

Nanostructured molybdenum oxides and their catalytic performance in the alkylation of arenes†

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We report for the first time that nanostructured MoO₃ is an excellent catalyst for the alkylation of a wide range of arenes with substituted benzyl alcohols as alkylating agents.

Molybdenum oxide is widely used as a catalyst.¹ Generally, molybdenum species are dispersed on oxides, like ZrO₂,² Al₂O₃,³ SiO₂,⁴ *etc.* Recent years have seen a surge in the design and preparation of molybdenum oxides. Much effort has been focused on preparing new morphologies of nano-crystalline MoO₃, such as rods,^{5,6} wires,⁷ tubes,⁸ belts,⁹ *etc.* A search we undertook through the SciFinder[®] Scholar database (keyword: molybdenum oxide) returned more than 20 000 papers, most of which were devoted to material synthesis. Notably, there was no report on employing nanostructured MoO₃ as an alkylation catalyst.

Recently we found that nanostructured MoO₃ exhibited an unexpected catalytic performance in benzylation reactions. By treating benzyl alcohol in toluene with a catalytic amount of MoO₃, we could obtain benzyl toluene isomers in a quantitative yield. Benzylation is a traditional and very important Friedel–Crafts alkylation reaction, and it represents a satisfactory route to synthesize diphenylmethane derivatives.¹⁰ In comparison with processes using H₂SO₄, AlCl₃, metal complexes,^{11–13} supported solid acids,^{14,15} metal ion-incorporated zeolite catalysts¹⁶ and complex oxides,^{17,18} our method possesses the advantages of high performance, and easy catalyst preparation and reusability. Herein, we wish to communicate the first protocol of a benzylation reaction using a nanostructured MoO₃ catalyst.

Several molybdenum oxides were prepared and tested in the benzylation of toluene with benzyl alcohol. The detailed procedures of catalyst preparation and our catalytic tests are described in the ESI.† The results of these reactions are listed in Table 1. In the absence of a catalyst, no reaction took place (Table 1, entry 1). Surprisingly, the catalyst prepared by the precipitation method (MP) exhibited the best result (Table 1, entry 2), with >99% conversion of benzyl alcohol and 95% isolated yield of the alkylated products in 20 min at 110 °C

(reflux in toluene). The regioselectivity of the reaction was 44 : 10 : 46 (*ortho* : *meta* : *para*). Extending the reaction duration to 30 min did not lead to any by-products, such as polymers.¹⁹ Different batches of catalyst gave very similar results, suggesting that the catalyst preparation is reproducible. Due to its excellent performance, we selected the MP catalyst for further evaluation. In contrast, the catalysts prepared by a hydrothermal method (MH),²⁰ molybdate salt calcination (MM), β-MoO₃,²¹ and commercial MoO₃ (MC-MoO₃) and MoO₂ (MC-MoO₂), showed less activity and selectivity. The by-product benzyl diether (BDE) was formed by the dehydration reaction between two benzyl alcohol molecules. A similarly good result using the MP catalyst was achieved by employing benzyl chloride instead of benzyl alcohol as the alkylating agent. Because of its lower toxicity and easier handling, benzyl alcohol was preferred to benzyl chloride in this research.

The MP catalyst was separated simply by membrane filtration and washing with toluene, and could be reused several times. The catalytic performances of reused catalysts were similar to those of fresh ones (Fig. 1) and their structures did not change after seven uses, as shown by XRD (ESI Fig. S1†). Removal of the MP catalyst during the course of the reaction completely stopped conversion of the benzyl alcohol, while addition of the catalyst immediately triggered the reaction (ESI Fig. S2†), suggesting that the nature of the reaction was heterogeneous catalysis. ICP-mass analysis revealed that no Mo species leached into the reaction media.

Having established a method for the benzylation of toluene, we were interested in the alkylation of other substituted arenes with benzyl alcohol (Table 2). As expected, a variety of electron-rich arenes, like anisole (Table 2, entry 2, yield 94%), *para*-xylene (Table 2, entry 3, yield 93%), ethylbenzene (Table 2, entry 4, yield 93%) and mesitylene (Table 2, entry 5, yield 95%) gave the corresponding benzylation products in excellent yield. Due to the activated benzene ring in anisole, the benzylation reaction occurred solely at the *para* and *ortho* positions with respect to the methoxy group. For Table 2, entries 3–5, these reactions were complete after 5–10 min at a slightly enhanced temperature, with a 93–95% isolated yield. The benzylation of non-activated arenes such as benzene (Table 2, entry 6, 94% yield) and naphthalene (Table 2, entry 7, 85% yield) proceeded smoothly. The more challenging benzylation of acetophenone (Table 2, entry 8) gave the corresponding product in 15% yield, with an 88% selectivity for the *para* isomer. We have noted that substituent effects greatly influenced the reactivity of arenes. For example, the reaction rate of benzyl alcohol with toluene was 12 times that of acetophenone. The least reactive arene, trifluoromethyl

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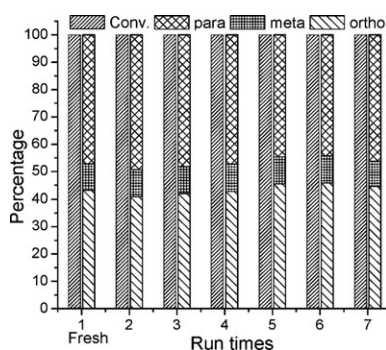
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† Electronic supplementary information (ESI) available: Experimental procedures, XRD and SEM characterization of the catalyst, catalyst separation and triggering test, competitive test, and ¹H NMR, ¹³C NMR and mass spectra data of new compounds. See DOI: 10.1039/b803205j

Table 1 Alkylation of toluene using molybdenum oxides^a

Entry	Catalyst ^b	Catalyst colour	Alkylating agent	t/min	Conversion (%) ^c	Major product Regioselectivity (%) ^d	Isolated yield (%)	BDE selectivity (%)
1	—	—	Benzyl alcohol	30	0	—	—	—
2	MP	Light blue	Benzyl alcohol	10	76	44 : 10 : 46	ni ^e	0
			Benzyl alcohol	20	>99	44 : 10 : 46	95	0
			Benzyl alcohol	30	>99	44 : 10 : 46	ni	0
			Benzyl alcohol	30	>99	44 : 10 : 46	93	0
3	MH	White	Benzyl alcohol	30	82	44 : 14 : 42	ni	5
			Benzyl alcohol	40	90	44 : 9 : 47	ni	10
4	MM	Light gray	Benzyl alcohol	40	90	44 : 9 : 47	ni	10
5	β-MoO ₃	Bright yellow	Benzyl alcohol	60	0	—	—	—
6	MC-MoO ₃	Light gray	Benzyl alcohol	30	54	44 : 9 : 47	ni	46
7	MC-MoO ₂	Brown	Benzyl alcohol	260	11	48 : 6 : 46	ni	55
8	MP	Light blue	Benzyl chloride	20	>99	44 : 8 : 48	92	0

^a Reaction conditions: alcohol 0.24 mL, arene 15.0 mL, hexadecane (internal standard) 0.1 mL, reaction temperature 110 °C, catalyst 0.3 g, argon atmosphere. ^b Detailed information regarding catalyst preparation is shown in the ESI. ^c Conversion was determined by GC based on benzyl alcohol using an internal standard. ^d Isomeric ratio of *ortho* : *meta* : *para*. ^e ni = not isolated. ^f Catalytic results using different batches of MP catalyst.

**Fig. 1** Reusability of the MP catalyst.

benzene (Table 2, entry 9), did not react with benzyl alcohol after 120 min.

Moreover, the MP catalyst could efficiently catalyze intramolecular benzylation (Table 3). 5-, 6- and 7-membered rings could be formed by connecting two phenyl rings. For instance, when (2-benzylphenyl)methanol was treated with the MP

Table 2 Reaction of benzyl alcohol with different arenes^a

Entry	Arene	T/ °C	t/ min	Conversion (%)	Regioselectivity (%)	Isolated yield (%)
1	Toluene	110	20	>99	46 : 10 : 44 (<i>para</i> : <i>meta</i> : <i>ortho</i>)	95
2	Anisole	110	20	>99	51 : 49 (<i>para</i> : <i>ortho</i>)	94
3	<i>para</i> -Xylene	135	10	>99	>99	93
4	Ethylbenzene	135	5	>99	46 : 12 : 42 (<i>para</i> : <i>meta</i> : <i>ortho</i>)	93
5	Mesitylene	135	5	>99	>99	95
6	Benzene	80	90	>99	>99	94
7	Naphthalene ^b	100	120	95	74 : 26 (1- : 2-)	85
8	Acetophenone	110	60	25	88 : 12 (<i>para</i> : <i>ortho</i>)	15
9	Trifluoromethyl benzene	110	120	0	0	—

^a For reaction conditions, see Table 1 footnote a. ^b Naphthalene 0.78 mmol, benzyl alcohol 26 μmol, hexadecane 2.7 μL, catalyst 30 mg, under reflux in 1,4-dioxane 2 mL.

catalyst in refluxing 1,4-dioxane for 4 h, 9,10-dihydroanthracene (**3b**) was formed as the sole product in 92% yield. Likewise, compounds 9*H*-fluorene (**3a**, yield 88%) and 10,11-dihydro-5*H*-dibenzo[*a,d*]cycloheptene (**3c**, yield 91%) were isolated as the sole products when employing biphenyl-2-ylmethanol and (2-phenethylphenyl)methanol as substrates, respectively. The reaction rates decreased in the sequence: **3b** > **3c** > **3a**, which could be explained by the increasing order of ring strain energy ($\Delta H_c^\circ/\text{kcal mol}^{-1}$): cyclohexane (−0.6) < cycloheptane (5.6) < cyclopentane (6.0).²²

We expected that the MP catalyst could also be applied to substituted benzylic alcohol alkylating agents. Catalytic reactions were carried out using *para*-xylene and various substituted benzylic alcohols (Table 4). As a result, electron-rich alcohols such as *para*- and *ortho*-methyl benzyl alcohol (Table 4, entries 2 and 3) afforded the corresponding benzylation in excellent yield (95%). Even with bulky substituents at the benzylic carbon, such as 1-phenylethanol (Table 4, entry 4) and diphenylmethanol (Table 4, entry 5), quantitative yields of benzylation were obtained. Benzylation with electron-poor alcohols also proceeded smoothly

Table 3 Intramolecular benzylation^a

Arenes	Product	t/ h	Conversion (%) ^b	Isolated yield (%)
		4 10	40 97	ni 88
		4	>99	92
		4 10	42 95	ni 91

^a Reaction conditions: substrate 2 mmol, solvent 1,4-dioxane 10 mL, catalyst 0.3 g, argon atmosphere, under reflux conditions. ^b Determined by ¹H NMR.

Table 4 The reaction of *para*-xylene with different alcohols^a

Entry	Alcohol	T/°C	t/min	Conversion (%)	Regioselectivity (%)	Isolated yield (%)
1	Benzyl alcohol	135	10	>99	>99 ^b	93
2	<i>para</i> -Methyl benzyl alcohol	110	15	>99	>99 ^b	95
3	<i>ortho</i> -Methyl benzyl alcohol	110	20	>99	>99 ^b	95
4	1-Phenylethanol	110	45	>99	>99 ^b	96
5	Diphenylmethanol	110	60	98 ^c	>99 ^c	88
6	4-Biphenylmethanol	130	180	>99 ^c	>99 ^c	90
7	<i>ortho</i> -Chlorobenzyl alcohol	130	180	>99 ^c	>99 ^c	93
8	<i>para</i> -(Trifluoromethyl) benzyl alcohol	130	180	0 ^c	—	—

^a For reaction conditions, see Table 1 footnote a. ^b Determined by GC. ^c Determined by ¹H NMR.

by increasing the reaction time and temperature (Table 4, entries 6 and 7). Most interestingly, the reaction of chlorobenzyl alcohol with *para*-xylene resulted in a spectacular yield (93%). It is worth noting that the latter reaction is one of the few successful Friedel–Crafts benzylation reactions that work well with deactivated arenes. However, the *p*-CF₃ substituted benzyl alcohol (Table 4, entry 8) was unreactive under the conditions used.

X-Ray diffraction patterns showed that MP, as well as MC-MoO₃, exhibiting typical (020), (110), (021) and (111) planes (JCPDS #05-0508), were α -phases (ESI Fig. S1†). Field emission scanning electron microscopy (FE-SEM) showed that both MP and MC-MoO₃ had a pellet morphology (ESI Fig. S3†). The MP catalyst had a narrow distribution of 400–500 nm and MC-MoO₃ had a broad distribution of 1–2 μ m. Notably, the thickness of MP was *ca.* 30 nm, which is much smaller than that of MC-MoO₃ (*ca.* 800 nm) and the other catalysts. The excellent performance of the MP catalyst is attributed to the increased number of surface defect sites, generated by the remarkable reduction of particle dimensions to nanoscale. The light blue colour of the MP catalyst indicates the existence of specific point defects, such as F centres.^{23,24} It has been reported that such sites could efficiently catalyze the activation of benzylic C–OH bonds.^{17,25} We evaluated *p*-Me, *p*-H and *p*-CF₃ substituted benzyl alcohols in a one-pot competitive test (ESI Fig. S4†). The rate ratio of the *p*-Me reaction over the *p*-H reaction after 2.5 min was 38, indicating that the formation of a carbocation intermediate may be involved at some stage.²⁶ The heterolytic cleavage of the PhCH₂–OH bond on defect sites leads to the formation of the carbocation species, which further reacts with an arene molecule to form the product.

In summary, we have demonstrated that nanostructured MoO₃ (MP) can efficiently catalyze the benzylation of a broad range of arenes, with various benzylic alcohols as alkylating agents. The catalytic reaction is clean and quick, which enables the method to be feasible at either the bench or pilot plant level. Further research will be devoted to broadening the application of the catalyst into other reactions and investigating the mechanisms involved.

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