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MICROWAVE-INDUCED BISMUTH TRIIODIDE-CATALYZED FACILE SYNTHESIS OF OCTAHYDROXANTHENES

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Abstract:
Microwave-induced reaction of 1,3-cyclohexanedione with numerous aldehydes using bismuth iodide is performed successfully toward the synthesis of important octahydroxanthenes. A most probable mechanism is suggested to explain the formation of products.

Key Words:
Microwave, Bismuth Iodide, Mechanism, Octahydroxanthenes

Introduction:

Benzoxanthenes are privileged chemotypes' present in numerous medicinally active substrates. Xanthenedione system is found in many natural compounds and dyes. Due to their importance, a several synthetic methods have been developed for'the preparation of xanthenes and their functionalized analogues. For examples, xanthenes were synthesized by condensation of activated methylene compounds with aldehydes in the presence of mineral acids [1], ring-closure reaction of polycyclic aromatic triflate ester derivatives [2], reaction of Grignard reagent with triethylorthoformate [3], selective *O*-alkylation reaction of monopodal xanthenes [4], reaction with nano-WO_3-supported sulfonic acid [5], reaction with Amberlite IR-120H [6], and reaction with proline-triflate in water [7]. Some of these methods are designated as good methods although minor or major limitations are seen in all of them. Drawbacks of these reported methods include use of toxic organic solvents and costly reagents or catalysts combinations and with low yields of the products. In continuation of our research on bismuth salts-catalyzed reactions for the efficient synthesis of diverse organic compounds, we report herein an expeditious method for the preparation of various xanthenes using catalytic amounts of non-toxic bismuth iodide under microwave-induced conditions [8-9].

Results and Discussions:

Microwave-induced reactions have received significant attention from scientists. This method has accelerated reaction rates significantly of many chemical reactions. Some reactions which were difficult to perform under conventional methods are made possible with microwave. Our research group has been engaged in bismuth salts-induced and microwave-induced chemical processes for many years [8-9]. Our studies in these areas have culminated in the synthesis of a variety of organic molecules. During this study, we realize octahydroxanthenes can be easily prepared following our protocol.

Reaction of 1,3-cyclohexanedione with various aromatic aldehydes in the presence of several

SCHEME1

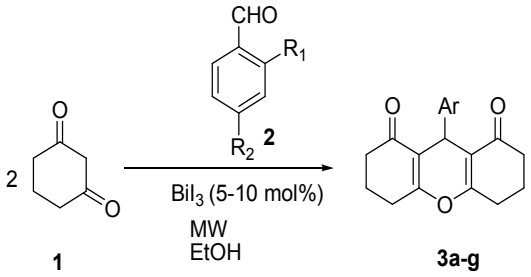


TABLE 1: Bismuth Idodide catalyzed Microwave-Induced synthesis of 9-aryl-1,8-dioxo-octahyroxanthenes

Entry	R^1	R^2	Time (min)	Compound(s)	Yeild(s)[a] (%)
1	H	H	2	**3a**	90
2	CH_3	H	5	**3b**	85
3	H	CH_3	4	**3c**	92
4	OCH_3	H	3	**3d**	87
5	H	OCH_3	4	**3e**	95
6	H	Cl	5	**3f**	85
7	Cl	H	6	**3g**	80

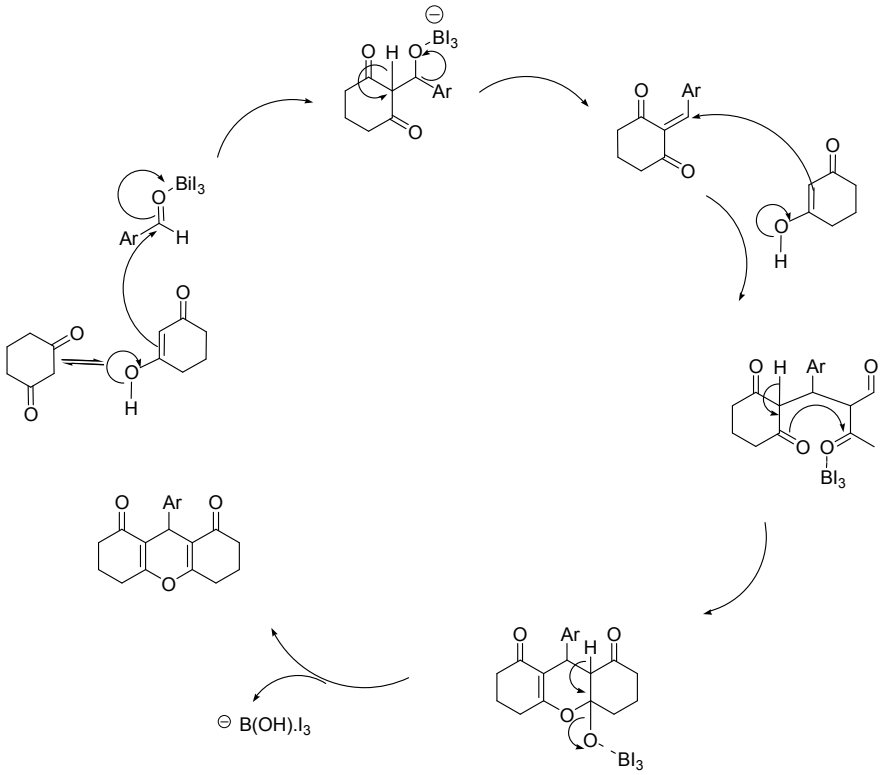
a : Isolated yeild after short column pad purification followed by crystalization. Ar: 2,4-disubstitued benzaldehyde(**2**)

bismuth (III) salts as a catalyst was conducted. For example, bismuth nitrate pentahydrate, bismuth chloride, bismuth bromide, bismuth iodide, bismuth oxide and bismuth subnitrate was used to identify the best catalyst system in this reaction. Bismuth iodide in ethanol was proved to be the best catalyst for this goal. Microwave-induced reactions accelerated the process significantly and the reaction was completed within 6-7 min at medium power and 60^0C temperature. The yield of the product was found to be approximately 70-75%. The tested substrates indicate substituents in the aromatic ring has no effects on this reaction [**Scheme 1, Table 1**].

The mechanistic route of this reaction is not investigated in detail. However, the formation of octahydroxanthenes is explained considering the nature of the substrates and catalyst. The cyclohexane diketone exists in its enol form in the presence of acidic bismuth iodide and undergoes reaction with aromatic aldehydes to create ortho-quinonemethide intermediate. Enolization is highly possible through a coordination of the electronegative oxygen with the empty d-orbital of bismuth atom. This intermediate is well-suited to follow a Michael-type of condensation with highly reactive diketone. A facile dehydration takes place and this produces the cyclic product. Clearly the formation of the enol, coordination of the oxygen

with the vacant d-orbital of bismuth and dehydration are facilitated by microwave irradiation due to high energy release

[**Scheme 2**].



SCHEME 2: Proposed mechanism for Bismuth iodide-catalyzed microwave-assisted synthesis of 9-aryl-1,8-dioxo-octahydroxanthene

Experimental:
To a mixture of the diketone (2 mmol) and aldehyde (1 mmol) was added bismuth iodide (10 mol%) in ethanol (1 mL). The reaction mixture was irradiated in a CEM microwave oven at 60^0C at power 300 watts for 6 min. After the reaction, dichloromethane (10 mL) and water (2 mL) was added to the reaction mixture, organic layer was collected and dried with sodium sulfate. The crude product was isolated after evaporation of the solvent which was purified by a short column of silica gel using ethylacetate and hexanes as the solvent (20: 80). The products obtained from this study have shown identical physicochemical data as reported [1-2, 4-7].

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