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Barium manganate in microwave-assisted oxidation reactions: synthesis of lactones by oxidative cyclization of diols

Mark C. Bagley *, Zhifan Lin, David J. Phillips, Andrew E. Graham *

School of Chemistry, Main Building, Cardiff University, Park Place, Cardiff CF10 3AT, UK

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ABSTRACT

Microwave irradiation of a range of diols at 150 °C in acetonitrile in the presence of three equivalents of barium manganate facilitates a novel tandem oxidation/heterocyclocondensation to give the corresponding lactone, including both small and medium ring lactones, in only one hour and in high yield without the need for chromatographic purification.

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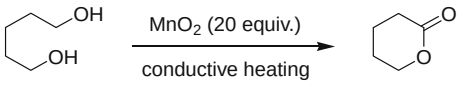
The oxidative cyclization of diols to lactones is an effective route to valuable targets of broad applicability that has seen use in natural product synthesis[1] and in the preparation of synthetic building blocks for fine chemical production.[2] Despite the potential for broad utility of this methodology, current procedures[3] employ expensive reagents or metal-based catalysts, which often require prior preparation, very high temperatures, co-oxidants or hydrogen acceptors, protracted reaction times, inert conditions, specialist equipment, for example, in electrochemical processes,[4] or rigorous chromatographic purification of the products.

We recently reported the desymmetrization of unactivated diols by reaction with stabilized Wittig reagents in the presence of an excess of manganese dioxide to give α,β-unsaturated hydroxyesters in a highly efficient one-pot procedure.[5] It was noted during these studies that in the case of 1,4- and 1,5-diols, the yields of α,β-unsaturated hydroxyesters were reduced by a competing oxidative cyclization which produced the corresponding lactones.[6] Tandem oxidation processes involving manganese dioxide are of particular current interest, especially those which involve the formation of reactive carbonyl intermediates, and a number of transformations have been described.[7] Our own studies[8] have shown that a tandem oxidation/heterocyclocondensation approach provides direct access to pyridines and pyrimidines from propargylic alcohols. However, given the considerable attention afforded to the desymmetrization of symmetrical diols, and the lack of convenient methods by which this transformation can be carried out,[9] we set out to realize a new procedure for the desymmetrization of diols by oxidative cyclization that was effective and efficient in short reaction times, used commercially available and cheap reagents, exhibited broad substrate scope, and provided the lactone product without the need for lengthy purification regimes. Given previous successes in realizing rapid methods to functionalized heterocyclic targets using microwave irradiation,[10] our previous findings that MnO_2 can mediate the rapid oxidation of heterocyclic precursors under microwave dielectric heating,[11] and the precedent that MnO_2 is an effective reagent for the oxidation of lactols to lactones,[12] we set out to investigate the desymmetrization of diols using this reagent.

The manganese dioxide-mediated oxidative cyclization of 1,5-pentanediol was studied initially under conductive heating (Table 1). Reactions were carried out with a large excess of oxidant (20 equiv) in dichloromethane at room temperature which proceeded to give moderate amounts of δ-valerolactone in addition to considerable quantities of the corresponding lactol. It was found that it was most efficient to carry out these reactions in chloroform under reflux conditions to maximize the yield, although considerable quantities of the desired product were obtained at room temperature after extended reaction times. Surprisingly, reactions employing activated manganese dioxide produced no lactone product at all with only starting material isolated, providing another example of the importance in choosing the correct grade of oxidant.[5]

The cyclization reactions of a range of unactivated diols were investigated under these conditions to assess the utility of the con-

Table 1
Comparing conversions for the oxidative cyclization of pentane-1,5-diol using MnO_2 (10 μm) under conductive heating



Entry	Conditions[a]	Conversion[b] (%)
1	CH_2Cl_2, rt, 20 h	30[c]
2	$CHCl_3$, rt, 20 h	57[c]
3	$CHCl_3$, reflux, 4 h	29[c]
4	$CHCl_3$, reflux, 20 h	91

[a] rt = room temperature.
[b] Determined by ^1H NMR spectroscopic analysis of the crude reaction mixture.
[c] Contained ~40% lactol.

* Corresponding authors.
E-mail address: bagleymc@cardiff.ac.uk (M.C. Bagley).

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Table 2
Comparing the isolated yield of δ-valerolactone from the $BaMnO_4$- and MnO_2-mediated oxidative cyclization under microwave irradiation with or without a SiC passive heating element

Entry	Conditions[a]	Yield[b] (%)
1	MnO_2 (10 μm), μω, MeCN, 150 °C, 1 h	60[b]
2	$BaMnO_4$, μω, MeCN, 150 °C, 1 h	88[c]
3	MnO_2 (10 μm), μω, SiC PHE, MeCN, 150 °C, 1 h	84[b]
4	$BaMnO_4$, μω, SiC PHE, MeCN, 150 °C, 1 h	86[c]

[a] Reaction was carried out under microwave irradiation (μω) at 150 °C for 1 h with 3 equiv of oxidant in MeCN in a sealed tube (10 mL) using a CEM Discover® microwave synthesizer by moderating the initial microwave power (150 W). SiC PHE refers to the addition of a silicon carbide passive heating element (as supplied from Anton Paar).
[b] Yield% refers to isolated yield of lactone after purification by column chromatography on silica gel.
[c] Yield% refers to isolated yield of lactone after only a simple filtration through Celite.

ductive heating reaction (see later in Table 3). Gratifyingly, diols containing either primary, or both primary and secondary, alcohol functionality underwent efficient oxidative cyclization to produce lactone products in good to high yields. Interestingly, the oxidation of 1,4-pentanediol and 1,5-hexanediol produced quantities of the corresponding acyclic dicarbonyl compound (10 and 25%, respectively) produced by oxidation of both the primary and the secondary alcohol functions. The method was effective for activated alcohols which are much more readily oxidized and so shorter reaction times could be employed. Thus, reaction of 1,2-benzenedimethanol at room temperature for 8 h produced the corresponding lactone, but also gave quantities of the corresponding dialdehyde. Disappointingly, however, reactions involving either 2-butene-1,4-diol or diols containing heteroatoms in the chain gave only a trace of the desired lactone product and were accompanied by considerable amounts of degradation. Thus, although the method appeared to offer promise, its somewhat limited substrate scope, long reaction time, requirement for a large excess of oxidant, reliance upon chlorinated solvents, and requirement for chromatographic purification identified formidable challenges to overcome.

In order to reduce the large excess of oxidant that was needed and simultaneously accelerate the process, the transformation was next studied at elevated temperatures in a sealed vessel under microwave irradiation. The oxidative cyclization of 1,5-pentanediol at 150 °C in an alternative non-chlorinated solvent, acetonitrile, using only three equivalents of MnO_2 did provide the δ-valerolactone product; however the heating profile (Fig. 1) of reaction demonstrated that at an initial power of 150 W the set temperature was not attained and the yield of the product was compromised as a consequence (Table 2, entry 1). By switching

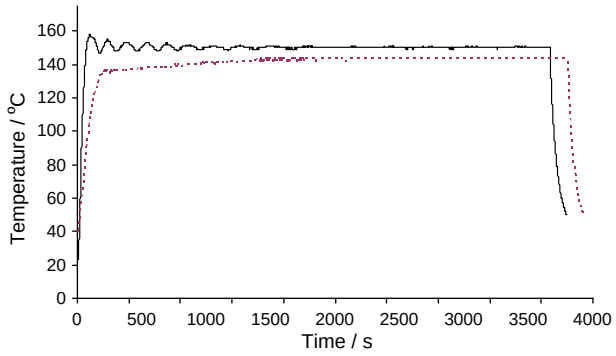
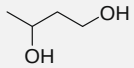
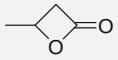
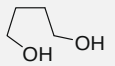
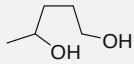
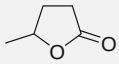
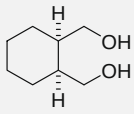
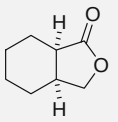
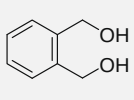
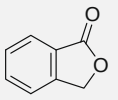
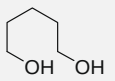
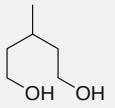
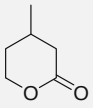
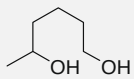
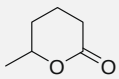
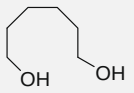
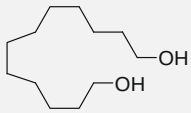
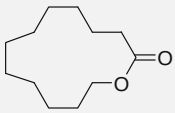


Figure 1. Heating profile under microwave irradiation with MnO_2 (purple) and $BaMnO_4$ (black) without a SiC passive heating element.

Table 3
Comparing the microwave-assisted oxidative cyclization of diols using $BaMnO_4$ with a MnO_2-mediated conductive heating reaction

Entry	Diol[a]	Lactone product[b]	Yield%[c] MnO_2/Δ	Yield%[d] $BaMnO_4/\mu\omega$
1			0[e]	76
2			72	70
3			44	60
4			87	80
5			64	80
6			74	88
7			81	87
8			62[f]	80
9			0[e]	84
10			0[e]	78

[a] All diols were used as supplied.
[b] All products gave satisfactory spectroscopic and spectrometric data.
[c] Reactions carried out in $CHCl_3$ at reflux using 20 equiv of MnO_2 (10 μm). Yield% refers to isolated yield of lactone after purification by column chromatography on silica gel.
[d] Reaction was carried out under microwave irradiation (μω) at 150 °C for 1 h with 3 equiv of $BaMnO_4$ in MeCN in a sealed tube (10 mL) using a CEM Discover® microwave synthesizer by moderating the initial microwave power (150 W). Yield% refers to isolated yield of lactone after only a simple filtration through Celite.
[e] The reaction failed to give any more than a trace (<10%) of the desired lactone product.
[f] The reaction was heated at reflux for 48 h.

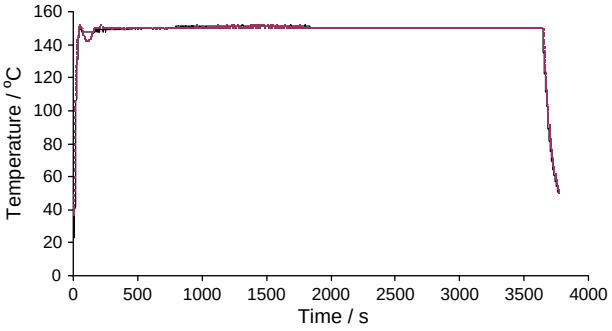


Figure 2. Heating profile under microwave irradiation with MnO_2 (purple) and $BaMnO_4$ (black) in the presence of a SiC passive heating element.

oxidant from MnO_2 to $BaMnO_4$ (3 equiv), difficulties in coupling with the microwave irradiation were overcome (Fig. 1) and this was reflected in an increase in the isolated yield (Table 2, entry 2). The $BaMnO_4$-mediated reaction was more efficient, both in terms of energy transfer under microwave irradiation, presumably as a consequence of its ionic character, and isolated yield and provided the product without the need for chromatographic purification, thus achieving many of the goals we had set out to reach. In order to verify that it was the heating profile that was the significant factor, reactions using MnO_2 and $BaMnO_4$ were repeated under microwave irradiation with a SiC passive heating element present.[13] Under these conditions, the heating profiles (Fig. 2) and isolated yield of product (Table 2, entries 3 and 4) were near identical, thus verifying that the higher temperature of the microwave-assisted $BaMnO_4$-mediated reaction in MeCN had caused the increase in yield.

With successful conditions established[14] using microwave irradiation, the scope of the $BaMnO_4$-mediated method was reviewed using the same range of diols (Table 3), for convenience in the absence of the SiC heating element. It was apparent that the efficiency of the microwave-assisted method was comparable if not improved over the conductive heating procedure (Table 3), as well as offering considerable advantages in terms of convenience, speed and facility. Furthermore, most surprisingly, it enabled the synthesis of both small and medium ring lactones where the conductive heating method failed, providing for example, β-butyrolactone (entry 1) in 76% yield and the 13-membered ω-dodecanolactone in an astonishing 78% isolated yield (entry 10) without the need for chromatographic purification.

In conclusion, we have shown that the $BaMnO_4$-mediated oxidative cyclization of unactivated diols proceeds rapidly and efficiently under microwave irradiation to give high yields of the corresponding lactone products. The benign nature of the oxidant, in addition to its low cost and ease of use, the simple experimental and work-up procedures, and the fact that no chromatographic purification is required demonstrate that $BaMnO_4$ is an attractive replacement for MnO_2 in microwave-mediated tandem oxidation processes.

Acknowledgments

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14. In a typical experimental procedure, a mixture of 1,5-pentanediol (0.58 mmol, 1 equiv) and $BaMnO_4$ (1.74 mmol, 3 equiv) in MeCN (5 mL) was irradiated at 150 °C, at an initial power of 150 W, using a self-tuned single mode CEM Discover® Focused Synthesizer for 1 h in a pressure-rated Pyrex reaction tube (10 mL). The mixture was then cooled rapidly to room temperature, by passing compressed air through the microwave cavity for 5 min, and then filtered through Celite and washed with MeCN, to give δ-valerolactone (50 mg, 88%), with spectroscopic and spectrometric characterization data that agreed with literature values.