Amination of Arenes with *N*,*N*-Dimethyl-2-imidazolidinone *O*-Methoxyacetyloxime

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Treatment of nucleophilic arenes with *N*,*N*-dimethyl-2-imidazolidinone *O*-methoxyacetyloxime and $SnCl_4$ produced the corresponding *N*-arylimines, which were converted to anilines by hydrolysis with CsOH and to *N*-methylanilines by $LiAlH_4$ reduction.

Direct amination of arenes has been considered as a straightforward method for the synthesis of aniline derivatives.[1] In the course of our study on the utilization of oxime derivatives as electrophilic amination reagents,[2] it was found that in the presence of Lewis acids, cyclic *O*-sulfonyl- or *O*-acyloximes could be used for the amination of nucleophilic arenes. This process involves the formation of imines from the oximes and arenes and the successive hydrolysis leading to the corresponding anilines (Figure 1).

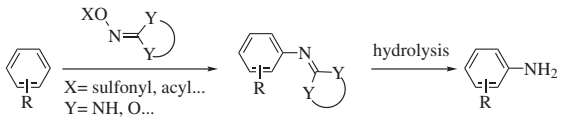
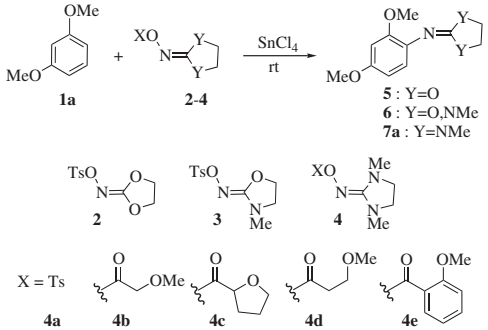


Figure 1. Amination of arenes with oxime derivatives.

First, the amination of 1,3-dimethoxybenzene (**1a**) was investigated with several *O*-sulfonyloxime derivatives **2**,**3**,**4a**[2e] and $SnCl_4$ as Lewis acid (Table 1, Entries 1–3). As expected from the properties of the oximes of ureas and carbonates, we hoped that these reagents would not suffer from unwanted side reactions such as Beckmann rearrangement and Neber reaction. *O*-sulfonyloxime of cyclic carbonate **2** led to a complex mixture in which only a small amount of 2,4-dimethoxyaniline was identified after acidic hydrolysis (Entry 1). Imine **6** was formed in a poor yield from 1,3-oxazolidinone *O*-sulfonyloxime **3** and could not be hydrolyzed by the subsequent acidic treatment (Entry 2). *O*-sulfonyloxime of cyclic urea **4a** proved to be more interesting. Its corresponding imine **7a** was formed in 81% yield, but was also resistant to acidic hydrolysis (Entry 3). We investigated then more closely the properties of the *N*,*N*-dimethyl-2-imidazolidinone oxime fragment by replacing the tosyl group of **4a** with another type of leaving group. Our first experiments with the methoxyacetyl group were very encouraging as **4b** reacted exothermically to afford the expected *N*-arylimine **7a** in high yield (Entry 4), and even with an equimolar amount of **1a** in dichloromethane at 0 °C, the reaction was rapidly completed, giving a similar yield of **7a** (Entry 5).

This result prompted us to explore the reactivity of other methoxyacyl analogues. Compounds **4b**–**e**[3] were treated at room temperature with an equimolar amount of **1a** and 2.5 molar amounts of $SnCl_4$ for 15 min (Entries 6–9). As expected from the precedent results, **4b** gave a 86% yield of imine **7a**

Table 1. Amination of 1,3-dimethoxybenzene **1a** with **2**-**4**[a]



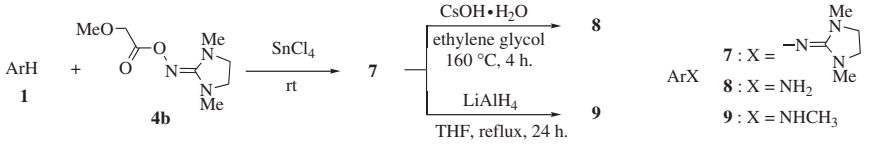
Entry	Oxime	**1a**/equiv.	Time	Yield/%	
1	**2**	10	24 h	**5**	—[b]
2	**3**	10	24 h	**6**[c]	<10
3	**4a**	10	24 h	**7a**[c]	81[d]
4	**4b**	10	1.5 h	**7a**[c]	86
5[e,f]	**4b**	1	7 min	**7a**[c]	87[d]
6[e]	**4b**	1	15 min	**7a**[c]	86
7[e]	**4c**	1	15 min	**7a**[c]	81
8[e]	**4d**	1	15 min	**7a**[c]	5
9[e]	**4e**	1	15 min	**7a**[c]	<8

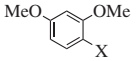
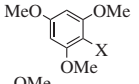
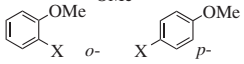
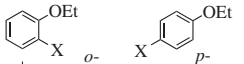
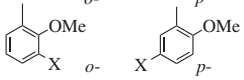
a) **2**-**4** : $SnCl_4$ = 1 : 2.5. b) Imine **5** was directly hydrolysed without isolation (HCl, MeOH, reflux 1.5 h) to give 2,4-dimethoxyaniline in 13%. c) Imines **6** and **7a** were not hydrolysed in acidic conditions. d) Yield was determined by ^1H NMR spectroscopy with anthracene as an internal standard. e) Reaction was carried out in CH_2Cl_2 (0.5 M). f) Reaction was carried out at 0 °C.

(Entry 6), and compound **4c** which can be seen as a conformationally restricted analogue of **4b** afforded a slightly lower yield of **7a** (Entry 7). The *O*-β-methoxypropionyl oxime **4d** led only to 5% of the desired product (Entry 8), together with unreacted dimethoxybenzene, and the *o*-methoxybenzoyl derivative **4e** afforded also a low yield of **7a** (Entry 9). The *O*-tosyloxime **4a** was also included in this study, and while a good yield of imine was obtained with dimethoxybenzene (**1a**) used as a solvent in 24 h (Entry 3), no product formation was detected when it was treated with a stoichiometric amount of **1a** in CH_2Cl_2 for a short time.

Interestingly, only $SnCl_4$ promoted the reaction of **4b** with dimethoxybenzene (**1a**). All our experiments with another Lewis acid or Lewis acids combination resulted in poor yields of imine **7a** or surprisingly, no imine formation at all with most of the conventional Lewis acids such as $TiCl_4$, $EtAlCl_2$, $ZnCl_2$, and $MgBr_2$. The reaction described in this work involves probably a nucleophilic attack of the arene on the nitrogen atom of the oxime.[4] Tin chloride would assist the cleavage of the N-O bond by coordination of Sn^{4+} with the oxygen atom, in analogy

Table 2. Synthesis of anilines and *N*-methylanilines by the reaction of **4b** with aromatic compounds[a]



Entry	ArH (equiv.)	ArX	Yield from ArH/% [ratio *o*- : *p*-] 7[b]	8[c]	9[c]
1	 **1a** (1)		88[d]	53	62
2	 **1b** (1)		96[d]	12	94[e]
3	 **1c** (10)		85 [54:46]	80 [52:48]	75 [54:46]
4	 **1d** (10)		87 [52:48]	86 [51:49]	77 [57:43]
5	 **1e** (10)		61 [23:77]	58 [22:78]	50 [6:94]

a) **4b** : $SnCl_4 = 1 : 2.5$. b) Yield was determined by ^1H NMR spectroscopy with anthracene as an internal standard. c) Isolated yield. d) Reaction was carried out in CH_2Cl_2 (0.5 M). e) $LiAlH_4$ reduction conducted at rt.

with the Beckmann rearrangement. Calculation studies showed that the rate-determining step for the Beckmann rearrangement was the 1,2-proton shift from the *N*-protonated oxime to the *O*-protonated form, which can be strongly assisted by solvent participation.[5] The highest reactivity of **4b** may thus be explained by a similar 1,2 shift of tin cation assisted by the participation of the methoxy group of the methoxyacetyl substituent.

Finally, the transformation of imine **7a** into dimethoxyaniline **8a** was studied. While the hydrolysis of this type of imines did not proceed by acid treatment, a careful investigation showed that the best results are obtained by treatment with $CsOH{\cdot}H_2O$ in ethylene glycol at 160 °C. Alternatively, the reduction of **7a** with $LiAlH_4$ gives access to the *N*-methyldimethoxyaniline.[2e]

The present method was then applied to the amination of various aromatic substrates as listed in Table 2. The most electron-rich arenes **1a** and **1b** reacted rapidly with an equimolar amount of **4b** and afforded excellent yields of the corresponding imines, while less nucleophilic arenes such as **1c**–**1e** had to be used in 10 molar excess and required a longer reaction time. The hydrolysis of **7** into aniline **8** was nearly quantitative for the monoalkoxyarylimines (Entries 3–5) but led only to a 53% overall yield with the dimethoxyarylimine and 12% for the trimethoxyarylimine sustaining oxidation of the corresponding anilines (Entries 1 and 2). Conversely, most imines were efficiently converted to *N*-methylanilines **9** and a 94% overall yield was achieved for the methylamination of trimethoxybenzene **1b**. However, the ortho-isomer of the imine obtained from **1e** could not be reduced completely (Entry 5).

As described above, *O*-acyloxime derivatives such as **4b** can be used as electrophilic aminating reagents of nucleophilic arenes, giving anilines or *N*-methylanilines after subsequent basic hydrolysis or $LiAlH_4$ reduction.

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References and Notes

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3 **4b**–**e** were obtained by conventional esterification of *N*,*N*-dimethyl-2-imidazolidinone oxime with the corresponding acid chlorides in the presence of triethylamine or with tetrahydro-2-furoic acid, DCC and DMAP in the case of **4c**.

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