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Arylglyoxals as precursors for synthesis of N-hydroxyhydantoins, N-alkoxyhydantoins and thiohydantoins in mild conditions

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It is known that hydantoins are used as drugs and precursors for drugs synthesis. But the easy method for synthesis of N-hydroxyhydantoins and N-alkoxyhydantoins was not known before. We have proposed that interaction of arylglyoxals with N-hydroxyurea or with N-alkoxyureas may be a simple route to 3-hydroxy-5-arylhydantoins and to 3-alkoxy-5-arylhydantoins respectively. As we found, arylglyoxals reacted with N-hydroxyurea in an aqueous solution at room temperature according to exact scheme. At the first stage the substituted urea formed. At the second stage urea cyclizes into 3,4,5-trihydroxyimidazolidine-2-ones. Compounds were protonized by N-hydroxyurea with further elimination of the water molecule from C-5 atom. Then 1,2-shift of hydrogen atom from atom C(4) to atom C(5) occurs, yielding 3-hydroxyl-5-arylhydantoin. This interaction may be stopped on different stages. It depends not only on nature of arylglyoxal, but also on the reaction conditions. In these conditions the products of stages I, II, III may be isolated depending of the arylglyoxal structure and temperature. Thus, the reaction of arylglyoxals with N-hydroxyurea in acetic acid at room temperature selectively yields only 3-hydroxy-5-arylimidazolidine-2,4-diones. The reaction of arylglyoxals with N-alkoxyureas in acetic acid at room temperature also selectively yields 3-alkoxy-5-arylimidazolidine-2,4-diones. Also in acetic acid arylglyoxals react with thiourea selectively yielding 5-arylimidazolidine-4-one-2-thiones at room temperature.

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