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C–S bond formation in aromatic substrates using Mn(II)-promoted montmorillonite clays

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Direct introduction of –SCH_3 groups into activated aromatic and hetero aromatic compounds has been achieved by reaction with dimethyldisulfide over a $MnCl_2$-promoted K-10 montmorillonite. Unlike $ZnCl_2$/K-10, the Mn-promoted clay appears to promote reaction by coordination of the aromatic substrate at the active site followed by attack of the disulfide at the activated aromatic.

Keywords: montmorillonite, K-10, Mn(II), aromatics, disulfides, C–S bond formation

1. Introduction

In general, formation of C–S bonds in aromatic and hetero aromatic compounds has been possible only by indirect methods such as reaction of diazonium salts with xanthates [1], quenching of organo-lithium derivatives with electrophilic sulfur species [2–6] or by nucleophilic displacement of chloride or bromide from organohalo compounds under forcing conditions [7]. One of the few examples of direct aromatic C–S bond formation utilized a combination of S_2Cl_2 and $FeCl_3$ [8,9] but neither this method nor any other direct method appears to have been applied generally.

Recently, we have described a method for direct introduction of –SMe substituents into thiophene and benzothiophene by reaction with dimethyldisulfide (DMDS) over Zn(II)-promoted K-10 clay [10]. K-10 is a commercially available acid-treated montmorillonite with a high mesopore volume ($0.36\ \mathrm{ml\ g^{-1}}$) and a large surface area ($230\ \mathrm{m^2\ g^{-1}}$) [11]. Thiolation is believed to occur by coordination of one sulfur atom of DMDS to Zn(II) on the catalyst surface and attack of the aromatic reagent at the adjacent electrophilic sulfur (scheme 1). The soft Lewis acid, $ZnCl_2$, seems to be particularly effective because of its ability to coordinate disulfides. Interestingly, it was noted [10] that this reaction proceeds better in air, most likely as a result of oxidation and removal of methanethiol by-product bound to active sites (see scheme 1).

Overall, the clay-promoted introduction of –SMe groups into thiophenic systems occurred under very mild conditions [10] and, by removal of the Me group with Na/NH_3, it allows a simple preparation of thiophene thiols. In general, we have found that K-10/$ZnCl_2$ also promotes thiolation of simple benzenoid aromatics but in low overall yields. In an attempt to improve the reaction with aromatics such as benzene and toluene, K-10 was impregnated with other metal species (e.g. Fe(III), Cu(II)). These catalysts did promote the thiolation of thiophenes and very reactive hydrocarbon aromatics, but were ineffective using only moderately reactive aromatics. Interestingly, K-10 impregnated with 2 mmol/g of Mn(II)Cl_2 proved to be the most active catalyst for thiolation of thiophenes and aromatics. This is a very surprising observation as Mn(II) is a poor Lewis acid and would not be expected to activate disulfides by coordination.

The purpose of this letter is to disseminate our early results on this interesting observation and suggest a pathway by which Mn(II) may promote reaction with aromatics.

2. Results

Table 1 summarizes results of reactions of various aromatic and hetero aromatic species with DMDS using catalysts prepared by impregnation of K-10 with 2 mmol g^{-1} of either $ZnCl_2$, H_2SO_4 or $MnCl_2$. In order to put these results into context, it is useful to note that K-10 without added metal species or H_2SO_4 gives only poor yields of products after very long contact times. This low activity of K-10 is, most likely, due to some Brønsted acid sites within its structure.

It was found that benzene was inert towards DMDS with all catalysts and that toluene reacted only slowly with K-10/H^+ and K-10/$MnCl_2$. *o*-xylene is more susceptible to reaction with DMDS with the best yield of the 4,5-diSCH_3 product being obtained with the Mn(II)-promoted catalyst. In this case it was not possible to restrict reaction to a mono-thiolated product. Both anisole and thioanisole gave 4-SCH_3 products in reasonable

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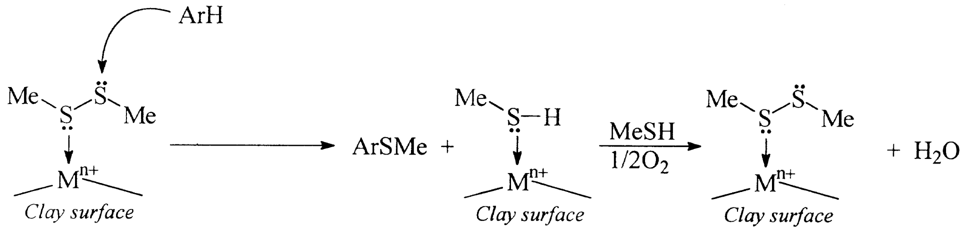


M^{n+} = Zn(II), Cu(II) and Fe(III)
ArH = Reactive aromatic

Scheme 1.

yield and some poly-substituted products when using the Mn(II) catalyst. Lower yields were obtained with either the Zn(II) or H$^+$-promoted catalysts. The pattern of higher reactivity of K-10/MnCl$_2$ is followed for reaction of DMDS with naphthalene, thiophene and benzothiophene (BT). In all cases reactions promoted by K-10/MnCl$_2$ were much cleaner in comparison to reactions promoted by the other catalysts. In particular, dimethylpolysulfides ($CH_3S_xCH_3$), which were formed as by-products with K-10/ZnCl$_2$, were not produced in the K-10/MnCl$_2$-catalyzed processes. Reactions with BT are particularly noteworthy as significant quantities of tetra- and penta-substituted products were obtained using the Mn(II) catalyst. In contrast, only 2,3-diSCH$_3$ and very poor yields of poly-substituted products could be obtained using K-10/ZnCl$_2$ and K-10/H$_2$SO$_4$ respectively.

Elsewhere, we have reported the reaction of DMDS with cyclohexene and other alkenes over clay catalysts [12]. In this type of reaction, K-10/ZnCl$_2$ promotes addition of DMDS across the double bond. As may be seen from table 1, whereas both K-10/ZnCl$_2$ and K-10/H$_2$SO$_4$ promote this reaction, K-10/MnCl$_2$ does not catalyze addition of DMDS to cyclohexene beyond the level observed with unmodified K-10.

3. Discussion

Besides the somewhat surprising observation that K-10/MnCl$_2$ is an excellent catalyst for promoting C–S bond formation in aromatics, it is noteworthy that the same catalyst does not promote addition of DMDS to isolated double bonds, especially since K-10/ZnCl$_2$ is an excellent catalyst for the addition reaction. Overall, these observations would suggest that Zn(II) and Mn(II) catalysts promote thiolation of aromatics by a different mechanism.

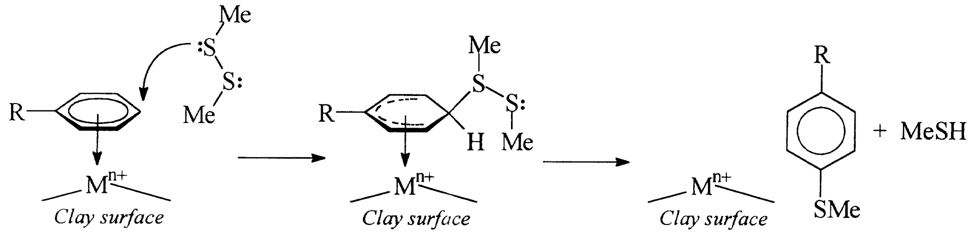
Scheme 1 proposes that reaction occurs via coordination of DMDS to an active site (Zn(II), or another metal species) and subsequent attack of the aromatic at the activated sulfur of the disulfide. This mechanism explains why oxygen (in the form of air) assists the process as conversion of methanethiol, now coordinated to

Table 1
Thioalkylation of aromatics, heteroaromatics and cyclohexane

Starting material	Conditions (°C, *t* h)	Product	Isolated yield (%)		
			K-10/ZnCl$_2$	K-10/H$_2$SO$_4$	K-10/MnCl$_2$
benzene	130, 24	none	–	–	–
toluene	130, 24	2,4,5-triSCH$_3$	0	11	5
o-xylene	130, 24	4,5-diSCH$_3$	0	23	38
thioanisole	130, 24	1,4-diSCH$_3$	< 5	33	44
		1,2,4,5-tetraSCH$_3$	0	0	12
anisole	130, 24	4-SCH$_3$	46	15	66
		2,4,5-triSCH$_3$	0	9	12
naphthalene	130, 24	1,4-diSCH$_3$	21	0	64
thiophene	150, 8	2,3,4,5-tetraSCH$_3$	50	0 [a]	50
benzo[*b*]thiophene	130, 24	2,3-diSCH$_3$	74	0 [a]	0
		2,3,6-triSCH$_3$	0	0	5
		2,3,5,6-tetraSCH$_3$	0	5	35
		2,3,6,7-tetraSCH$_3$	0	7	44
		2,3,5,6,7-pentaSCH$_3$	0	0	16
cyclohexane	20, 2	1,2-diSCH$_3$	88	0 [a]	50 [b]

[a] Extensive polymerization was observed in these reactions.

[b] This experiment was conducted over 24 h; only minimal product formation was observed after 2 h. Also K-10 without MnCl$_2$ gave similar results.



Scheme 2.

the active site, back to DMDS should enhance reaction rates. (Note: methanethiol is unlikely to act as a thiolating agent in a substitution process as it would require loss of H^- from the transition state.) The fact that K-10/$MnCl_2$ does not promote addition of DMDS to cyclohexene strongly suggests that DMDS does not coordinate to Mn(II). Thus, a probable explanation for the activity of the Mn(II)-promoted catalyst for the thiolation of aromatics is that it is the aromatic which is activated by coordination at the Mn(II) site (scheme 2). The inactivity of the Mn(II) catalyst towards addition of DMDS to double bonds can then be explained by the inability of the Mn sites to coordinate either DMDS or an isolated double bond.

K-10/Zn(II)-promoted reactions invariably result in significant polysulfide formation (e.g. CH_3SSSCH_3) in addition to causing thiolation of the aromatic substrate. Most likely, these by-products arise by reaction of DMDS with a Zn-coordinated DMDS (scheme 3). Interestingly, Mn(II)-promoted K-10 thiolation of aromatics and thiophenes resulted in product mixtures in which no dimethylpolysulfide product could be detected. This indicates further that DMDS does not coordinate to Mn(II), and, therefore, cannot form polysulfides as suggested in scheme 3.

As has been discussed previously [10], K-10/H_2SO_4 catalyzes thiolation of aromatics by protonation of DMDS at a Brønsted site on the catalyst surface followed by reaction of the electron-rich aromatic at the "electrophilic sulfur" created by this process. Although this catalyst appears to be reasonably active, only low isolated yields were obtained, particularly in cases (e.g. thiophene, cyclohexene) where the substrate is sensitive to acid-catalyzed polymerization.

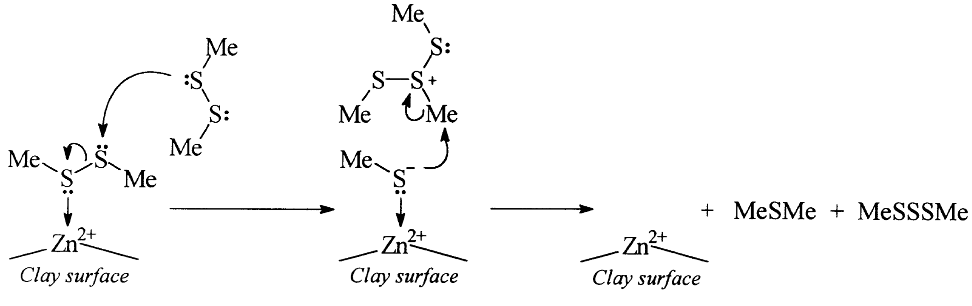
Overall, we conclude that K-10/$MnCl_2$ is a very active catalyst for promoting thiolation of aromatic compounds allowing a facile direct synthesis of these materials. Most likely, the reaction pathway involves coordination of the aromatic to a Mn(II) site and subsequent reaction with DMDS from the bulk solution.

4. Experimental

Reagents and materials. K-10 was purchased from The Fluka Chemical Company and was used as received. Other materials were purchased from the Aldrich Chemical Company and, with the exception of DMDS, were used as received. DMDS was stored over alumina and was redistilled prior to use to remove the traces of triethylamine frequently present in commercial DMDS.

Catalyst preparation. K-10 was modified with either $MnCl_2$, $ZnCl_2$, or H_2SO_4 (in amounts to achieve 2 mmol g^{-1} active phase) using wet impregnation techniques described previously[13]. The catalysts were activated by heating at 150°C for 24 h and were stored in a desiccator prior to use.

General procedure. In a typical experiment, a mixture of the aromatic or alkene substrate (7.5 mmol), DMDS (75 mmol) and the catalyst (10 g) in chlorobenzene (30 ml) was stirred and heated under reflux for 2–24 h (see table 1). After removal of the catalyst by filtration, solvent and excess DMDS were removed by distillation and the residual oils were purified by a combination of



Scheme 3.

distillation and crystallization. All compounds were identified by a combination of mass and NMR spectrometry. Details of these analyses are given in the following material.

Product identification of new compounds

1-methyl-2,4,5-tris(methylthio)benzene. Mp. 87–88°C; δ_H (400 MHz) 2.33 (s, 3H), 2.46 (s, 3H), 2.47 (s, 3H), 2.48 (s, 3H), 7.02 (s, 1H) and 7.09 (s, 1H); δ_C (100 MHz) 16.04 (CH_3), 16.67 (CH_3), 16.98 (CH_3), 19.61 (CH_3), 125.65 (CH), 128.86 (CH), 134.75 (q), 134.83 (q), 135.25 (q) and 135.49 (q); m/z 230 (M^+, 100%).

1,2-dimethyl-4,5-bis(methylthio)benzene. Mp. 85–88°C; δ_H (400 MHz) 2.36 (s, 6H), 2.43 (s, 6H), and 7.09 (s, 2H); δ_C (100 MHz) 16.5 (CH_3), 16.8 (CH_3), 124.4 (CH), 134.8 (q), and 135.4 (q); m/z 198 (M^+, 70%).

4-(methylthio)anisole. Bp. 58°C/ 0.01 mmHg; δ_H 2.45 (s, 3H), 3.80 (s, 3H), 6.86 (d, 2H), and 7.28 (d, 2H); δ_C 18.0 (CH_3), 55.3 (CH_3), 114.6 (CH), 128.8 (q), 130.2 (CH), and 158.22 (q); m/z 154 (M^+, 77%).

2,4,5-tris(methylthio)anisole. Mp. 93–94°C; δ_H 2.44 (s, 6H), 2.48 (s, 3H), 3.92 (s, 3H), 6.71 (s, 1H), and 7.18 (s, 1H); δ_C 15.2 (CH_3), 16.3 (CH_3), 17.9 (CH_3), 55.9 (CH_3), 108.9 (CH), 127.7 (q), 129.1 (CH), 138.0 (q), and 155.9 (q); m/z 246 (M^+, 100%).

1,2,4,5-tetrakis(methylthio)benzene. Mp. 110–112°C; δ_H 2.49 (s, 12H), and 7.11 (s, 2H); δ_C 16.7 (CH_3), 126.5 (CH), and 135.7 (q); m/z 262 (M^+, 100%).

2,3,4,5-tetrakis(methylthio)thiophene. Mp. 34–35°C; δ_H (200 MHz) 2.52 (s, 6H), and 2.42 (s, 6H); δ_C (50 MHz) 19.2 (CH_3), 19.6 (CH_3), 136.4 (q), and 140.8 (q); m/z 268 (M^+, 100%).

1,4-bis(methylthio)naphthalene. Mp. 78–81°C; δ_H (200 MHz) 2.53 (s, 6H), 7.35 (s, 2H), 7.57 (dd, 2H), and 8.32 (dd, 2H); δ_C (50 MHz) 16.7 (CH_3), 124.6 (CH), 125.1 (CH), 126.5 (CH), 132.1 (q), and 133.8 (q); m/z 220 (M^+, 100%).

2,3,5,6,7-pentakis(methylthio)benzo[b]thiophene. Mp. 130–131°C; δ_H (400 MHz) 2.40 (s, 3H), 2.42 (s, 3H), 2.56 (s, 6H), 2.67 (s, 3H), and 6.94 (s, 1H); δ_C (100 MHz) 15.9 (CH_3), 16.2 (CH_3), 17.3 (CH_3), 17.8 (CH_3), 21.0 (CH_3), 118.0 (CH), 121.0 (q), 123.3 (q), 134.2 (q), 135.9 (q), 139.4 (q), 147.0 (q), 148.7 (q); m/z 364 (M^+, 100%).

Other compounds in table 1 were identified by comparison of spectral data to published information.

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