

0040-4039(95)00281-2

A Mild Oxidation of Aromatic Amines

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Abstract: Several primary aromatic amines have been converted to the corresponding nitro compounds in good yields. The oxidant was oxone[®] (potassium peroxymonosulfate) and the reactions were performed in 5 to 20% aqueous acetone and buffered with sodium bicarbonate.

We have recently reported a mild, selective and high-yielding oxidation of sulfides to sulfones² using oxone[®] in aqueous acetone. Our method² and similar ones using oxone[®] in the presence of a ketone catalyst have already appeared in the literature for the oxidation of sulfides to sulfoxides.³ The ease and utility of our method prompted us to investigate the reaction of aromatic primary amines with oxone[®] in aqueous acetone, and the purpose of this note is to disclose some of our preliminary results.

Murray⁴ has demonstrated the usefulness of dimethyldioxirane in acetone and in the absence of light to oxidize aniline to nitrobenzene, while Zabrowski⁵ has reported the use of oxone[®] in an aqueous acetone / methylene chloride mixture for the oxidation of aromatic amines to nitro compounds in the presence of electron-rich aromatic systems. Zabrowski's method required a phase transfer catalyst and he reported that poor yields were obtained for the oxidation of anilines containing either a carboxylic acid or an alcohol functionality substituted on the aromatic ring. These reports encouraged us to try our method² for the oxidation of 4-aminobenzoic acid and we were pleased to find that we were able to obtain 4-nitrobenzoic acid in 73% isolated yield.

This method appears to be general for anilines containing carboxylic acid and alcohol functionalities and Table 1 illustrates the usefulness of this oxidation procedure. All of the oxidations were performed at 8 °C in 5 - 20% aqueous acetone with 2.6 to 5.2 equivalents⁶ of oxone[®] and buffered with excess sodium bicarbonate. Lower yields were obtained if the reaction was performed at 20 to 25 °C, and the aqueous acetone and the oxone[®] solution must be added simultaneously in order to obtain optimal yields.⁷ It is particularly noteworthy that *in all cases* lower yields were obtained when the reactions were performed without the addition of acetone. This observation strongly suggests the generation of dimethyldioxirane competing with oxone[®] for reaction with the substrate.

Table 1 Oxidation of aromatic amines with Oxone® in aqueous acetone⁷

Amine	Product	Yield (%) ^a
4-Aminobenzoic acid	4-Nitrobenzoic acid	73 [57] ^b
4-Aminophenethyl alcohol	4-Nitrophenylethyl alcohol	73 [61]
4-Aminophenylacetic acid	4-Nitrophenylacetic acid	81 [41]
3-Aminophenylacetic acid	3-Nitrophenylacetic acid	81 [37]
4-(4-Aminophenyl)butyric acid	4-(4-Nitrophenyl)butyric acid	84 [69]
5-Aminosalicylic acid	5-Nitrosalicylic acid	74 [68]

a) All compounds were characterized by ¹H NMR and FT-IR. The reported yields are representative for material which gave satisfactory elemental analysis.

b) Yields [] obtained when the reactions were performed in the absence of acetone.

Acknowledgement. We are indebted to the Analytical and Physical & Structural Chemistry Departments for the analytical data: Ms. E. Reich for combustion analyses and Ms. P. Offen for FT-IR data.

References and Notes

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6. Only the oxidation of 4-aminobenzoic acid required 5.6 equivalents of oxone®, 4-(4-aminophenyl)butyric acid required 3.2 equivalents of oxone® and all others required 2.6 equivalents of oxone®.
7. A vigorously stirred solution of sodium hydroxide (0.321 g) and deionized water (55 mL) was cooled to 2 °C and treated with 3-aminophenylacetic acid (1.026 g) and sodium bicarbonate (5.679 g). The mixture was stirred for 10 minutes followed by the simultaneous addition of an oxone® solution (10.625 g in 60 mL of 4 x 10⁻⁴ M EDTA) and an aqueous acetone solution (25 mL of acetone and 30 mL of deionized water). **Note:** The rate of addition of the oxone® was double that of the acetone while maintaining the internal temperature below 8 °C. The reaction was allowed to slowly warm to 18 °C over four hours and quenched with sodium bisulfite. Ethyl acetate (250 mL) was added and the solution was acidified with 6N (aq) HCl (10 mL). The organic layer was isolated, washed with deionized water (5 X 100 mL) and concentrated via rotary evaporation to afford a solid. The solid was titrated with ethyl acetate (50 mL), filtered and concentrated via rotary evaporation to obtain 1.212 g of a solid. The solid was recrystallized from hot ethyl acetate (5 mL) and hot hexane (10 mL). The crystals were isolated and dried in a vacuum oven (23 inches at 80 °C for 8 hours) to afford 0.989 g (81%) of pure 3-nitrophenylacetic acid: mp 117-119°C; Anal Calcd. for C₈H₇NO₄: C, 53.04; H, 3.90; N, 7.73. Found: C, 53.43; H, 3.93; N, 7.49.

(Received in USA 27 October 1994; revised 31 January 1995; accepted 6 February 1995)