

Application of Multicomponent Reactions in Synthesis of Diimines as Salen Homologues

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One of the most powerful chiral ligands utilized in asymmetric processes is the Salen-type ligand.¹⁾ The abbreviation Salen (**B**) was initially introduced to indicate diimines derived from the condensation of salicylaldehydes and 1,2-ethylenediamine; however, at present all the structurally correlated chiral and achiral Schiff bases of such a class of compounds are generally indicated Salen (Fig. 1).²⁾ Dihydroxydiimines (**A**) can be represented as salen type (**A'**). They have been used as ligands for metal complexes³⁾ as well as precursor for imidazolidenes (**C**).⁴⁾ Synthetic methods for the preparation of diimines, which have the same substituents such as **1** and **2** (Fig. 2), have been widely reported.⁵⁻⁸⁾ However, only a few synthetic methods have been revealed for the formation of diimines, which have different substituents (**3**, **4**, **5** in Fig. 2).⁹⁻¹⁰⁾ In this report facile synthetic methods to prepare different substituted diimines are introduced.

Multicomponents reactions (MAR) have been used to develop efficient synthesis of complicated natural products or pharmaceutically important substances.¹¹⁻¹³⁾ In a typical MCR, starting compounds and intermediates and elementary reactions are in a mobile equilibrium. However, partial irreversible reaction or irreversible last step reaction drives the whole reaction to one isolable product, which makes MCR useful in organic synthesis. For the formation of different substituted diimines, multicomponents reaction was applied. Three components of the starting materials, salicylaldehyde **6**, substituted aromatic aldehyde **7** and ammonium acetate are mixed together in THF at room temperature, forming crystalline yellow solid as the main product a 71-88% yield (Fig. 3). Nitrogen reacts with salicylaldehyde to give intermediate imine **9** which maintains intramolecular hydrogen

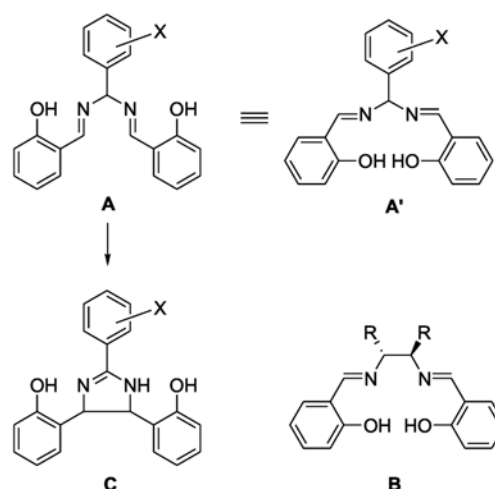


Fig. 1. Chemical structure of Salen **B** and dihydroxydiimide **A** as Salen homologue **A'**.

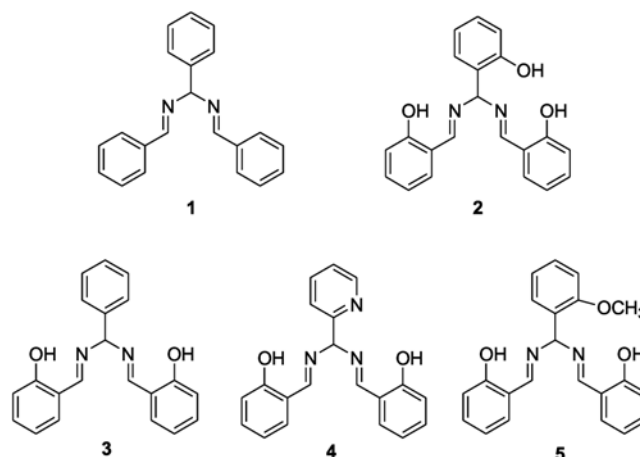


Fig. 2. Structures of diimides with same substituents (**1**, **2**) and diimides with different substituents (**3**, **4**, **5**).

bond. Resonance-stabilized intramolecular hydrogen bond¹⁴⁻¹⁵⁾ is sustained when tetrahedral intermediate **10** is made by the reaction between imine **9** and aromatic aldehyde **7**. Another imine **9** is added to the intermediate **10** to form a stable dihydroxydiimine **A**, which has two resonance-stabilized intramolecular hydrogen bonds. Another possible dihydroxydiimide **D** has only one resonance-stabilized intramolecular hydrogen bond and, therefore, cannot be formed, because it is less stable than dihydroxydiimide **A**. Driving force of the multicomponents reaction is the formation of two resonance-stabilized intramolecular hydrogen bonds¹⁴⁻¹⁵⁾ in a dihydroxydiimide molecule **A**. Two dihydroxydiimides **A** and **D** can be differentiated by comparison of their 1H-NMR spectra. Resonance-stabilized intramolecular hydrogen bond makes its OH proton extremely downfielded around 13 ppm. Diimide **A**, which has two resonance-stabilized intramolecular hydrogen bonds, displays double integration value around 13 ppm as compared to the

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Abbreviations: MCR, Multicomponent Reactions; NMR, nuclear magnetic resonance.

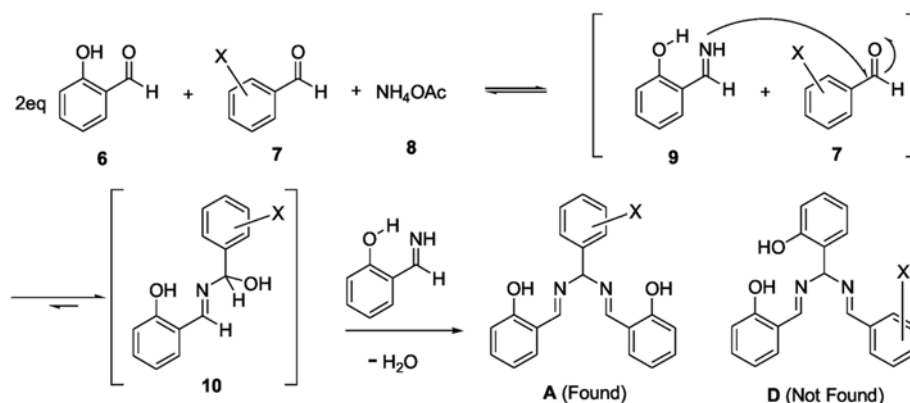


Fig. 3. Multicomponent reaction toward formation of differently substituted diimides.

methine proton adjacent to two nitrogens around 9 ppm. Diimide **D** which has one resonance-stabilized intramolecular hydrogen bond shows the same integration value around 13 ppm as that of methine proton around 9 ppm. Three isolated final products (**3-5**) reveal double integration value of hydrogen bond proton, compared to that of the methane proton.

Typical procedures for synthesis of dihydroxy diimides 3-5. Salicylaldehyde **6** (12.2 g, 10.0 mmol, 2eq.), benzaldehyde (5.3 g, 5 mmol, 1eq.), and ammonium acetate (6.7 g, 11 mmol, 2.1eq.) were mixed together in 150 ml tetrahydrofuran and the reaction mixture was warmed to 50°C and cooled to room temperature, affording a yellow crystal, which was stirred overnight at room temperature. Solid was filtered and washed with methanol and dried.

Compound 3. yield 88.3%, mp 123-124°C, ¹H-NMR (400 MHz, DMSO_{d6}); δ 6.13 (s, 1H, CHNN), 6.87-6.96 (m, 4H), 7.33-7.38 (m, 3H), 7.40-7.45 (m, 2H), 7.49-7.52 (m, 2H), 7.56 (dd, 2H), 8.87 (s, 2H, C = NH), 12.96 (s, 2H, OH), ¹³C-NMR (100 MHz); δ. 89.47, 116.48 (double intensity), 118.65 (double intensity), 118.99 (double intensity), 126.71 (double intensity), 128.27, 128.85 (double intensity), 132.12 (double intensity), 133.08 (double intensity), 141.09, 160.13 (double intensity), 165.41(double intensity).

Compound 4. yield 71.2%, mp 132-143°C, ¹H-NMR (400 MHz, DMSO_{d6}); δ 6.18 (s, 1H, CHNN), 6.90-6.96 (m, 5H), 7.36-7.41 (m, 3H), 7.58-7.61 (m, 3H), 8.59 (d, 1H), 8.90 (s, 2H, C = NH), 12.90 (s, 2H, OH), ¹³C-NMR (100 MHz); δ. 90.44, 116.12 (double intensity), 118.73 (double intensity), 119.02 (double intensity), 121.30, 123.55, 132.14 (double intensity), 133.15 (double intensity), 137.54 (double intensity), 149.41 158.78, 160.15, 166.12 (double intensity).

Compound 5. yield 82.5%, mp 141-142°C, ¹H-NMR (400 MHz, DMSO_{d6}); δ 3.83 (s, 3H, CH₃), 6.36 (s, 1H, CHNN), 6.89-6.92 (m, 4H), 7.00-7.07 (m, 2H), 7.32-7.43 (m, 4H), 7.52-7.55 (m, 2H), 8.78 (s, 2H, C = NH), 13.12 (s, 2H, OH), ¹³C-NMR (100 MHz); δ. 56.34, 84.46, 112.32, 117.21 (double intensity), 119.37 (double intensity), 119.63 (double intensity), 121.47, 128.01, 128.99, 130.37, 132.89 (double intensity), 133.69, 157.07 (double intensity), 161.00 (double intensity), 166.13(double intensity).

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