A Novel Synthetic Method for the Preparation of Aliphatic Aldehydes from the Corresponding Carboxylic Acids

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A novel synthetic method for the preparation of aliphatic aldehydes from the corresponding carboxylic acids via 1,3-dimethylbenzimidazolium salts is provided. 1,3-Dimethylbenzimidazolium salts were rapidly reduced with sodium/ethanol and then hydrolyzed with hydrochloric acid to obtain aliphatic aldehydes, in which the 1,3-dimethylbenzimidazolium salts can be readily achieved from the corresponding carboxylic acids. The mechanism for the reductive reaction of 1,3-dimethylbenzimidazolium salts with sodium/ethanol was discussed.

Keywords aliphatic aldehydes, 1,3-dimethylbenzimidazolium salts, reduction, sodium, synthetic method

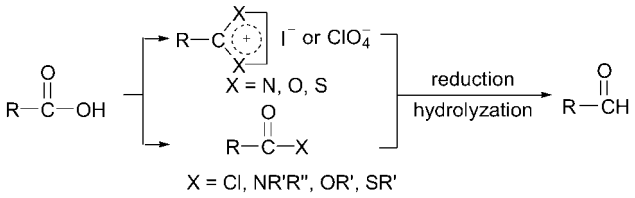
Introduction

Aldehydes are an important class of compounds in view of their distinct structural feature and wide utility in organic synthesis.[1] Many of the straight-chain "fatty" aldehydes have been recognized as odor-imparting components in natural compounds.[2] A common approach to obtain aldehydes is in fact the oxidation of primary alcohols or the reduction of carboxylic acids and their derivatives. However, aldehydes are very sensitive toward further oxidation to the corresponding carboxylic acids or reduction to the corresponding alcohols. Therefore, a large number of aldehydes are not available by direct oxidation or reduction. The development of general, facile and convenient methods for transformation of alcohols or carboxylic acids and their derivatives into the corresponding aldehydes is one of the most desirable subjects in organic synthesis.[3]

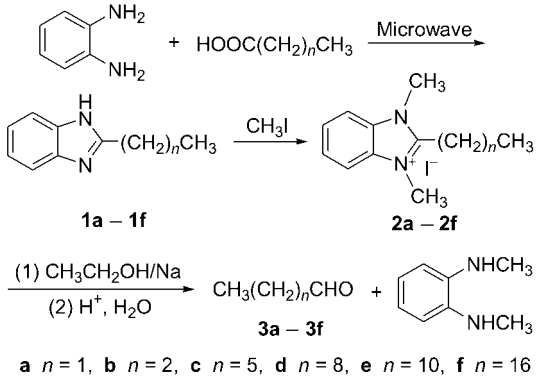
General synthetic method (Scheme 1) of aliphatic aldehydes from the corresponding carboxylic acids in literature involves the step of transformation of the carboxylic acids into the corresponding carboxylic acid derivatives which subsequently are reduced.[4]

In this paper, we first converted carboxylic acids to the corresponding aldehydes via the quaternary 1,3-dimethylbenzimidazolium salts which were rapidly reduced with sodium/ethanol and then hydrolyzed with hydrochloric acid to obtain aliphatic aldehydes. The mechanism for the reductive reaction of 1,3-dimethylbenzimidazolium salts with sodium/ethanol was discussed. A novel synthetic method for the preparation of straight-chain “fatty” aldehydes is provided. The route of the new synthetic method is shown in Scheme 2.

Scheme 1 General synthetic method of aliphatic aldehydes from the corresponding carboxylic acids in literature



Scheme 2 The route of the novel synthetic method for preparation of aliphatic aldehydes



In our experiments, 2-substituted benzimidazoles (**1a—1f**) were effectively synthesized in few minutes from the corresponding carboxylic acids and *o*-phenylenediamine under microwave irradiation.[5]

1,3-Dimethylbenzimidazolium salts (**2a—2f**) can be

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prepared via quaternization of the benzimidazoles (**1a—1f**) with iodomethane in benzene.[6] The quaternary benzimidazolium salts (**2a—2f**) were rapidly reduced with sodium/ethanol and then hydrolyzed with hydrochloric acid to obtain aliphatic aldehydes (**3a—3f**), which were directly converted into the corresponding 2,4-dinitrophenylhydrazones due to instability of aldehyde. Thus a novel synthetic method for aliphatic aldehydes from the corresponding carboxylic acids was accomplished.

Experimental

Apparatus and materials

Melting points were taken on an XT-4 micro-melting apparatus (Beijing) and uncorrected. TLC analysis was carried out on glass plates coated with silica gel-G, and spots were visualized using an ultraviolet (UV) lamp. Infrared (IR) spectra were recorded on a Bruck EQUIOX-55 spectrometer (Germany). ^{1}Proton magnetic resonance (^{1}H NMR) spectra were recorded at 400 MHz on a Varian INOVA-400 spectrometer (USA), and chemical shifts were reported relative to internal Me_4Si. All reagants of analytical grade were obtained from a commercial source and used without further purification.

General procedure for the preparation of benzimidazolium salts (2a—2f)

The 2-substituted benzimidazoles (**1a—1f**) were prepared from *o*-phenylenediamine and the corresponding carboxylic acids under microwave irradiation according to the literature.[5] A solution of sodium (0.01 mol) in ethanol was treated with benzimidazoles (0.01 mol) (**1a—1f**), iodomethane (0.03 mol) and benzene (12 mL), then the mixture was refluxed for 18 h. The solvent was removed and the residue was recrystallized from water (**2a—2d**) or water-ethanol (*V*/*V*, 1∶1) (**2e**, **2f**) to give benzimidazolium salts (**2a—2f**).

Compound 2a White solid, yield 95%, m.p. 252 ℃ (Lit.[6] 252 ℃); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.43 (t, J=8.0 Hz, 3H, CH_3), 3.63 (q, J=7.7 Hz, 2H, N=CCH_2), 4.14 (s, 6H, 2×NCH_3), 7.26—7.70 (m, 4H, 4×Ar-H); IR (KBr) ν_{max}: 3020, 2962, 2935, 2850, 1608 ($\nu_{C=N}$), 1531, 1479, 768 cm^{-1}; MS *m*/*z*: 175 (M^+−I).

Compound 2b White solid, yield 91%, m.p. 230—232 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.14 (t, J=7.4 Hz, 3H, CH_3), 1.80—1.89 (m, 2H, CH_2), 3.57 (t, J=8.0 Hz, 2H, N=CCH_2), 4.14 (s, 6H, 2×NCH_3), 7.61—7.72 (m, 4H, 4×Ar-H); IR (KBr) ν_{max}: 3010, 2960, 2925, 2866, 1612 ($\nu_{C=N}$), 1530, 1473, 760 cm^{-1}; MS *m*/*z*: 189 (M^+−I).

Compound 2c White solid, yield 90%, m.p. 186—188 ℃ (Lit.[6] 182—184 ℃); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.90 (t, J=7.0 Hz, 3H, CH_3), 1.30—1.78 (m, 8H, 4×CH_2), 3.54 (t, J=8.0 Hz, 2H, N=CCH_2), 4.12 (s, 6H, 2×NCH_3), 7.60—7.74 (m, 4H, 4×Ar-H); IR (KBr) ν_{max}: 3013, 2953, 2925, 2854, 1614 ($\nu_{C=N}$), 1532, 1475, 1251, 766 cm^{-1}; MS *m*/*z*: 231 (M^+−I).

Compound 2d White solid, yield 90%, m.p. 172—174 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.88 (t, J=6.8 Hz, 3H, CH_3), 1.27—1.74 (m, 14H, 7×CH_2), 3.57 (t, J=8.2 Hz, 2H, N=CCH_2), 4.12 (s, 6H, 2×NCH_3), 7.61—7.70 (m, 4H, 4×Ar-H); IR (KBr) ν_{max}: 3015, 2956, 2925, 2854, 1616 ($\nu_{C=N}$), 1533, 1478, 1258, 767 cm^{-1}; MS *m*/*z*: 273 (M^+−I).

Compound 2e White solid, yield 88%, m.p. 167—168 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.88 (t, J=6.8 Hz, 3H, CH_3), 1.25—1.74 (m, 18H, 9×CH_2), 3.55 (t, J=8.0 Hz, 2H, N=CCH_2), 4.12 (s, 6H, 2×NCH_3), 7.61—7.72 (m, 4H, 4×Ar-H); IR (KBr) ν_{max}: 3015, 2953, 2924, 2852, 1615 ($\nu_{C=N}$), 1534, 1479, 1262, 767 cm^{-1}; MS *m*/*z*: 301 (M^+−I).

Compound 2f White solid, yield 83%, m.p. 173—174 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.88 (t, J=6.6 Hz, 3H, CH_3), 1.25—1.77 (m, 30H, 15×CH_2), 3.53 (t, J=8.0 Hz, 2H, N=CCH_2), 4.12 (s, 6H, 2×NCH_3), 7.60—7.75 (m, 4H, 4×Ar-H); IR (KBr) ν_{max}: 3014, 2922, 2850, 1614 ($\nu_{C=N}$), 1532, 1468, 1356, 1263, 765 cm^{-1}; MS *m*/*z*: 385 (M^+−I).

General procedure for the preparation of aliphatic aldehydes (3a—3f)

A solution of benzimidazolium salts (2 mmol) (**2a—2f**) in ethanol (50 mL) was stirred in three-necked flask under a nitrogen atmosphere. Small particles of sodium (10 mmol) were added to the solution in batches at room temperature under stirring. After 45 min, The reaction mixture was quenched by 10 mL water and then acidify by hydrochloric acid to pH=4—5. The resulting mixture was stirred at 60 ℃ for 1 h, then 2,4-dinitrophenylhydrazine reagent was added. Yellow precipitate was appeared, filtered off and recrystallized from 95% ethanol to give compounds **3a—3f** 2,4-dinitrophenylhydrazone.

Propionaldehyde (3a) 2,4-dinitrophenylhydrazone Yellow solid, yield 51.4%, m.p. 153—154 ℃ (Lit.[7] 154—155 ℃); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.22 (t, J=7.4 Hz, 3H, CH_3), 2.44—2.51 (m, 2H, N=CCH_2), 7.58 (t, J=4.8 Hz, 1H, N=CH), 7.93—9.13 (m, 3H, 3×Ar-H), 11.03 (s, 1H, NH); IR (KBr) ν_{max}: 3423, 3292, 3109, 2984, 2924, 1616 ($\nu_{C=N}$), 1585, 1510, 1453, 1413, 1329, 1258, 850, 743, 716 cm^{-1}; MS *m*/*z*: 238 (M^+).

Butyraldehyde (3b) 2,4-dinitrophenylhydrazone Yellow solid, yield 58.7%, m.p. 121—122 ℃ (Lit.[8] 122—123 ℃); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.03 (t, J=7.4 Hz, 3H, CH_3), 1.62—1.71 (m, 2H, CH_2), 2.40—2.44 (m, 2H, N=CCH_2), 7.54 (t, J=5.2 Hz, 1H, N=CH), 7.92—9.13 (m, 3H, 3×Ar-H), 11.03 (s, 1H, NH); IR (KBr) ν_{max}: 3449, 3296, 3088, 2954, 2928, 2869, 1620 ($\nu_{C=N}$), 1590, 1518, 1422, 1331, 1218, 827, 763, 742 cm^{-1}; MS *m*/*z*: 252 (M^+).

Heptaldehyde (3c) 2,4-dinitrophenylhydrazone Yellow solid, yield 68.5%, m.p. 107—108 ℃ (Lit.[9] 107—108 ℃); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.91 (t, J=6.4 Hz, 3H, CH_3), 1.33—1.42 (m, 6H, 3×CH_2),

1.58—1.65 (m, 2H, CH_2), 2.41—2.46 (m, 2H, N=CCH_2), 7.54 (t, J=5.2 Hz, 1H, N=CH), 7.92—9.13 (m, 3H, 3×Ar-H), 11.03 (s, 1H, NH); IR (KBr) ν_{max}: 3448, 3295, 3089, 2926, 2851, 1621 ($\nu_{C=N}$), 1592, 1518, 1424, 1331, 1220, 829, 743, 723 cm^{-1}; MS *m*/*z*: 294 (M^+).

Capraldehyde (3d) 2,4-dinitrophenylhydrazone Yellow solid, yield 75.3%, m.p. 106—107 ℃ (Lit.[10] 104 ℃); ^1H NMR ($CDCl_3$, 400 MHz) δ: 0.88 (t, J=6.8 Hz, 3H, CH_3), 1.28—1.39 (m, 12H, 6×CH_2), 1.58—1.65 (m, 2H, CH_2), 2.40—2.46 (m, 2H, N=CCH_2), 7.54 (t, J=5.0 Hz, 1H, N=CH), 7.92—9.13 (m, 3H, 3×Ar-H), 11.02 (s, 1H, NH); IR (KBr) ν_{max}: 3446, 3295, 3088, 2913, 2847, 1622 ($\nu_{C=N}$), 1593, 1518, 1425, 1332, 1221, 829, 743, 722 cm^{-1}; MS *m*/*z*: 336 (M^+).

Lauraldehyde (3e) 2,4-dinitrophenylhydrazone Yellow solid, yield 78.0%, m.p. 105—106 ℃ (Lit.[11] 105—106 ℃); ^1H NMR ($CDCl_3$, 400 MHz) δ: 0.88 (t, J=6.6 Hz, 3H, CH_3), 1.27—1.41 (m, 16H, 8×CH_2), 1.58—1.65 (m, 2H, CH_2), 2.41—2.46 (m, 2H, N=CCH_2), 7.54 (t, J=5.4 Hz, 1H, N=CH), 7.92—9.13 (m, 3H, 3×Ar-H), 11.03 (s, 1H, NH); IR (KBr) ν_{max}: 3295, 3090, 2914, 2847, 1621 ($\nu_{C=N}$), 1593, 1518, 1466, 1425, 1331, 1221, 829, 763, 743 cm^{-1}; MS *m*/*z*: 364 (M^+).

Stearaldehyde (3f) 2,4-dinitrophenylhydrazone Yellow solid, yield 65.6%, m.p. 98—99 ℃; ^1H NMR ($CDCl_3$, 400 MHz) δ: 0.88 (t, J=6.6 Hz, 3H, CH_3), 1.26—1.41 (m, 28H, 14×CH_2), 1.58—1.65 (m, 2H, CH_2), 2.41—2.46 (m, 2H, N=CCH_2), 7.54 (t, J=5.4 Hz, 1H, N=CH), 7.92—9.13 (m, 3H, 3×Ar-H), 11.02 (s, 1H, NH); IR (KBr) ν_{max}: 3295, 3090, 2916, 2848, 1620 ($\nu_{C=N}$), 1592, 1518, 1467, 1425, 1330, 1220, 828, 764, 743 cm^{-1}; MS *m*/*z*: 448 (M^+).

Results and discussion

The mechanism for the reductive reaction of benzimidazolium salt

Two mechanisms universally accepted for the reduction of ketones with sodium/ethanol were suggested.[12] One is thermodynamic control mechanism involving carbanion intermediate. The other one is kinetic control mechanism involving free radical intermediate.

The mechanism for the reductive reaction of benzimidazolium salt with sodium/ethanol has not been reported in literature. However, the reaction can be reasonably explained by the above two mechanisms because the properties of the polarized C=N bond of benzimidazolium salt which belongs to good electron acceptor[13] are similar to those of the C=O bond of ketone.

In order to investigate which one in the above two mechanisms is operative, the effect of the reduction temperature on the yield of compound **3d** was studied. As shown in Table 1, the temperature of the reductive reaction has little effect on the yield of compound **3d**. Thus we can assume that the kinetic control should be dominant.

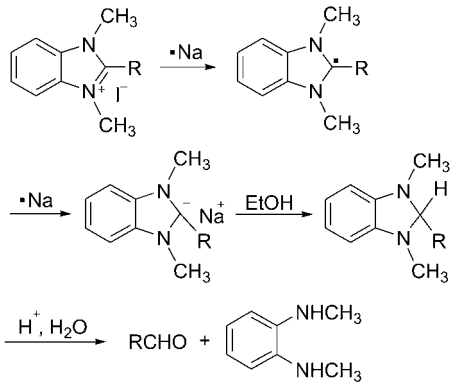
The mechanism for the reductive reaction of benzimidazolium salt described in this paper can be reasonably explained by Scheme 3.

Table 1 Yields of the compound **3d** at different reductive reaction temperatures

Entry	Temperature/℃	Yield[a]/%
1	5—10	73.8
2	20—25	74.5
3	40—45	75.3
4	70—75	75.6

[a] Yield of isolated 2,4-dinitrophenylhydrazone (**3d**); reaction time is 45 min.

Scheme 3 Possible reaction mechanism of reduction of 1,3-dimethylbenzimidazolium salt with sodium/ethanol



The polarized C=N bond of benzimidazolium salt was first added two electron from two free radicals of sodium to give a carbanion, followed by protonation with ethanol to give benzimidazolidine, which can be hydrolyzed in acidic solution to give the corresponding aldehyde.

Conclusion

In conclusion, a novel synthetic method for aliphatic aldehydes from the corresponding carboxylic acids was provided. A reasonable mechanism for the reductive reaction of 1,3-dimethylbenzimidazolium salts with sodium/ethanol was proposed. The present results will help to facilitate the synthesis of various aldehydes.

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