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MICROWAVE ASSISTED SYNTHESIS OF 1,8-DIOXOOCTAHYDROXANTHENE DERIVATIVES

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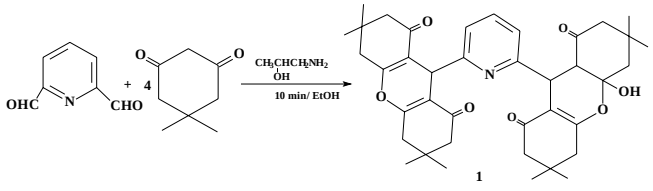
The synthesis of some new 1,8-dioxooctahydroxanthene derivatives been performed under microwave irradiation. It has been detected the catalytic role of primary amino group containing compounds in these reactions. Structureof all synthesized compounds confirmed by x-ray crystallography.
Keywords: *microwave irradiation, 1,8-dioxooctahydroxanthene, dimedone*

1,8-Dioxooctahydroxanthene derivatives and related pyrans exhibit wide spectrum of biological and pharmaceutical properties such as antibacterial, antiviral and anti-inflammatory activities as well as photo toxicity and antagonist activity [1–4]. There are some xanthene derivatives that are used in industry, such as florescent material for visualization of biomolecules [5], in laser technologies due to their useful spectroscopic properties [6] and as dyes [7]. Xanthenedione derivatives are valuable synthons because of inherent reactivity of the inbuilt pyran ring [8]. They are also found as core units in several natural products [9, 10]. From this point of view, the development of new methods for the synthesis of xanthene derivatives is an important area of synthetic research. Although numerous classes of pyrans have been conventionally synthesized, their synthesis have been suffered due to the multiple steps of procedures as well as quite long reaction time, low yields of products, strongly acidic conditions [11-14]. Therefore, to avoid these limitations, the development of a new suitable synthetic approach, with shortened reaction time and simple work-up for the preparation of 1,8-dioxooctahydroxanthenes is highly desirable. Herein we report on synthesis of 1,8-dioxooctahydroxanthene derivatives in the microwave irradiation condition. The products were obtained in good yields within few minutes during the reaction of aromatic bisaldehyde with dimedone in ethanol in the presence of aminoalcohol or ethylenediamine hydrochloride as catalyst. Interestingly, when in case of 1-aminopropan-2-ol as catalyst has been formed the 4a-hydroxy derivative **1** of desired compound (Scheme 1).



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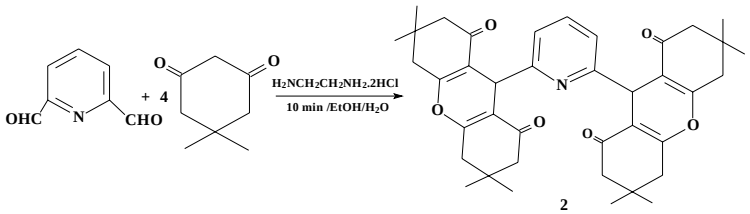
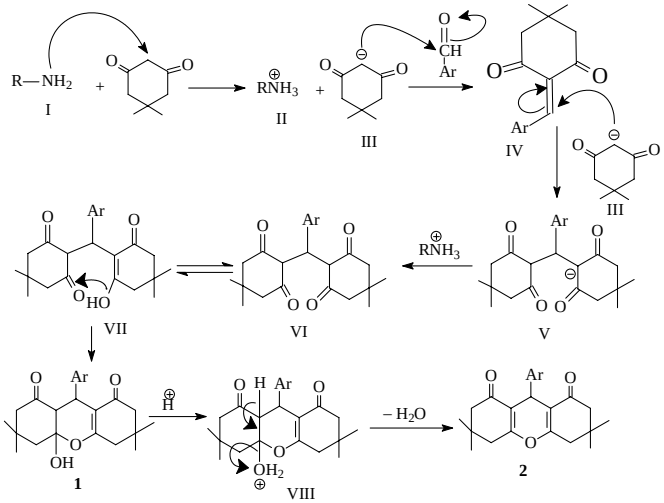
Scheme 1

But when ethylenediamine hydrochloride used in this reaction has been formed the corresponding xanthene derivative without any hydroxyl group in molecule (scheme 2) is as follow:



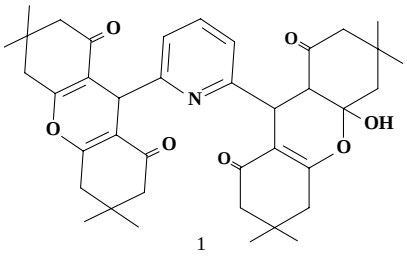
Scheme 2

Formation of the 1,8-dioxooctahydroxanthene derivative may be rationalized by an initial formation of the dimedone cation **III** which formed in presence of amino compounds **I** (Scheme 3). By attacking the cation of dimedone **III** to the aromatic aldehyde which undergoes partially polarization on carbonyl group formed arylidene derivative **IV**, by attacking another dimedone cation **III** on the formed arylidene derivative **IV** Michael addition affords the formation of adduct (Knoevenagel condensation product) **VI**. Knoevenagel product **VI** underwent internal attack of hydroxy group to carbonyl group to form stable structure of the hydroxy 1,8-dioxooctahydroxanthene derivative **1** (Scheme 1), in case of ethelenediamine hydrochloride afforded 1,8-dioxooctahydroxanthene by elimination of a molecule of water in the intermediate of **VIII** which formed 1,8-dioxooctahydroxanthene derivatives **2** (Scheme 2).



Scheme 3

Structure of both synthesized compounds investigated x-ray crystallography. The pyridine ring in the compound **1** ($C_{39}H_{47}NO_7$-$0.5C_2H_5OH$-$0.5H_2O$) is connected with one 3,3,6,6-tetramethyl-1,8-dioxoxanthenyl and one 4a-hydroxy-3,3,6,6-tetramethyl-1,8-dioxodecahydroxanthenyl substituent in the 2- and 6-positions of the ring. In the former substituent, the six-membered xanthenyl ring adopts a flattened envelope conformation (with the methine C atom as the flap) while in the latter, the six-membered xanthenyl ring adopts a twisted envelope conformation (with the C atom bearing the hydroxyl group representing the flap). The hydroxy H atom forms an intramolecular hydrogen bond to the pyridyl N atom. An ethanol solvent molecule is disordered with respect to a water molecule in a 1:1 ratio. The water molecule itself is disordered over two positions of equal occupancy [15] (fig 1).



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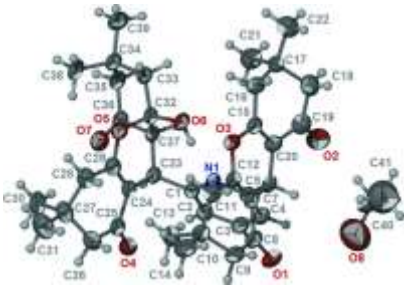
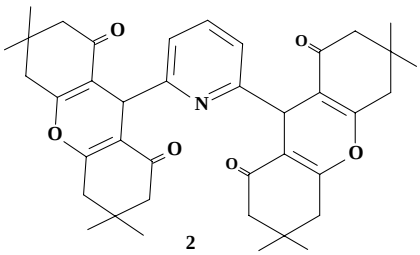


fig 1

The compound **2** ($C_{39}H_{45}NO_6$), the two tetramethyloctahydroxanthen-1,8-dione substituents are arranged approximately parallel to each other and approximately perpendicular to the plane of the pyridine ring. The six-membered xanthene rings adopt flattened boat conformations with the O and methine C atoms deviating from the plane of the other four atoms. [16] (Fig. 2).



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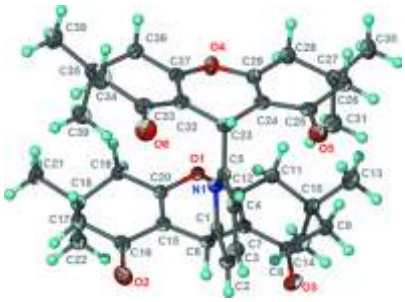

fig 2

To sum up, the use of amino compounds as catalyst under MW irradiation condition makes it possible to develop easier method for the synthesis of corresponding xanthene derivatives. Nature of amino compound influence to the reaction pathway.

EXPERIMENTAL

All reactions were performed in a monomodal EmrysTM Creator. Melting points were determined using open glass capillaries on a Gallenkamp digital melting point apparatus and are uncorrected. X-ray analyses have been determined by X-ray Bruker Smart Apex II X-ray diffractometer.

General procedure for the synthesis of title compounds: Typically, in a 20 mL EmrysTM reaction vial aromatic aldehyde (1 mmol), dimedone (4 mmol) and 1-aminopropan-2-ol (1 mmol) in case compound **1** (92%, MP 175^{0}C) or ethylenediamine hydrochloride in case compound **2** (Yield 40%, MP 200^{0}C) in ethanol (10 mL) were mixed and then capped. The mixture was irradiated by microwave at 200W and 80^{0}C for a given time. Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature and washed with 2 mL distilled water, filtered to give the crude products, which were further purified by recrystallization from 95% EtOH.

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MİKRODALĞALI ŞÜALANDIRMA ŞƏRAİTİNDƏ 1,8-DİOKSOOKTAHİDROKSANTEN TÖRƏMƏLƏRİNİN SİNTEZİ

Antar Ahmed Abdelhamid

Bəzi 1,8-dioksooktahidroksanten törəmələrinin sintezi mikrodalğalı şüalandırma şəraitində həyata keçirilmişdir. Bu reaksiyalarda birli amin qrupu saxlayan birləşmələrin katalitik rolu müəyyən edilmiş və aydınlaşdırılmışdır ki, amin qrupunun təbiəti reaksiyanın istiqamətinə təsir edir. Sintez olunmuş birləşmələrin quruluşu müasir rentgen kristalloqrafiyası üsulu ilə sübut olunmuşdur.
Açar sözlər: *mikrodalğalı şüalandırma, 1,8-Dioksooktahidroksanten, dimedon*

СИНТЕЗ ПРОИЗВОДНЫХ 1,8- ДИОКСООКТАГИДРОКСАНТЕНОВ ПОД ДЕЙСТВИЕМ МИКРОВОЛНОВОГО ОБЛУЧЕНИЯ

Антар Ахмед Абдельгамид

Осуществлен синтез некоторых новых производных 1,8-диоксооктагидроксантенов под действием микроволнового облучения. Была установлена каталитическая роль соединений, содержащих первичные аминогруппы. Структура всех синтезированных соединений подтверждена данными рентгеноструктурного анализа.
Ключевые слова: *микроволновое облучение, 1.8-диоксооктагидроксантен, димедон*

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