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Synthesis of polymer-supported TEMPO catalysts and their application in the oxidation of various alcohols

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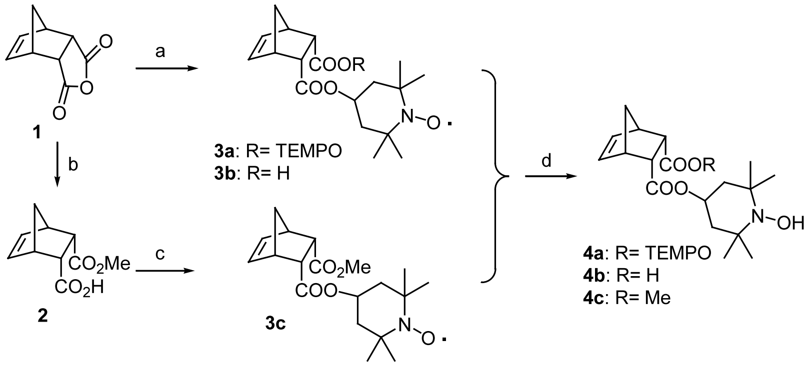
Abstract—We describe the synthesis of a recyclable polymer-supported TEMPO as a catalyst in the Anelli oxidation of various primary alcohols to afford the corresponding aldehydes in good yields. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

Oxidations of alcohols to carbonyl groups are fundamental transformations in organic chemistry. The application of free nitroxyl radicals is an alternative approach in this area.[1] The most useful ones are TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) derivatives.[2] Typically, such oxidations are carried out in the presence of 1 mol% of catalyst and a stoichiometric amount of a terminal oxidant such as bleach,[3] sodium chlorite,[4] *N*-chlorosuccinimide,[5] MCPBA[6] according to the protocol introduced by Anelli et al.[7] Although this method is successful for efficient oxidation, there is still a demand for catalyst recycling and simplified workup conditions. Fey and Bolm reported silica supported TEMPO catalyst systems.[8] Several publications concerning the application of polymer-supported catalysts and the use of norbornene systems in controlled polymerisation reactions prompted us towards the development of a new catalyst system.[9] We attempted to prepare one and two TEMPO bound norbornene systems and to polymerise these monomers by the ROMP method in a controlled way.[10] We describe here the synthesis of the new TEMPO based polymer catalyst systems and the results obtained from their applications in the oxidation of various primary alcohols.

2. Results and discussions

Monomers **4a–c** having polymerisable norbornene elements and TEMPO units were readily assembled from *cis*-5-norbornene-*endo*-2,3-dicarboxylic anhydride which was chosen as the starting compound because it



Scheme 1. (a) 4-hydroxy-TEMPO, 2-chloro-1-methyl-pyridinium iodide, DMAP, Et_3N, under Ar, 24 h, 72% **3a** and 25% **3b**. (b) MeOH, Et_3N, rt, 12 h, 98%. (c) 4-hydroxy-TEMPO, DMAP, DCC, 0°C, 12 h, 92% **3c**. (d) Isoascorbic acid, EtOH, 5 min.

Keywords: polymer support; nitroxides; ROMP and oxidation.

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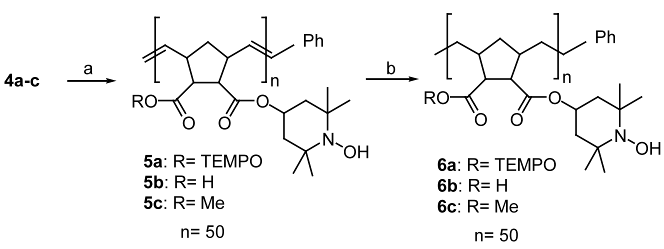
is easily available and inexpensive. The syntheses of TEMPO bound monomers are summarised in Scheme 1. In this synthetic approach, two TEMPO units were anchored to the host norbornene system **1** by a Mukaiyama reaction[11] to afford monomer **3a**.[12] However, the monomer containing only one TEMPO unit **3b** was also obtained as a side product.[12] The following typical procedure for route 'a' was applied: To a stirred solution of 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (2.00 g, 12.0 mmol) and *cis*-5-norbornene-*endo*-2,3-dicarboxylic anhydride (0.95 g, 6.0 mmol) in CH_2Cl_2 (50 mL) at room temperature, 2-chloro-1-methylpyridinium iodide (1.78 g, 7.0 mmol), DMAP (0.29 g, 2.4 mmol) and triethylamine (2.45 mL) were added and the reaction mixture was stirred for 16 h. H_2O (40 mL) was added and extracted with CH_2Cl_2 (2×50 mL). The organic phase was washed with brine (40 mL), dried over $MgSO_4$ and evaporated in vacuo. As the third monomer system **3c**,[13] the norbornene anhydride derivative **1** was opened in MeOH followed by anchoring one active TEMPO unit via a DCC-coupling reaction. For the attachment of one TEMPO unit, the general procedure given as route 'c' was followed. To a stirred solution of 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (0.65 g, 5 mmol) and monomethyl-5-norbornene-2,3-dicarboxylate (1.00 g, 5 mmol) in CH_2Cl_2 (25 mL) at 0°C under argon, DCC (1.03 g, 5 mmol) and DMAP (0.153 g, 1.25 mmol) were added and the reaction mixture was stirred for 12 h at room temperature. The solid materials formed were filtered off and the filtrate was washed with 1 M HCl (5 mL) followed by saturated $NaHCO_3$ (10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$ and evaporated in vacuo. In order to avoid some possible side reactions in the ROMP process and also to characterise the structures of the monomers using NMR, free nitroxyl radical containing monomers **3a**–**c** were reduced to the corresponding compounds **4a**–**c** by isoascorbic acid.[14] In the route 'd', each of the monomers **3a**, **3b** or **3c** (3.4 mmol) was dissolved in 15 mL EtOH and isoascorbic acid (4.8 mmol) was dissolved in 1 mL H_2O. These two solutions were mixed at room temperature. Reduction was monitored by disappearance of the pink colour after a few minutes. Ethanol was removed in vacuo, H_2O (5 mL) was added and the mixture was extracted with ether (3×20 mL). The organic phase was dried over $MgSO_4$ and evaporated in vacuo to afford the products **4a**, **4b** and **4c** in quantitative yields.[15]

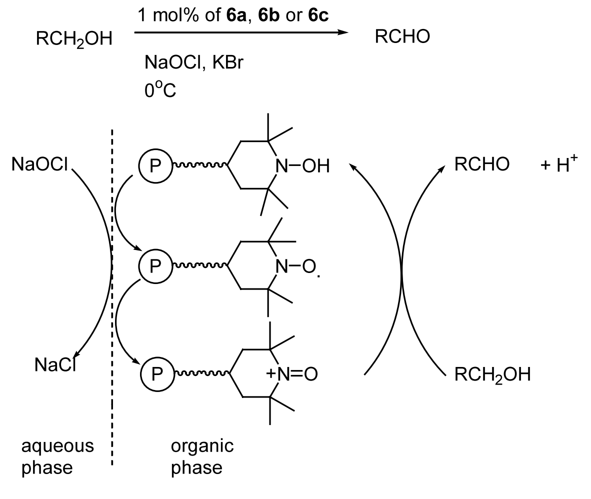
Grubbs's ruthenium based catalyst[16] reacted with the monomers **4a**–**c** efficiently, allowing the preparation of the desired polymers **5a**–**c** in quantitative yields (Scheme 2). The termination of the polymerisation reactions was done with *tert*-butyl vinyl ether after complete consumption of the monomers. In the polymerisation, the general procedure given below was applied. Monomer **4a**, **4b** or **4c** (3 mmol) was dissolved in CH_2Cl_2 (1 mL) under argon. Grubbs' catalyst, $(Cy_3P)_2Cl_2RuCH_2Ph$ (0.048 g, 5.8×10^{-3} mmol) was added. The resultant deep-purple solution was stirred for 6 days at room temperature, the *tert*-butyl vinyl ether (0.20 mL) was added. After 1 h stirring at room temperature, the crude polymer was precipitated by addition of ether (5 mL). The crude polymer was washed with ether (10 mL) until the colour turned from deep-purple to yellow. NMR analysis revealed complete conversion of the monomer. ^1H NMR of all the polymers showed very broad signals. Among these, the characteristic olefinic protons of the polymers were used to elucidate the structures. Polymer **5a** afforded a very broad signal in the range 5.78–6.24 ppm, **5b** in the range 5.87–6.31 ppm and **5c** in the range 5.85–6.36 ppm.



Scheme 2. (a) Grubbs' catalyst $(Cy_3P)_2Cl_2RuCH_2Ph$, under Argon, 6 d. (b) H_2, Pd–C, EtOH.

Pd–C mediated hydrogenation afforded the corresponding saturated polymers **6a**–**c** in quantitative yields. Polymer (1.0 g) was dissolved in ethanol (100 mL) and Pd–C (0.35 g) was added. Hydrogen gas pressure was adjusted to 20 lbs/sq. inch and the reaction mixture was shaken for 10 h. The reaction mixture was filtered through celite to remove Pd–C and the solvent was evaporated in vacuo to afford polymers **6a**–**c** in quantitative yields. The ^1H NMR spectra of all the polymers showed the disappearance of the signals in the region δ 5.78–6.36 and indicated complete saturation of the polymer backbones.

In these preliminary studies, 1 mol% of the catalyst was employed in all runs, setting the number of TEMPO units per molecule (*n*) at about 50. The performance of catalysts **6a**–**c** in oxidations of various primary alcohols was investigated under the conditions shown in Scheme 3. Both the alcohols and the TEMPO containing poly-



Scheme 3.

Table 1. Oxidation of primary alcohols catalysed with TEMPO polymers **6a**–**c**

Substrate	Polymer **6a** conv. (%)[a]	Polymer **6b** conv. (%)[a]	Polymer **6c** conv. (%)[a]
Butanol	71	75	72
Pentanol	84	82	85
Hexanol	87	83	85
Heptanol	85	79	82
Octanol	80	78	77
Benzyl alcohol	70	67	69

[a] GC was used to determine the conversions of alcohols to the corresponding aldehydes using DB-wax 15 m×0.32 mm, 0.13 micron column and dodecane as internal standard.

mers were soluble in two-phase systems (H_2O:CH_2Cl_2). Catalysts **6a**–**c** were all homogeneous catalysts. After the oxidation, the resultant carbonyl compounds could easily be separated from the reaction medium by phase separation methods. Also the catalysts could be recovered by decreasing the polarity of the medium and filtration. For up to three runs of the recovered catalysts, no drastic decrease was observed in their catalytic activity. The following general procedure was applied for all runs: an alcohol (0.8 mmol) and dodecane (0.24 mmol) used as the internal standard in GC-analysis were dissolved in CH_2Cl_2 (1 mL). Polymer catalyst dissolved in CH_2Cl_2 (1 mL) and KBr (0.16 mL, 0.5 M) were added to the reaction mixture at 0°C. NaOCl (2.7 mL, 0.37 M) buffered to pH 9.1 with $NaHCO_3$ was added and the reaction mixture stirred vigorously for 1 h. The reaction was stopped by the addition of $Na_2S_2O_3$ (1 mL, 1 M). The two phases were separated. Polymer catalyst was recovered by addition of ether (2 mL). The filtrate was used for GC-analysis. The most significant results of this study are summarised in Table 1.

The performance of the polymeric systems **6a**–**c** in catalysing the oxidation of alcohols to the corresponding aldehydes was comparable with the monomeric TEMPO unit. This study can be extended to other oxidation reactions i.e. oxidation of secondary alcohols to the corresponding ketones.

In conclusion, the possibility of anchoring of TEMPO units to various strained norbornene systems and generating the homogeneous polymeric systems having active TEMPO units by ROMP have been demonstrated. We are studying how to optimise the polymerisation conditions and to improve the efficiency of the catalyst systems and recovery.

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12. The crude products were separated by flash column chromatography using ethyl acetate/hexane, 1:4. **3a**: *m*/*z* (EI) 490 (3), 350 (100), 337 (14), 141 (23%); HRMS (EI): M^+, found 490.3029. $C_{27}H_{42}N_2O_6$ requires 490.3045. **3b**: *m*/*z* (EI) 336 (62), 285 (35), 211 (42), 156 (84), 140 (100), 124 (43%); HRMS (EI): M^+, found 336.1798. $C_{18}H_{26}NO_5$ requires 336.1811.
13. The crude product was separated by flash column chromatography using ethyl acetate/hexane, 1:4 as eluent to afford the product **3c** ($R_f=0.35$). **3c**: *m*/*z* (EI) 350 (100), 336 (12), 156 (11), 140 (33), 124 (21%); HRMS (EI): M^+, found 350.1982. $C_{19}H_{28}NO_5$ requires 350.1968.
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15. **4a**: IR: 3742, 2990, 1723, 1174 cm^{-1}. ^1H NMR: δ 1.13 (s, 12H), 1.17 (s, 12H), 1.25–1.45 (AB system, $J=8.6$ Hz, 2H), 1.51–1.85 (m, 8H), 3.07 (bs, 2H), 3.15 (bs, 2H), 4.84–4.95 (m, 2H), 6.20 (s, 2H). ^{13}C NMR: δ 14.5, 15.7, 20.8, 23.1, 30.1, 32.3, 48.7, 49.2, 60.1,

66.2, 66.9, 77.2, 135.2, 172.4. HRMS (EI): M^+, found 492.3198. $C_{27}H_{44}N_2O_6$ requires 492.3201.

4b: IR: 3742, 2990, 1736, 1170 cm^{-1}. ^{1}H NMR: δ 1.13 (bs, 12H), 1.37–1.47 (AB system, J = 8.0 Hz, 2H), 1.77–1.85 (m, 4H), 2.55 (bs, 1H), 3.02 (s, 1H), 3.17 (s, 1H), 3.25 (s, 1H), 4.92–4.99 (m, 1H), 6.00 (s, 1H), 6.21 (s, 1H). ^{13}C NMR: δ 18.9, 20.1, 30.1, 32.3, 44.2, 46.1, 47.7, 58.7, 59.6, 67.5, 67.7, 135.4, 138.1, 173.3, 174.4. HRMS (EI): M^+, found 337.1878. $C_{18}H_{27}NO_5$ requires 337.1890.

4c: IR: 3735, 2985, 1738 cm^{-1}. ^{1}H NMR: δ 1.25 (bs, 12H), 1.32–1.47 (AB system, J = 8.0 Hz, 2H), 1.61–1.94 (m, 4H), 3.16 (s, 2H), 3.26 (s, 2H), 3.62 (s, 3H), 4.91–5.01 (m, 1H), 5.29 (s, 1H), 6.26 (bs, 2H). ^{13}C NMR: δ 16.1, 26.6, 38.6, 38.7, 41.8, 43.5, 47.2, 51.0, 56.5, 61.5, 130.2, 130.6, 167.3, 168.2. HRMS (EI): M^+, found 351.2048. $C_{19}H_{29}NO_5$ requires 351.2046.

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