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Abstract

Synthesis and biological evaluation of new naphthoquinones derivatives by catalytic oxidation

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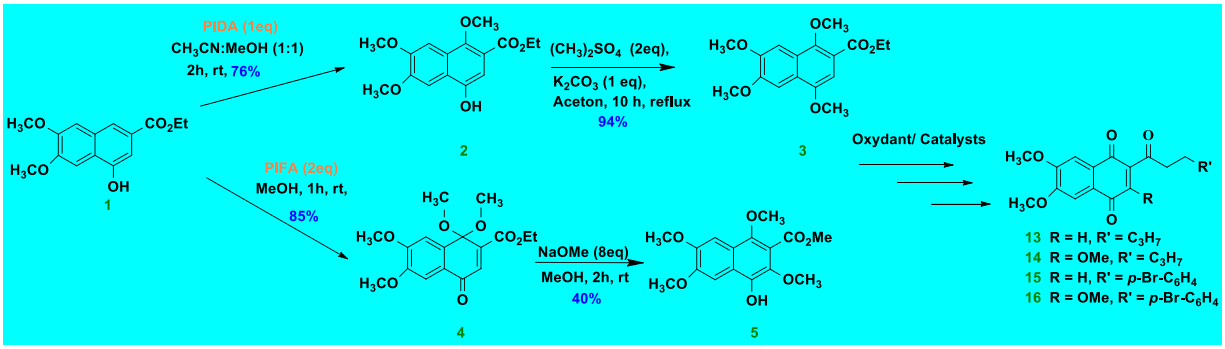
The catalytic utilization of hypervalent iodine reagents, largely in consideration of economical and environmental viewpoints, is a most attractive strategy due to their unique features as extremely useful oxidants, with mild, safe, and environmentally friendly characteristics. Oxidation reactions constitute of a number of important transformations in organic synthesis. They are widely in the productions of a variety of fine chemicals including pharmaceuticals, natural products, and their intermediates.[1] As oxidants, hypervalent iodine reagents have recently received much attention due to their low toxicity, mild reactivity, ready availability, high stability, easy handling, etc.[2–6] For examples, phenyliodine(III) diacetate (PIDA) and phenyliodine(III) bis (trifluoroacetate) (PIFA)-induced oxidations of phenols and related reactions have been applied to many total syntheses of biologically important natural products and their pivotal intermediates.[7–9] This study reports a new synthetic methodology that was optimized to prepare new naphthoquinones derivatives 13-16 via catalytic oxidation. The latter were prepared in 5-6 steps from naphtol **1** in overall yields (11-34%). The synthetic pathway of these new analogs is depicted in Scheme. Hypervalent iodine is the most common method to oxidize methoxy phenols or methoxy naphthols in naphtoquinones. On the one hand, treatment of **1** with phenyliodonium diacetate) (PIDA) in a mixture of acetonitrile/methanol (1/1) led efficiently to naphthol **2** (76% yield) which after methylation furnished compound **3** in excellent yield (94%). On the other hand, the oxidation of phenol into quinone monoacetal was frequently observed in the alcoholic solvent. Hence, compound **1** was treated with phenyliodonium bis(trifluoroacetate) (PIFA) in methanol (2 eq.) to give quinone monoacetal **4** in 85% yield. Nucleophilic substitution of sodium methylate furnished naphthol **5** (40% yield). The conversion of naphthols to the corresponding naphthoquinones **13-16** were reacted with either cerium (IV) ammonium nitrate (CAN) or phenyliodonium diacetate (PIDA), the results were disappointing. Therefore, the experimental conditions were optimized by varying the time of reaction and solvent ratio.



Scheme1. The synthetic pathway of naphthoquinones derivatives via catalytic oxidation.

Keywords: Naphthoquinones; naphthols; phenyliodine(III) diacetate (PIDA), phenyliodine(III) bis(trifluoroacetate) (PIFA), catalytic oxydation; cerium (IV) ammonium nitrate (CAN)

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