Molybdenum-Catalyzed Aromatic Substitution with Olefins and Alcohols

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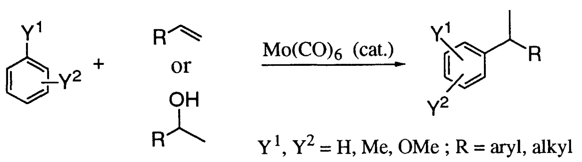
A new type of electrophilic aromatic substitution without using organic halides has been realized by using $Mo(CO)_6$ catalyst.

Electrophilic aromatic alkylation with alkyl halides, known as Friedel-Crafts alkylation reaction, is one of the most useful synthetic methods for preparation of substituted aromatic compounds.[1] Recently due to the imperative necessity of environmentally benign synthesis, catalytic reactions without using organic halides become of great importance to avoid use and/or production of unnecessary halogen containing compounds. We have reported previously that the allylation of aromatic compounds can be achieved with allylic esters or alcohols using a catalytic amount of $Mo(CO)_6$.[2] In this paper we report a facile aromatic substitution with olefins or alcohols in the presence of $Mo(CO)_6$ catalyst.



(1)

Y^1, Y^2 = H, Me, OMe ; R = aryl, alkyl

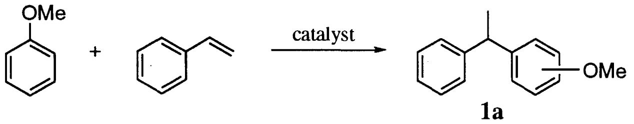
Reaction of styrene with methoxybenzene at 80 °C in the presence of $Mo(CO)_6$ (10 mol%) for 20 h gave a 4:1 mixture of 1-*p*- and 1-*o*-methoxyphenyl-1-phenylethane **1a** in 99% yield.[3] As shown in Table 1, the same product in a similar ratio was obtained in 72% yield when as little as 1 mol% of the catalyst was used. Whereas $MoCl_5$ showed a similar reactivity as $Mo(CO)_6$, the chromium analog $Cr(CO)_6$ proved inactive and $W(CO)_6$ and $H_2IrCl_5 \cdot 6H_2O$ showed much lower catalytic activities. The carbonyl complexes of late transition metals such as $Ru_3(CO)_{12}$ and $Co_2(CO)_8$ had no reactivity either. Although the reaction of methoxybenzene and styrene can be promoted by protonic acids or Lewis acids such as *p*-toluenesulfonic acid, Nafion-H,[4] and $Sc(OTf)_3$,[5] the catalytic activities of these acids were much less than that of $Mo(CO)_6$.

Similar aromatic substitution reaction of 1,2-dimethoxybenzene (65%), *p*-xylene (39%), and methoxynaphthalene (73%) with styrene gave the corresponding products in good to fair yields as shown in the parentheses, whereas reaction with electron deficient aromatic compounds such as acetophenone and nitrobenzene did not proceed.

The reaction of various substituted styrenes with methoxybenzene gave its substitution products with styrenes coupled at the α position in high yields (Table 2).

Not only aromatic olefins but cyclohexenes also react to give cyclohexylmethoxybenzene. Reaction of 1-methylcyclohexene afforded **2b** in 94% yield but the reaction

Table 1. Transition metal- or acid-catalyzed reaction of methoxybenzene with styrene[a]

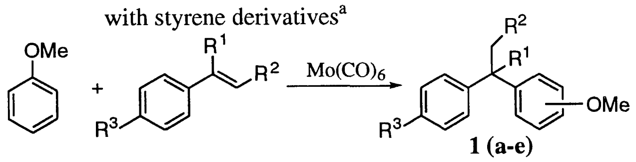


1a

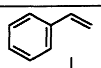
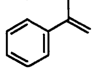
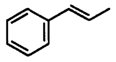
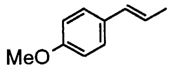
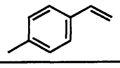
Catalyst	Time/h	Yield/%	Selectivity[e] (*o*, *m*, *p*)
$Mo(CO)_6$	20	99	(1, 0, 4)
$Mo(CO)_6$[b]	20	72	(1, 0, 4)
$W(CO)_6$[c]	70	26	(1, 0, 5)
$Cr(CO)_6$	20	0	
$Ru_3(CO)_{12}$	40	0	
$Co_2(CO)_8$	72	0	
$MoCl_5$	20	84	(1, 0, 4)
$H_2IrCl_5 \cdot 6H_2O$	20	39	(1, 0, 5)
p-TsOH	40	26	(1, 0, 8)
Nafion-H[d]	40	57	(1, 0, 3)
$Sc(OTf)_3$	37	34	(1, 0, 4)

[a] Methoxybenzene (10 ml), styrene (1 mmol), and the catalyst (10 mol%) at 80 °C under Ar. [b] $Mo(CO)_6$ (1 mol%) was used. [c] Reaction at 120 °C. [d] Nafion-H (10 wt%) was used. [e] Determination by GC.

Table 2. $Mo(CO)_6$-catalyzed substitution of methoxybenzene with styrene derivatives[a]

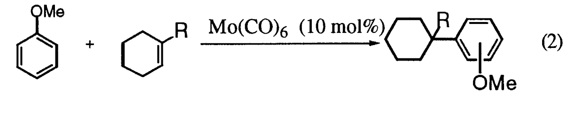


1 (a-e)

Styrene	Time/h	Yield/%	Selectivity[b] (*o*, *m*, *p*)
	20	96	(1, 0, 4)
	20	79	(1, 0, 12)
	47	79[c]	(1, 0, 4)
	70	97	(1, 0, 19)
	20	92	(1, 0, 9)

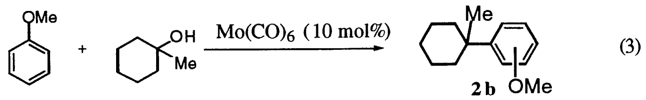
[a] Methoxybenzene (10 ml), styrene derivative (1 mmol), and $Mo(CO)_6$ (10 mol%) at 80 °C under Ar. [b] Determination by GC.
[c] $Mo(CO)_6$ (10 mol%) was used.

with cyclohexene gave **2a** only in 28% yield.



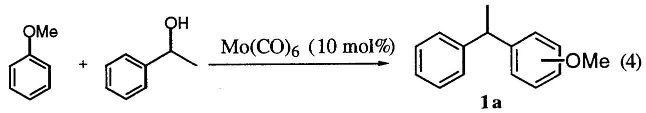
R = H 120 °C 40 h **2a** 28% (*o*, *m*, *p* = 1, 0, 1)
R = Me 80 °C 20 h **2b** 94% (*o*, *m*, *p* = 1, 0, 27)

These results of the reaction of aromatic compounds with olefins, especially the feature of high *o*,*p*-direction, implicates that the reaction proceeded by electrophilic substitution of arene by olefins promoted by the molybdenum complexes. In addition to olefins,[6] aromatic substitution proceeds with oxygen containing compounds such as alcohols affording dehydrative addition products of alcohols substituted with methoxybenzene. Thus the reaction of 1-methylcyclohexanol or 1-phenylethanol in methoxybenzene gave (1-methylcyclohexyl)methoxybenzene **2b** and 1-methoxyphenyl-1-phenylethane **1a** in 73% and 91% yields respectively. Although the direct 1,2-addition to carbonyl compounds[7,8] did not give good results, ring opening addition of styrene oxide provided alcohol **3** in 21 % yield.



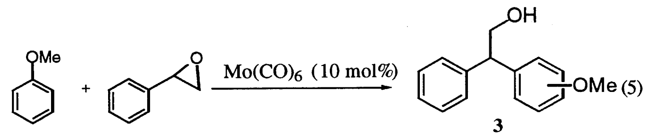
2b

73% (*o*, *m*, *p* = 1, 0, 32)



1a

91% (*o*, *m*, *p* = 1, 0, 4)



3

21% (*o*, *m*, *p* = 1, 0, 4)

These reactions provide a simple and useful synthetic method for preparation of substituted aromatic compounds.

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References and Notes

1 G. A. Olah, R. Krishnamurti, and G. K. Surya, "Comprehensive Organic Synthesis," ed by B. M. Trost, Pergamon Press, Oxford (1991), Vol. 3, pp. 293-339.

2 I. Shimizu, T. Sakamoto, S. Kawaragi, Y. Maruyama, and A. Yamamoto, *Chem. Lett.*, **1997**, 137. Also for palladium-catalyzed processes using allylic alcohols, see; M. Sakamoto, I. Shimizu, and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **69**, 1065 (1996); Y. Tada, A. Satake, I. Shimizu, and A. Yamamoto, *Chem. Lett.*, **1996**, 1021.

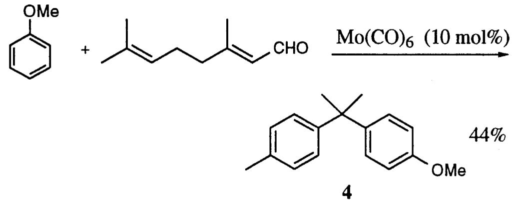
3 As a typical procedure for alkylation of methoxybenzene, the reaction mixture containing styrene (1.0 mmol), $Mo(CO)_6$ (0.1 mmol), and dodecane (an internal standard, 50 mg) in methoxybenzene (10 ml) was refluxed for 20 h. The reaction mixture was concentrated in vacuo. Chromatographic separation of the residue on SiO_2 (Wakogel C-300) with 2% AcOEt in hexane gave 1-methoxyphenyl-1-phenylethane (99%). The ratio of *o*-, *m*-, and *p*-isomers (1: 0 : 4) was determined by GC (SE-30, 2 m).

4 H. Hasegawa and T. Higashimura, *Polym. J.*, **13**, 915 (1981); T. Yamato, C. Hideshima, G. K. S. Prakash, and G. A. Olah, *J. Org. Chem.*, **56**, 2089 (1991); T. Yamato, M. Fukumoto, N. Sakaue, T. Furusawa, and M. Tashiro, *Synthesis*, **1991**, 699.

5 A. Kawada, S. Mitamura, and S. Kobayashi, *Synlett*, **1994**, 545; A. Kawada, S. Mitamura, and S. Kobayashi, *J. Chem. Soc., Chem. Commun.*, **1993**, 1157; T. Tsuchimoto, K. Tobita, T. Hiyama, and S. Fukuzawa, *Synlett*, **1996**, 557.

6 Recently ruthenium-catalyzed aromatic substitution using olefins through C-H activation process has been reported. S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, and N. Chatani, *Nature*, **366**, 529 (1993); F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, and S. Murai, *Bull. Chem. Soc. Jpn.*, **68**, 62 (1995).

7 Cationic cyclization of citral followed by reaction with methoxybenzene took place to give 2-(4-methoxyphenyl)-2-(4-methylphenyl)propane **4** in 44% yield.



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8 S. Fukuzawa, T. Tsuchimoto, and T. Hiyama, *J. Org. Chem.*, **62**, 151 (1997).