

NaIO₄/Br⁻ AS A MILD SYSTEM FOR THE OXIDATION OF 1-METHYL-ANTHRA-9,10-QUINONES

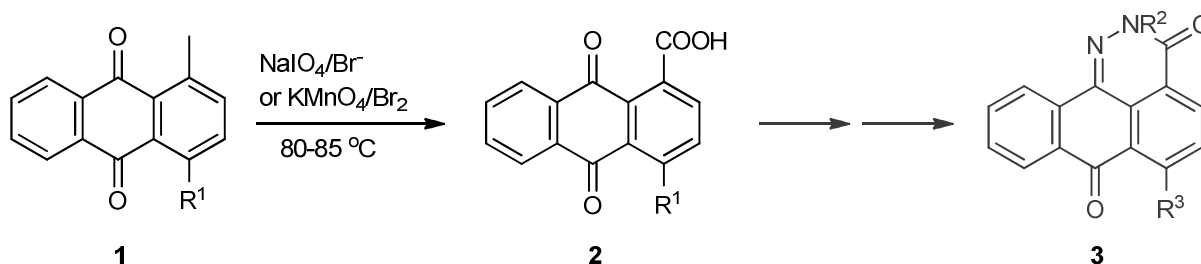
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One of the anthraquinone classes comprises compounds with a carbonyl group. These natural or synthetic anthraquinones find their application as building blocks in the synthesis of the compounds with a biological activity.

Recently, 4-substituted anthra-9,10-quinone-1-carboxylic acids (**2**) have been used as key intermediates in the synthesis of patented compounds (**3**) with anticancer activity against multidrug resistant cell lines [1, 2]. Although 2,7-dihydro-3*H*-dibenz[de,h]cinnolin-3,7-diones (**3**) were successfully synthesized in a small laboratory scale, several problems were observed during the preparation of their acid intermediates (**2**) in a multi-gram scale.



The known methods for the preparation of **2** are based on the oxidation of the methyl group in anthra-9,10-quinones (**1**). The most common are: the oxidation with the diluted nitric acid under high pressure in a sealed tube at the temperature of 195-220 °C [3, 4], the oxidation in nitrobenzene by passing chlorine gas through the reaction mixture at the temperature of 160-170 °C [5] or in a presence of the fuming sulphuric acid [6, 7]. The mentioned methods require aggressive reagents and specific reaction conditions including high pressure and temperature. Thus, there was a need to find a new efficient, cost-effective and reproducible synthetic method of preparation of **2**. While searching literature it was found that the direct oxidation of alkylarenes mediated by the sodium periodate/lithium bromide combination produces benzyl acetates throughout benzyl bromides in the acetic acid, or benzylic acids in the diluted inorganic acid [8, 9]. Based on these results we examined a variety of reaction conditions with or without the bromine source and the oxidizing anion. As a result, a novel procedure for the preparation of highly pure 4-substituted anthra-9,10-quinone-1-carboxylic acids (HPLC > 99.5%) using oxidizing anion/ brominating reagent system was developed. It enabled **2** isolation by the simple filtration of the reaction mixture and was applied in the scale-up of 2,7-dihydro-3*H*-dibenz[de,h]cinnolin-3,7-dione derivatives.

Acknowledgments

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