A method for the direct bromination of hydrocarbons with Br₂ using a ubiquitous and inexpensive catalyst is highly desirable. Herein, we report the selective monobromination of hydrocarbons in good yield using Li₂MnO₃ 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, as well as enjoying functional applications in bioactive materials. Classically, alkyl bromides have been prepared from the reaction of the corresponding alkyl alcohols with Br₂, HBr, and other brominating reagents. They can also be synthesized from the corresponding alkanes by reaction with brominating reagents, such as NBS, CBr₄, and Et₃NB₃. Although alkyl bromides can be synthesized from the corresponding alkanes by reaction with Br₂ under photolysis or high temperature conditions without any catalyst, the reactions do not exhibit any selectivity, 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 Br₂ in the presence of an excess of AcOH, a stoichiometric amount of t-BuONO, a catalytic amount of AlCl₃ at a low temperature, and an excess of MnO₂, have been reported. 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 MnO₂-promoted reaction, because it has been proposed that the Br₂ is activated on the MnO₂ surface. An issue associated with the use of MnO₂, however, is that the HBr byproduct formed during the course of the reaction poisons the MnO₂ to give non-active MnBrO(OH) species. During our initial attempts to use a catalytic amount of MnO₂ in the bromination of cyclohexane, however, the formation of MnBr₂ 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. 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, Li₂MnO₃, was identified as a suitable catalyst and promoted the bromination reaction to afford the monobrominated product 2a in 70% yield (Scheme 1). It is worthy of note that trans-1,2-dibromocyclohexane (3a) was only formed in 2% yield. 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).

Toluene was then used as a substrate to determine the nature of the reaction pathway (radical or ionic). Thus, if Br₂ was homolytically dissociated to form bromine radicals, the bromination would occur at the C-H bond on the benzyl position, whereas if cationic bromine was formed, electrophilic attack would occur on the aromatic ring. When the reaction was performed without the catalyst under photolysis, only benzylobromide (2b) was formed in 89% yield (Scheme 2, eq. 1). The same reaction profile was observed when the Li₂MnO₃ catalyst was used with and in the absence of light (Scheme 2, eq. 2). Furthermore, the kinetic isotope effect (KIE) of the bromination of cyclohexane (1a and 1a’) with and without Li₂MnO₃ was investigated. The KIE values in both cases were similar (3.3 and 3.4), which suggested that the reaction pathways were similar. These results indicated that Li₂MnO₃ 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 Li₂MnO₃ system. Unfortunately, however, the catalytic activity of Li₂MnO₃ in the bromination of benzene was lower than that previously observed using MnO₂, however, is that the HBr byproduct formed during the course of the reaction poisons the MnO₂ to give non-active MnBrO(OH) species. During our initial attempts to use a catalytic amount of MnO₂ in the bromination of cyclohexane, however, the formation of MnBr₂ 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. 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, Li₂MnO₃, was identified as a suitable catalyst and promoted the bromination reaction to afford the monobrominated product 2a in 70% yield (Scheme 1). It is worthy of note that trans-1,2-dibromocyclohexane (3a) was only formed in 2% yield. 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).

Toluene was then used as a substrate to determine the nature of the reaction pathway (radical or ionic). Thus, if Br₂ was homolytically dissociated to form bromine radicals, the bromination would occur at the C-H bond on the benzyl position, whereas if cationic bromine was formed, electrophilic attack would occur on the aromatic ring. When the reaction was performed without the catalyst under photolysis, only benzylobromide (2b) was formed in 89% yield (Scheme 2, eq. 1). The same reaction profile was observed when the Li₂MnO₃ catalyst was used with and in the absence of light (Scheme 2, eq. 2). Furthermore, the kinetic isotope effect (KIE) of the bromination of cyclohexane (1a and 1a’) with and without Li₂MnO₃ was investigated. The KIE values in both cases were similar (3.3 and 3.4), which suggested that the reaction pathways were similar. These results indicated that Li₂MnO₃ 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 Li₂MnO₃ system. Unfortunately, however, the catalytic activity of Li₂MnO₃ in the bromination of benzene was lower than that previously observed using MnO₂, however, is that the HBr byproduct formed during the course of the reaction poisons the MnO₂ to give non-active MnBrO(OH) species. During our initial attempts to use a catalytic amount of MnO₂ in the bromination of cyclohexane, however, the formation of MnBr₂ 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. 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, Li₂MnO₃, was identified as a suitable catalyst and promoted the bromination reaction to afford the monobrominated product 2a in 70% yield (Scheme 1). It is worthy of note that trans-1,2-dibromocyclohexane (3a) was only formed in 2% yield. 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).

Toluene was then used as a substrate to determine the nature of the reaction pathway (radical or ionic). Thus, if Br₂ was homolytically dissociated to form bromine radicals, the bromination would occur at the C-H bond on the benzyl position, whereas if cationic bromine was formed, electrophilic attack would occur on the aromatic ring. When the reaction was performed without the catalyst under photolysis, only benzylobromide (2b) was formed in 89% yield (Scheme 2, eq. 1). The same reaction profile was observed when the Li₂MnO₃ catalyst was used with and in the absence of light (Scheme 2, eq. 2). Furthermore, the kinetic isotope effect (KIE) of the bromination of cyclohexane (1a and 1a’) with and without Li₂MnO₃ was investigated. The KIE values in both cases were similar (3.3 and 3.4), which suggested that the reaction pathways were similar. These results indicated that Li₂MnO₃ 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 Li₂MnO₃ system. Unfortunately, however, the catalytic activity of Li₂MnO₃ in the bromination of benzene was lower than that previously observed using MnO₂, however, is that the HBr byproduct formed during the course of the reaction poisons the MnO₂ to give non-active MnBrO(OH) species. During our initial attempts to use a catalytic amount of MnO₂ in the bromination of cyclohexane, however, the formation of MnBr₂ 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. 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, Li₂MnO₃, was identified as a suitable catalyst and promoted the bromination reaction to afford the monobrominated product 2a in 70% yield (Scheme 1). It is worthy of note that trans-1,2-dibromocyclohexane (3a) was only formed in 2% yield. 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).
reported for other catalysts, including a zeolite and its analogues.\textsuperscript{17} With this in mind, we focused our own research on the bromination of aliphatic hydrocarbons.

\textbf{Scheme 2.} Mechanistic study of Li$_2$MnO$_3$-catalyzed bromination of hydrocarbons. (1) Bromination of toluene (1b) and KIE analysis using cyclohexane (1a) and cyclohexane-12 (1a’), (2) bromination of benzene (1c) and under irradiation was performed with weak light. Fluorescent room light was selected as a light source for the investigation and cyclohexane (1a) was consequently converted into bromocyclohexane (2a) in 70% yield using a lower reaction temperature and a shorter reaction time (Table 1, entry 1). When a strong light source was used, such as a high pressure mercury–vapor lamp (Ushio, UM-452, 450 W) or a xenon lamp (Asahi Spectra, MAX-302, 300 W), complex polybrominated products derived from the photoinduced formation of free bromine radicals were obtained. In the absence of light, 2a was not formed at 80 °C following a 10 min reaction period (Table 1, entry 2). It is known that HBr is converted into Br$_2$ under photolysis with oxygen.\textsuperscript{22} The effect of oxygen was envisaged that the rate of the reaction could be accelerated in the presence of a catalytic amount of Li$_2$MnO$_3$ and under irradiation with weak light.

Br$_2$ can be readily dissociated under irradiation of light with a wavelength of 350–550 nm to give bromine radicals.\textsuperscript{20} It was envisaged that the rate of the reaction could be accelerated in the presence of a catalytic amount of Li$_2$MnO$_3$ and under irradiation with weak light. Fluorescent room light was selected as a light source for the investigation and cyclohexane (1a) was consequently converted into bromocyclohexane (2a) in 70% yield using a lower reaction temperature and a shorter reaction time (Table 1, entry 1). When a strong light source was used, such as a high pressure mercury–vapor lamp (Ushio, UM-452, 450 W) or a xenon lamp (Asahi Spectra, MAX-302, 300 W), complex polybrominated products derived from the photoinduced formation of free bromine radicals were obtained. In the absence of light, 2a was not formed at 80 °C following a 10 min reaction period (Table 1, entry 2). It is known that HBr is converted into Br$_2$ under photolysis with oxygen.\textsuperscript{22} The effect of oxygen was envisaged that the rate of the reaction could be accelerated in the presence of a catalytic amount of Li$_2$MnO$_3$ and under irradiation with weak light.

Br$_2$ can be readily dissociated under irradiation of light with a wavelength of 350–550 nm to give bromine radicals.\textsuperscript{20} It was envisaged that the rate of the reaction could be accelerated in the presence of a catalytic amount of Li$_2$MnO$_3$ and under irradiation with weak light. Fluorescent room light was selected as a light source for the investigation and cyclohexane (1a) was consequently converted into bromocyclohexane (2a) in 70% yield using a lower reaction temperature and a shorter reaction time (Table 1, entry 1). When a strong light source was used, such as a high pressure mercury–vapor lamp (Ushio, UM-452, 450 W) or a xenon lamp (Asahi Spectra, MAX-302, 300 W), complex polybrominated products derived from the photoinduced formation of free bromine radicals were obtained. In the absence of light, 2a was not formed at 80 °C following a 10 min reaction period (Table 1, entry 2). It is known that HBr is converted into Br$_2$ under photolysis with oxygen.\textsuperscript{22} The effect of oxygen was envisaged that the rate of the reaction could be accelerated in the presence of a catalytic amount of Li$_2$MnO$_3$ and under irradiation with weak light.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Entry$^{[h]}$} & \textbf{conditions} & \textbf{atmosphere} & \textbf{yield / \%$^{[i]}$} \\
\hline
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 \\
\hline
\end{tabular}
\caption{Effect of Light and Oxygen in Bromination of Cyclohexane (1a).}
\end{table}

\textbf{Table 1} Effect of Light and Oxygen in Bromination of Cyclohexane (1a).

\textbf{Table 2} Scope of Substrates in the Li$_2$MnO$_3$-Catalyzed Bromination of Hydrocarbons Under Oxygen and Photo-Irradiation.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{entry$^{[k]}$} & \textbf{R}–\textbf{H} & \textbf{lamp / °C} & \textbf{time / h} & \textbf{product yield} \\
\hline
1 & 1d & 25 & 0.2 & 2d \ 2 \ quant \\
2 & 1a & 40 & 0.5 & 2e \ 59 \ 2e’ \ 23 \% \\
3 & 1f & 100 & 24 & 2f \ 42 \% \ 2f’ \ 5 \% \\
4 & 1b & 25 & 0.2 & 2b \ 93 \% \\
5 & 1g & 80 & 3 & 2g \ 86 \% \\
\hline
\end{tabular}
\caption{Scope of Substrates in the Li$_2$MnO$_3$-Catalyzed Bromination of Hydrocarbons Under Oxygen and Photo-Irradiation.}
\end{table}

\textbf{Scheme 3.} Bromination of cyclooctane (1d).
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 encourage 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 formation 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

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 Li₃MnO₃ exhibits both metal oxide and metalate chemical character towards Br₂.

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).

Notes and references


12. a) G. S. Silverman, P. E. Rakita, in Catalysis Research Center, Hokkaido University, Sapporo 001-0021, Electronic Supplementary Information (ESI) available: Methods and experimental procedure. See DOI: 10.1039/b000000x/; b) Products and yields are determined by GC comparing the standard sample, and using dodecan as an internal standard.

13. a) Li₃MnO₃ was synthesized from MnO₂ and Li₂CO₃ (see Supporting Information). Other alkali metal-modified manganese oxides were prepared in the same procedure, however, they were complex mixtures and XRD analysis could not determine their structures.


