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# Oxidation of 4-methoxyanilines to 1,4-benzoquinones using ceric ammonium nitrate (CAN)

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ABSTRACT

Treatment of substituted 4-methoxyanilines with ceric ammonium nitrate in a 1:1 mixture of water and acetonitrile resulted in the formation of 1,4-benzoquinones in acceptable yields.

## 1. Introduction

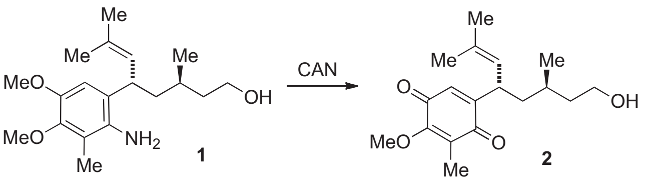
In the course of our work on the synthesis of various antitubercular terpenes[1] and related compounds,[2] we were challenged by the need to oxidize a relatively complex aniline to the corresponding benzoquinone.[3] This Letter summarizes our successful development of ceric ammonium nitriate for that purpose.

The oxidation of aromatic amines to quinones is a potentially convenient way to generate the latter, since anilines are readily available via a number of processes, including the reduction of nitroarenes. While a number of methods have been reported for this oxidation,[4–12] they can be tedious due to long reaction times, complicated work-up procedures, or low yields and often work best when using anilines soluble in water.

Ceric ammonium nitrate (CAN) is a powerful oxidant that has many uses in organic synthesis.[13] This reagent is well known to oxidize electron rich aromatic groups. The removal of *p*-methoxyphenyl and related electron rich aromatic groups from amines has been established.[14] For example, electron rich aromatics can be removed from secondary amines and secondary amides by oxidation with CAN.[15] It is likely that such deprotections proceed via the formation of a quinone, but generally in these processes, the quinone is not the desired organic material. Other electron rich systems are readily oxidized by CAN to quinones,[16] but it appears that the direct oxidation of substituted, unprotected anilines to quinones has not previously been reported.

## 2. Results and discussion

We specifically wanted to accomplish the conversion of **1** into **2** (Eq. 1). To this end, **1** was treated with a variety of oxidants. After several attempts with known procedures[17] that proved ineffective; we turned to ceric ammonium nitrate and found that a good yield of the quinone **2** could be obtained simply by stirring aniline **1** in the presence of the reagent in a 1:1 mixture of water and acetonitrile. Thus, an acetonitrile solution (4 mL) of 1 (0.6 mmol) was added dropwise into a 16 mL solution (acetonitrile/water = 1:1) of ceric ammonium nitrate (4.0 equiv) at room temperature with vigorous stirring. After 20 min, the reaction was quenched. Chromatographic work-up afforded a 73% yield of **2**. Compound **2** was obtained without any epimerization at the stereocenter adjacent to the quinone ring according to $^{1}$H NMR analysis.



(1)

This procedure turned out to be general and was applied to a small selection of other anilines that were available in our laboratories. The results are presented in Table 1. The results suggest that highly substituted anilines are best for this process, presumably as

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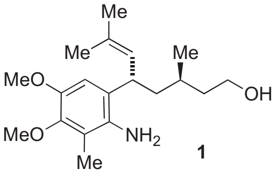
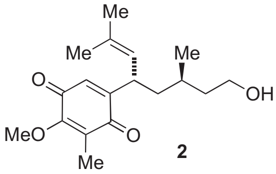
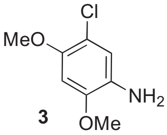
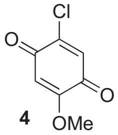
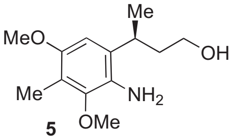
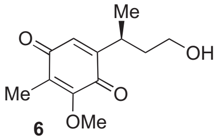
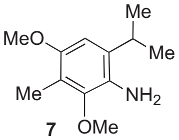
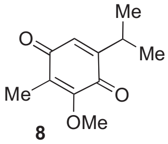
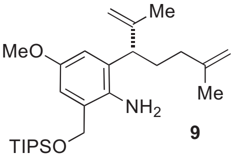
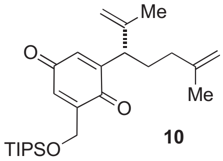
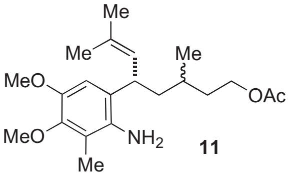
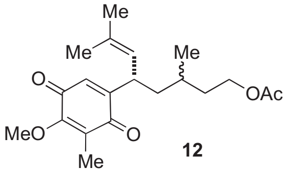
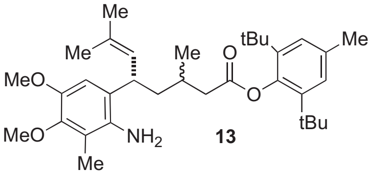
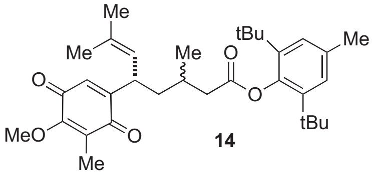
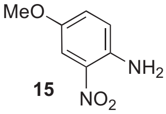
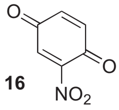
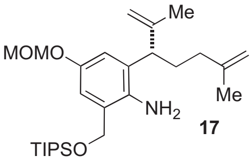
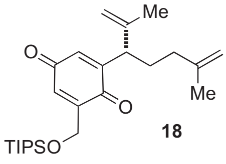
**Table 1**
Conversion of anilines to quinones with CAN

| Entry | Aniline | Quinone | Yield (%) |
|---|---|---|---|
| 1 |  **1** |  **2** | 73 |
| 2 |  **3** |  **4** | 51[b] |
| 3 |  **5** |  **6** | 76[c] |
| 4 |  **7** |  **8** | 75 |
| 5 |  **9** |  **10** | 69 |
| 6 |  **11** |  **12** | 57 |
| 7 |  **13** |  **14** | 42 |
| 8 |  **15** |  **16** | 11[a] |
| 9 |  **17** |  **18** | 0 |

[a] The reaction was conducted at 0.001 M. At 0.03 M, no quinone could be isolated.

[b] See Ref. 18.

[c] See Ref. 19.

that minimizes side reactions that might arise as a result of reactions between the starting materials and the products. Indeed, it should be noted that in general this reaction not only gave quinone but also resulted in the formation of a number of colored by products, none of which have been isolated and characterized.

## 3. Conclusion

We found that treatment of *p*-methoxyanilines with ceric ammonium nitrate afforded the corresponding 1,4-quinones in good yield. The efficacy of CAN as an oxidant suggests its potential applicability to many oxidation problems, some of which we plan to test. Results will be reported in due course.

## Acknowledgment

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## Supplementary data

Supplementary data (experimental procedures, charaterization data; $^1$H and $^{13}$C spectra for new compounds) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.11.070.

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