

SiliaCat[®] TEMPO: An Effective and Recyclable Oxidizing Catalyst

Annie Michaud · Valerica Pandarus ·
Lynda Tremblay · Rosaria Ciriminna ·
Mario Pagliaro · François Béland

Published online: 28 May 2010
© Springer Science+Business Media, LLC 2010

Abstract Organically modified silica-based SiliaCat TEMPO is an oxidizing catalyst that can efficiently replace other homogeneous stable nitroxyl radicals. Its high activity, reusability, leach-proof properties, selectivity towards the oxidation of alcohols into aldehydes/ketones and its capacity to carry out the oxidation in either organic solvents or water, with or without KBr as co-catalyst, have shown that this material is green chemistry driven.

Keywords TEMPO · Oxidation · Heterogeneous · Recyclable · Catalyst

1 Introduction

Aldehydes and ketones, either as starting materials, synthetic intermediates, or final products, are of great interest in synthetic chemistry. Such carbonyl containing products are of high importance as they can lead to carbon–carbon (i.e. Wittig, Aldol, alkylation) or carbon–nitrogen bond formation. Over the years, chemists have discovered various oxidizing agents such as pyridinium chlorochromate (PCC), MnO₂, Dess-Martin periodinane, or Swern oxidation conditions. Although all these conditions lead to the aldehyde (limited oxidation of the aldehyde to the carboxylic acid), they have drawbacks such as the hazard and toxicity associated to the residual metal contamination.

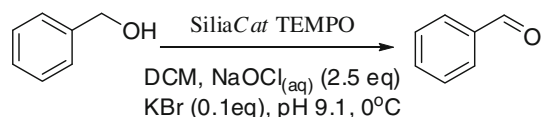
Development of environmentally friendly methods such as selective catalytic oxidation of alcohol substrates to aldehydes and ketones is of great interest as it can have significant impact on modern methods used in chemical synthesis. 2,2,6,6-Tetramethylpiperidin-1-oxyl (TEMPO) has proven to be very successful in such type of transformation and has led to the development of other nitroxyl radicals. SiliaCat TEMPO is a heterogeneous version that overcomes its homogeneous analogs, as well than heterogeneous ones, as it does not require activation prior to use. We would like to present that SiliaCat TEMPO can be used following the Montanari-Anelli procedure [1] or with alternative conditions (solvents, pH, reagents) for the oxidation of alcohols and that this catalyst is recyclable without compromising its activity.

2 Experimental Section

Organosilica-based SiliaCat TEMPO was made and characterized following the procedure described by Pagliaro et al. [2]. Typical Experimental Procedure for the oxidation of primary alcohol substrates: A solution of the alcohol in dichloromethane (0.4 M, 10–30 mmol, 1 equiv) was mixed with an aqueous solution of KBr (0.5 M, 0.1 equiv), and was maintained at 0 °C in an ice bath. The desired amount of SiliaCat TEMPO was added, followed by aqueous NaOCl (1.25 equiv) buffered at pH 9 (using NaHCO₃). The reaction is exothermic and NaOCl was added slowly over a 10 min period. The mixture was agitated at 1300 rpm for 60–90 min. After filtration, the organic phase was washed with deionized water and dried over MgSO₄. Results presented in Tables 1 and 2: Conversions with respect to the substrate were determined by GC/FID analysis based on a calibration curve prepared with *n*-decane as internal

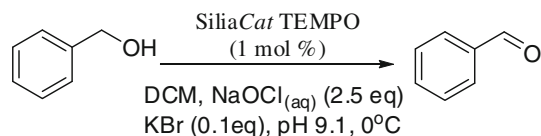
A. Michaud · V. Pandarus · L. Tremblay · F. Béland (✉)
SiliCycle®Inc., 2500 Parc-Technologique Blvd., Quebec City,
QC G1P 4S6, Canada
e-mail: francoisbeland@silicycle.com

R. Ciriminna · M. Pagliaro
Istituto per lo Studio dei Materiali Nanostrutturati, CNR,
via Ugo La Malfa 153, 90146 Palermo, Italy

Table 1 Catalytic performance and leaching

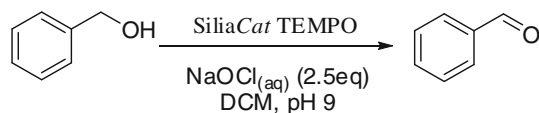
SiliaCat TEMPO (Mol %)	Time (h)	Conversion (%)	Si (ppm) ^a
0.1	1	95	–
0.02	2	96	–
0.02	3	100	2
0.01	2	83	3
0.01	3	95	1.6
0.01	4	97	1.5

^a The following levels of silicon were measured in the organic phase (solvent) using ICP-OES. The levels of silicon in the aqueous phase are ≤ 10 ppm

Table 2 SiliaCat TEMPO after recycling

Reusability ^a	Time (min)	Conversion (%)
1st	30	100
...
6th	30	100
7th	30/60	88/96
8th	30/60	95/100
9th	30/60	97/100
10th	30/60	90/100

^a SiliaCat TEMPO is recycled by post-reaction filtration, DCM washes and air drying

Table 3 Influence of co-catalyst KBr and of the temperature

Entry	SiliaCat TEMPO (mol %)	KBr (equiv)	Temperature (°C)	Time (min)	Conversion (%)
1	0.1	0.1	0	60	95
2	0.1	0	0	60 210	80 100
3	0.2	0	0	105	96
4	0.2	0	22	60 90	76 87

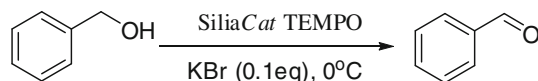
standard. Results presented in Tables 3, 4 and 5: Yields were determined by GC/FID analysis (with *n*-decane as internal standard for the Response Factors calculations [3]). Results presented in Table 6: Conversions with respect to the aldehyde were determined by GC/MS.

3 Results and Discussion

Montanari-Anelli conditions are widely used with TEMPOs. The catalytic cycle involves regeneration of the oxidative species with NaOCl (commercial bleach) in presence of KBr as co-catalyst to form the stronger anion OBr[−] [1, 4]. Investigation of the SiliaCat TEMPO using the Montanari-Anelli conditions has led to very interesting results. As shown in Table 1, the catalyst has an attractive catalytic performance as the reaction can be run with as low as 0.01 mol% while being a leach-proof material ([Si] ≤ 3 ppm) (Table 1) and the robustness of the organoceramic matrix allows it to be recycled many times for further uses (Table 2).

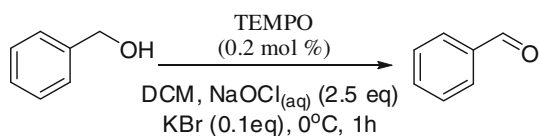
To optimize the reaction conditions, it was investigated if co-catalyst (KBr) was necessary for the reaction to proceed effectively. As shown in Table 3, although KBr is not required for the reaction (entries 2–4), it does have a significant impact on the kinetics. The reaction can still go to completion without KBr but require longer time (entry 2 vs. 1) and/or more SiliaCat TEMPO (entry 3). It was also demonstrated that the reaction can be pursued at room temperature without KBr (entry 4).

As shown in Table 4, the reaction can be carried out at pH 9.0 or at pH 7.5 in DCM with high conversion yields (entry 4 vs. 1) and the catalytic conditions are selective towards the aldehyde, rather than the carboxylic acid, even with 10 equiv of NaOCl (entry 2). At pH 7 in water, the reaction is slower, but it can be overcome by using more NaOCl_(aq) (entries 5, 6 vs. 3, 4). At pH 9, the conversion is

Table 4 Influence of solvents, pH, and NaOCl_(aq)

Entry	SiliaCat TEMPO (mol %)	NaOCl _(aq) (equiv)	Solvent	pH	Time (min)	Yield (%)
1	0.2	2.5	DCM	9.0	60	98
2	0.2	10.0	DCM	9.0	90	98
3	0.2	1.25	DCM	7.5	60	83
					90	86
4	0.2	2.5	DCM	7.5	60	94
					90	98
5	0.2	1.25	H ₂ O	7.5	60	57
					90	65
6	0.2	2.5	H ₂ O	7.5	60	87
					90	88
7	0.7	1.20	H ₂ O	9.0	60	83
					150	89
8	0.8	5.0	H ₂ O	9.0	60	60 (19) ^a
					18 h	7 (89) ^a
9	0.2	1.25	EtOAc	9.0	60	95
					90	96

^a Data in parenthesis indicate conversion to carboxylic acid

Table 5 Comparison of SiliaCat TEMPO vs homogeneous TEMPOs

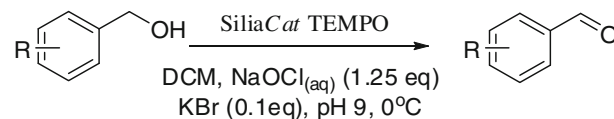
pH	SiliaCat TEMPO	4-MeO-TEMPO	4-Oxo-TEMPO
7.5	91	99	45
9.0	98	55 (40) ^a	73

^a Data in parenthesis indicate conversion to carboxylic acid

high (entry 7) but too much bleach and long reaction time in the aqueous media will lead to the corresponding carboxylic acid (entry 8). The reaction can be pursued in other organic solvent (entry 9).

Comparative analysis with homogeneous TEMPOs (Table 5) demonstrates the SiliaCat TEMPO to be comparable or better at neutral pH and significantly superior in basic conditions.

SiliaCat TEMPO is efficient with different substrates (Table 6) and can be used with phase transfer agent (entry 4). When an electron-rich benzylic alcohol cannot be

Table 6 Oxidation of alcohol substrates with SiliaCat TEMPO

Entry	Substrate (R)	SiliaCat TEMPO (mol %)	Time (min)	Conversion (%)
1	3-NO ₂	0.4	90	100
2	4-NO ₂	0.4	90	98
3	4-MeO	0.4	90	36
4	4-MeO	0.4	60	79 ^a
4	4-Cl	0.4	90	95
6	3-phenyl-1-propanol	0.4	60	97
7	1-phenyl-1-propanol	0.4	180	95 ^b
8	4-MeO	8.2	16 h	99 ^c
9	3-MeO	7.8	16 h	96 ^c
10	Piperonal	10	20 h	100 ^c

^a 0.05 equiv of Aliquat 336 were used as phase transfer agent

^b Conversion with respect to the ketone is determined by ¹H-NMR (300 MHz)

^c Reaction conditions: I₂(1.8 eq), NaHCO₃ (aq), pH 8, Toluene, 22 °C

oxidized successfully with NaOCl, conditions involving I₂ in toluene, at room temperature (as reported by Miller et al. [5]), will lead to the desired product (entry 8 vs. 3, entries 9–10).

4 Conclusion

SiliaCat TEMPO is an effective oxidizing catalyst presenting unique advantages such as high activity, robustness, leach-proof properties and selectivity toward the oxidation of alcohol into aldehyde and ketone, both very valuable products in organic chemistry.

References

1. Anelli PL, Biffi C, Monanari F, Quici S (1987) *J Org Chem* 52:2559
2. Michaud A, Gingras G, Morin M, Béland F, Ciriminna R, Avini D, Pagliaro M (2007) *Org Process Res Dev* 11:766
3. Swarup KM, Subhajt D, Ramgopal B (2008) *Tetrahedron Lett* 49:6205
4. Jiang B, Drouet E, Milas M, Rinaudo M (2000) *Carbohydr Res* 327:455
5. Miller AR, Hoerrner SR (2003) *Org Lett* 5:285