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OXIDATIVE DEAMINATION OF AMINES USING SODIUM NITRITE

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GRAPHICAL ABSTRACT



Abstract A novel synthetic utility of sodium nitrite for oxidative deamination is described. Aromatic and aliphatic amines compounds were successfully converted into the corresponding carbonyl compounds in the presence of sodium nitrite, potassium iodide, and molecular oxygen under reflux conditions. The method is applicable for both primary and secondary amines for moderate to good yields of corresponding carbonyl compounds.

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Keywords Aldehyde; amines; ketone; oxidation; sodium nitrite

INTRODUCTION

The oxidation of amines to generate a significant class of available building blocks and fundamental synthetic intermediates has received much attention from organic chemists. Oxidation of amines can lead to functional groups including imines, amides, nitro, oximes, nitriles, aldehydes, and ketones.^[1–4] The conversion of amines to carbonyl compounds has been reported with various metal oxidizing reagents such as KMnO₄, K₂FeO₄, Pb(OAc)₄, NiO₂, and HgO-I₂.^[5–8] A literature survey also indicates that Pd/C under microwave irradiation and RuO under pressure can be used for this transformation at higher temperatures.^[9] Very recently, ZnCr₂O₇ trihydrate was used for oxidative deamination at room temperature.^[10] There are several two-step processes available for conversion of amines to carbonyl compounds. However, these methods suffer from disadvantages such as the requirement for larger amount of reagents and poor yield of the products.

In our previous study of bromodecarboxylation using NaNO₂ and 48% HBr at room temperature,^[11] we observed that NaNO₂ in combination with other reagents

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Scheme 1. Formation of benzaldehyde using NaNO₂ and KI.

Table 1. Different halogen reagents for conversion of benzylamine to benzaldehyde

No.	Salt	Time (h)	Yield (%)
1	Tetraethylammonium bromide	4	NR
2	Tetrabutylammonium iodide	4	NR
3	KBr	4	5
4	NaBr	4	5
5	NaI	4	20
6	KI	3	90

can be used for the preparation of carbonyl compound from the corresponding amine at different reaction conditions.

Initially we selected benzylamine as a model substrate (Scheme 1). Exposure of sodium nitrite to benzylamine in the presence of potassium iodide in an acetonitrile/ water mixture in the presence of oxygen at reflux temperature resulted in the formation of benzaldehyde. In the absence of oxygen, no reaction was observed.

Further screening for the reaction conditions revealed that 1 equivalent of sodium nitrite and 2 equivalents of KI are required to furnish benzylamine to benzaldehyde in 90% yield. The reaction does not take place in dry organic solvents (CH_2Cl_2 , $CHCl_3$, CH_3CN), but 50% aqueous organic solvents (water–organic solvent, 1:1) gave benzaldehyde without affecting yield and reaction time. The reaction was also carried out at room temperature but a slower reaction rate was observed.

To check the possibility of substitution of KI with other halogen reagents, the reactions were carried out using KBr, NaI, NaBr, tetraethyl ammonium bromide, and tetrabutyl ammonium iodide instead of KI (Table 1).

Table 1 clearly indicates the iodine salts are suitable for this conversion, whereas as compared to KI lower yield was observed in the case of NaI. Almost negligible yields were observed when KI was replaced by bromide salts. No reactions were observed in the cases of tetraethylammonium bromide and tetrabutylammonium iodide.

RESULTS AND DISCUSSION

OXIDATIVE DEAMINATION OF AMINES

Entry	Substrate	Product	Time (h)	Yield ^b (%)
1	NH ₂	СНО	3	90
2	O2N NH2	O ₂ N CHO	3	90
3	H5C200C	H ₅ C ₂ OOC	3	92
4	H ₃ CO	Н3СОСНО	3	90
5	CH ₃ NH ₂	CH ₃ O	8	80
6	CI CH3	CI CH3	8	85
7	H ₃ C	H ₃ C	8	85
8	NH ₂		8	75
9	H ₂ N		8	75
10	H ₃ C NH ₂	Н₃С∕∕СНО	9	65
11	H ₃ C NH ₂	H ₃ C	12	65
12	N H	онс сно	12	70

Table 2. Oxidative deamination of amines in the presence of NaNO₂ and KI^{a}

^{*a*}Reaction conditions: substrate (10 mmol), NaNO₂ (10 mmol), KI (20 mmol) in 20 mL acetonitrilewater (1:1), reflux temperature.

^bIsolated yields after column chromatography and structures were confirmed by comparison of IR and ¹H NMR with authentic materials.

entries 8 and 9). Under these reaction conditions, ester and methoxy groups are stable (Table 2, entries 3 and 4). Both electron-withdrawing and electron-donating substitutes are suitable for this transformation (Table 2, entries 2, 3, 4, 6, and 7).

In conclusion, we have exploited a novel application of $NaNO_2$ in combination with KI for oxidative deaminations of primary and secondary amines for preparation of corresponding carbonyl compounds in moderate to good yields. The described method has simple workup and is used for both substituted primary and secondary aliphatic amines.

Representative Procedure for Oxidative Deamination of Benzylamine (Table 1, Entry 1)

In a mixture of 50% acetonitrile/water (20 mL), benzylamine (1.07 g, 10 mmol) and KI (3.30 g, 20 mmol) were stirred at room temperature. Aqueous solution (5 mL) of NaNO₂ (0.69 gm, 10 mmol) was added dropwise to that stirred solution. The reaction mixture was subjected to reflux. During the reaction, oxygen was bubbled in the reaction mixture. After completion of the reaction [as monitored by thin-layer chromatography (TLC)], ethyl acetate (20 mL) was added to the reaction mixture and stirring was continued for 2 min. The organic layer was separated; washed with dilute HCl (2 × 20 mL), 10% aqueous NaHCO₃ (2 × 20 mL) solution, followed by water (3 × 20 mL); dried over Na₂SO₄; and concentrated in vacuum. The remaining residue was purified by column chromatography on silica gel (hexane / ethyl acetate = 9/1) to yield benzaldehyde (0.954 g, 90%) as a colorless oil.

Benzaldehyde (Table 2, Entry 1)

Bp: 178 °C; IR (neat): 1694 cm⁻¹; ¹H NMR (CHCl₃, 60 MHz): δ 7.50–7.60 (3H, m), 7.85–7.90 (2H, m), 10.03 (1H, s). Mp, IR, and NMR values match with literature values.^[12a]

4-Nitrobenzaldehyde (Table 2, Entry 2)

Pale yellow solid; mp: 104 °C; IR (KBr): 1676 cm⁻¹; ¹H NMR (CHCl₃, 60 MHz): δ 8.0 (2H, d, J = 8.3 Hz), 8.50 (2H, d, J = 8.6 Hz), 10.10 (1H, s). Mp, IR, and NMR values match with literature values.^[12a]

4-Methoxylbenzaldehyde (Table 2, Entry 4)

Colorless liquid; bp: 247 °C; IR (neat): 1682 cm^{-1} ; ¹H NMR (CHCl₃, 60 MHz): δ 3.90 (3H, s), 7.0 (2H, d, J = 8.6 Hz), 7.80 (2H, d, J = 8.4 Hz), 9.80 (1H, s). Mp, IR, and NMR values match with literature values.^[12a]

Acetophenone (Table 2, Entry 5)

Colorless liquid; bp: 201 °C; IR (film): 1682 cm⁻¹; ¹H NMR (CDCl₃, 60 MHz) δ 7.7–7.9 (m, 2H), 7.0–7.5 (m, 3H), 2.5 (s, 3H). Bp, IR, and NMR values match with literature values.^[12b]

Cyclohexanone (Table 2, Entry 8)

Colorless liquid; bp: 155 °C; IR (neat): 1717 cm⁻¹; ¹H NMR (CDCl₃, 60 MHz) δ 2.2–2.4 (m, 4H), 1.7–1.9 (m, 6H). Bp, IR, and NMR values match with literature values.^[12b]

Pentanal (Table 2, Entry 10)

Colorless liquid; bp: $102 \,^{\circ}$ C; IR (neat): $1725 \,\text{cm}^{-1}$; ¹H NMR (CDCl₃, 60 MHz) δ 9.4 (s, 1H), 2.2 (m, 2H), 1.5 (m, 4H), 0.8 (m, 3H). Bp, IR, and NMR values are matches with literature values.^[12c]

Hexan-2-one (Table 2, Entry 11)

Yellow liquid; bp: $127 \,^{\circ}$ C; ¹H NMR (CDCl₃, 60 MHz) δ 1.5 (m, 4H), 2.4 (m, 5H), 0.9 (m, 3H). Bp and NMR values match with literature values.^[12d]

Glutaraldehyde (Table 2, Entry 12)

Colorless liquid; bp: 188 °C; IR (neat): 1715 cm⁻¹; ¹H NMR (CDCl₃, 60 MHz) δ 9.5 (t, 2H), 2.6 (m, 4H), 1.2 (m, 2H). Bp, IR, and NMR values match with literature values.^[12e]

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