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Citation	RSC Advances, 3(7), 2158-2162 https://doi.org/10.1039/c2ra22197g
Issue Date	2013
Doc URL	http://hdl.handle.net/2115/53760
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Type	article (author version)
Additional Information	There are other files related to this item in HUSCAP. Check the above URL.
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Cite this: DOI: 10.1039/c0xx00000x

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Direct Bromination of Hydrocarbons Catalyzed by Li_2MnO_3 under Oxygen and Photo-Irradiation Conditions

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Received (in XXX, XXX) Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXXX 20XX

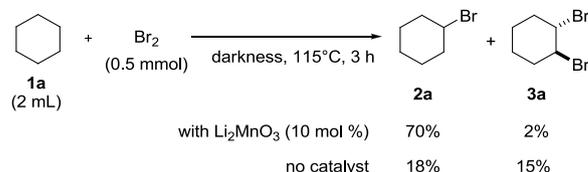
DOI: 10.1039/b000000x

A method for the direct bromination of hydrocarbons with Br_2 using a ubiquitous and inexpensive catalyst is highly desirable. Herein, we report the selective monobromination of hydrocarbons in good yield using Li_2MnO_3 as a catalyst under irradiation with a fluorescent room light. This new catalyst can be recyclable. The effect of light was investigated using action spectra, which revealed that the reaction occurred on the surface of the catalyst.

Organic bromides have been widely used as starting materials and intermediates in organic synthesis,¹ as well as enjoying functional applications in bioactive materials.² Classically, alkyl bromides have been prepared from the reaction of the corresponding alkyl alcohols with Br_2 , HBr , and other brominating reagents.³ They can also be synthesized from the corresponding alkanes by reaction with brominating reagents, such as NBS ,⁴ CBr_4 ,⁵ and Et_4NBr .⁶ Although alkyl bromides can be synthesized from the corresponding alkanes by reaction with Br_2 under photolysis or high temperature conditions without any catalyst, the reactions do not exhibit any selectivity,⁷ because the bromine radicals present in the reaction mixtures indiscriminately attack the C-H bonds of the starting material and the products (alkyl bromides). There have only been a limited number of reports in the literature concerning the selective synthesis of alkyl bromides from alkanes. For example, the reactions of alkanes with Br_2 in the presence of an excess of AcOH ,⁸ a stoichiometric amount of $t\text{-BuONa}$,⁹ a catalytic amount of AlCl_3 at a low temperature,¹⁰ and an excess of MnO_2 , have been reported.¹¹ Unfortunately, however, these reactions are relatively inefficient and cannot compete with the corresponding alcohol-mediated bromination processes.

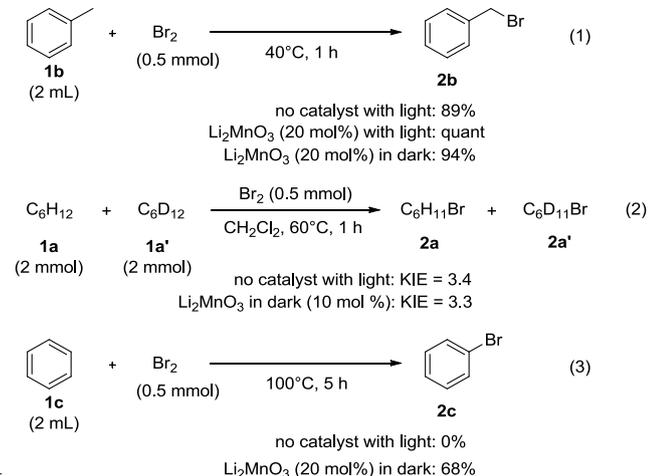
We envisaged that the formation of a bromine radical species on the surface of a catalyst would enable a more selective free radical bromination process. Of the previously reported alkane bromination processes, we were particularly interested in the MnO_2 -promoted reaction, because it has been proposed that the Br_2 is activated on the MnO_2 surface.¹¹ An issue associated with the use of MnO_2 , however, is that the HBr byproduct formed during the course of the reaction poisons the MnO_2 to give non-active $\text{MnBrO}(\text{OH})$ species.¹¹ During our initial attempts to use a catalytic amount of MnO_2 in the bromination of cyclohexane, however, the formation of MnBr_2 was observed following the reaction (See ESI[†]). The development of a form of

manganese oxide that is stable under acidic condition could potentially provide a platform for the effective catalytic bromination of alkanes. It is known that a manganese oxide containing an alkali metal is stable under acidic condition.¹² With this in mind, we synthesized a series of alkali metal-modified manganese oxides (See ESI[†]) and screened them as catalysts for the bromination of cyclohexane (**1a**). Consequently, the lithium-modified manganese oxide, Li_2MnO_3 , was identified as a suitable catalyst and promoted the bromination reaction to afford the monobrominated product **2a** in 70% yield (Scheme 1).^{13,14} It is worthy of note that *trans*-1,2-dibromocyclohexane (**3a**)¹⁵ was only formed in 2% yield.⁷ In the absence of the catalyst, the selectivity of the reaction was poor, in spite of the inclusion of a large excess of **1a** (Scheme 1).

Scheme 1. Bromination of Cyclohexane (**1a**).

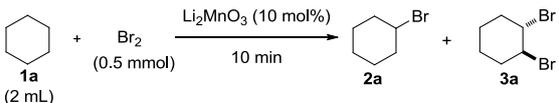
Toluene was then used as a substrate to determine the nature of the reaction pathway (radical or ionic). Thus, if Br_2 was homolytically dissociated to form bromine radicals, the bromination would occur at the C-H bond on the benzyl position,¹⁶ whereas if cationic bromine was formed, electrophilic attack would occur on the aromatic ring.^{16a,17} When the reaction was performed without the catalyst under photolysis, only benzylbromide (**2b**) was formed in 89% yield (Scheme 2, eq. 1). The same reaction profile was observed when the Li_2MnO_3 catalyst was used with and in the absence of light (Scheme 2, eq. 1).¹⁸ Furthermore, the kinetic isotope effect (KIE) of the bromination of cyclohexane (**1a** and **1a'**) with and without Li_2MnO_3 was investigated. The KIE values in both cases were similar (3.3 and 3.4),¹⁹ which suggested that the reaction pathways were similar. These results indicated that Li_2MnO_3 promoted the formation of bromine radicals. In contrast, when benzene (**1c**) was used as the substrate, bromobenzene (**2c**) was obtained in 68% yield (Scheme 2, eq. 3), which suggested that cationic bromine species were being formed in the Li_2MnO_3 system. Unfortunately, however, the catalytic activity of Li_2MnO_3 in the bromination of benzene was lower than that previously

reported for other catalysts, including a zeolite and its analogues.¹⁷ With this in mind, we focused our own research on the bromination of aliphatic hydrocarbons.



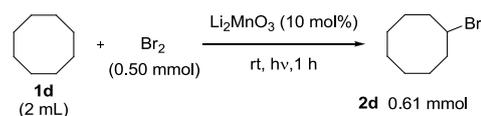
Scheme 2. Mechanistic study of Li_2MnO_3 -catalyzed bromination of hydrocarbons. (1) Bromination of toluene (**1b**), (2) KIE analysis using cyclohexane (**1a**) and cyclohexane-d12 (**1a'**), (3) bromination of benzene (**1c**).

Table 1 Effect of Light and Oxygen in Bromination of Cyclohexane (**1a**).



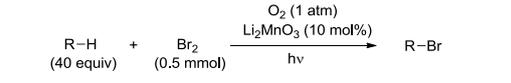
Entry ^[a]	conditions	atmosphere	yield / % ^[b]	
			2a	3a
1	hv, 80 °C	Ar (1 atm)	70	1
2	dark, 80 °C	Ar (1 atm)	0	2
3	hv, 80 °C	O ₂ (1 atm)	85	3
4	hv, 115 °C	O ₂ (1 atm)	84	4
5	hv, 80 °C	air (1 atm)	78	5
6	hv (5 min), 80 °C	O ₂ (1 atm)	62	6

^a Reaction conditions: Li_2MnO_3 (0.05 mmol), **1a** (2 mL, 40 equiv), Br_2 (0.5 mmol). ^b The ratio of **2a** to **3a** was determined by ¹H NMR.



Scheme 3. Bromination of cyclooctane (**1d**).

Table 2. Scope of Substrates in the Li_2MnO_3 -Catalyzed Bromination of Hydrocarbons Under Oxygen and Photo-Irradiation.



entry ^[a]	R-H	temp / °C	time / h	product yield
1		25	0.2	 2d quant
2 ^[b]		40	0.5	 2e 59%  2e' 23%
3 ^[c]		100	24	 2f 42%  2f' 5%
4		25	0.2	 2b 93%
5		80	3	 2g 86%

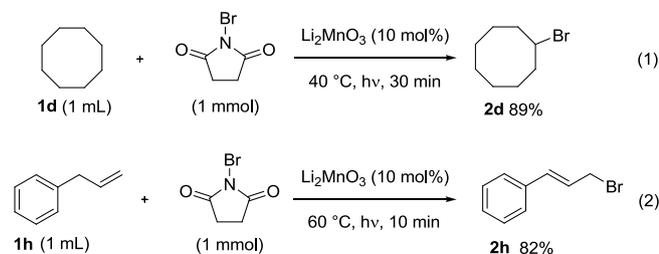
^a Reaction conditions: Li_2MnO_3 (0.05 mmol), **1** (40 equiv), Br_2 (0.5 mmol).

^b Yield was determined by ¹H NMR using $\text{CH}_2\text{ClCH}_2\text{Cl}$ as an internal standard. ^c Adamantane (**1f**) was used in 2 equivalent and CH_2Cl_2 (1 mL) was used as a solvent.

With the optimized conditions in hand from the bromination of cyclohexane, we then investigated the scope of the reaction conditions with other substrates (Table 2). Cyclooctane (**1d**) was converted into bromocyclooctane (**2d**) at room temperature (Table 2, entry 1). Although *n*-hexane (**1e**) consists of six 1° C-H bonds and eight 2° C-H bonds (four bonds at 2- and 3-positions, respectively), only the 2° C-H bonds were brominated.

Furthermore, a 2:1 selectivity for the 2-position over the 3-position was observed, which was attributed to steric hindrance (Table 2, entry 2). Adamantane (**1f**), which has four 3° C-H bonds and twelve 2° C-H bonds, was selectively brominated at the 3° C-H bonds (Table 2, entry 3). As indicated in Scheme 2, toluene (**1b**) was brominated exclusively at the benzylic position under the current bromination conditions to give benzylbromide (**2b**) (Table 2, entry 4). When the benzylic positions of toluene were blocked, the bromination occurred at the 1° or aromatic C-H bonds. Further to an investigation with *tert*-butylbenzene (**1g**), *p*-bromination of the aromatic ring was achieved, but required a higher reaction temperature and an extended reaction time to provide a good yield of the product (Table 2, entry 5). Based on these experiments, the order of C-H bond reactivity was proposed to be 3° > 2° > aromatic > 1°.²²

N-bromosuccinimide was also investigated in the current reaction system and performed effectively as a brominating reagent. Thus, cyclooctane (**1d**) was converted to bromocyclooctane (**2d**) following irradiation with a fluorescent light at 40°C for 30 min when NBS was used instead of Br₂ (Scheme 4, eq. 1). It is clear that more forcing conditions were required when NBS was used in this particular case relative to Br₂ (Table 2, entry 1). In spite of the requirement for more aggressive conditions, we were encouraged that NBS could be used for bromination of wide range of substrates, because Br₂ cannot undergo mono-bromination in the presence of an alkene and this discovery expanded the scope and utility of the current procedure.^{23,24} This increase in scope was exemplified by the conversion of allylbenzene (**1h**) to cinnamyl bromide (**2h**) when NBS was used as the brominating reagent (Scheme 4, eq. 2).



Scheme 4. Bromination of (1) cyclooctane (**1d**), and (2) allylbenzene (**1h**) with NBS.

The reusability of the catalyst was examined. X-ray diffraction (XRD) measurements were used to confirm that the structure of the catalyst did not change following the bromination of cyclohexane **1a** (Figure 1). The catalyst showed resistance to the formed HBr,¹² and was therefore recyclable and could be reused without any adverse impact on the product yields for at least five consecutive cycles (See ESI†).

Next, we investigated the wavelength dependency in the bromination of cyclohexane (**1a**) with and without Li₂MnO₃ (Figure 2). An action spectrum plot of apparent quantum efficiency against wavelength is recognized as a valid and feasible method for determining whether a reaction is or is not photocatalysed. The apparent quantum efficiency is defined as the ratio of the consumed photogenerated electrons to the incident photons.²⁵

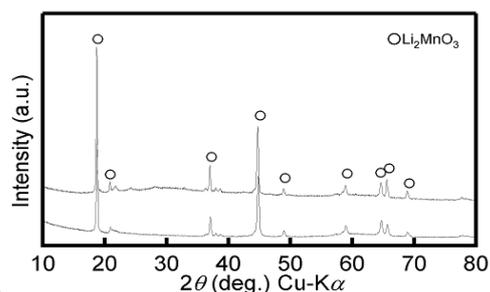


Figure 1 XRD Analysis of Li₂MnO₃ Before (above) and After (bottom) the Reaction.

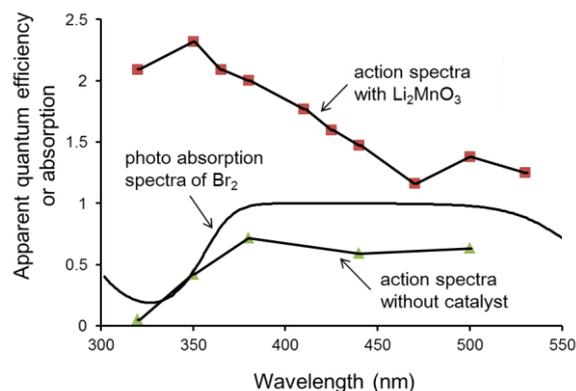


Figure 2 Action spectra of photoinduced bromination of cyclohexane in the presence (■) and absence (▲) of Li₂MnO₃, and the photo absorption spectrum of Br₂ (○) in cyclohexane.

A mixture of Br₂ in cyclohexane absorbed light at wavelengths of 380–500 nm (Figure 2, ○). A similar tendency was observed in the action spectrum for the bromination of cyclohexane (**1a**) without the catalyst (Fig. 2, ▲), which indicated that Br₂ itself was activated by light to promote the reaction. The action spectrum of the bromination reaction in the presence of Li₂MnO₃ contained a maximum peak at 350 nm (Fig. 2, ■) that had shifted to a shorter wavelength than those of in the former two spectra, indicating that the reaction with Li₂MnO₃ proceeded efficiently in the ultraviolet region. Stoimenov *et al.* reported that when Br₂ was adsorbed onto the surface of a metal oxide, its photo absorption spectrum shifted to a wavelength shorter than that of free Br₂.²⁶ Unfortunately, the photo reflection and absorption spectra of Li₂MnO₃ and its composite with Br₂ could not be measured because it was a black and solid-state material. Taken together, the shorter wavelength shift of the action spectrum with Li₂MnO₃ could indicate that Br₂ was adsorbed onto the Li₂MnO₃ surface and subsequently functioned as a photoabsorber. Furthermore, the fact that the apparent quantum efficiency with Li₂MnO₃ exceeded unity (1.0) suggests that the photoinduced bromination reaction involves a radical chain reaction. The formation of a bromine radical species on the surface could contribute to selective bromination and halogens could interact with metal oxides both with and without polarization.²⁶ This could well be true, because Li₂MnO₃ effectively promoted both the radical- (Scheme 2, eqs. 1-2 and Table 2, entries 1-4) and cationic- (Scheme 2, eq. 3 and Table 2, entry 5) derived bromination reactions. A simple metal oxide, such as Fe₂O₃ or

MnO₂, could not catalyze the bromination of an aromatic ring and it therefore clear that Li₂MnO₃ exhibits both metal oxide and metalate chemical character towards Br₂.¹⁷

Conclusions

We have successfully developed a novel bromination catalyst system for use under photo irradiation conditions. Furthermore, the catalyst is stable in the presence of HBr and recyclable. Selective mono-bromination reactions were achieved by surface reaction. Our future work will focus on modifications to the surface conditions and particle size, with the aim of developing further reactive and selective catalysts that are more effective than the existing systems for the halogenation of alkanes.

Acknowledgements

Financial support for this study was provided by the Development of Human Resources in Science and Technology, The Circle for the Promotion of Science and Engineering, and Hatakeyama Culture Foundation. We also received generous support from Mr. Noriyasu Kimura for XRD analysis, and Prof. Kazuhiko Takai for his generous support and comments on this research. This study was also supported by the Cooperative Research Program of Catalysis Research Center, Hokkaido University (Grant #11B2001).

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[†] Electronic Supplementary Information (ESI) available: Methods and experimental procedure. See DOI: 10.1039/b000000x/

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