



A new approach to the facile synthesis of 1,8-dioxooctahydroxanthene using nano-TiO₂/ CNT as an efficient catalyst

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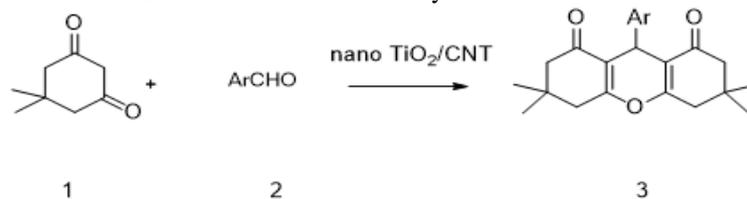
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ABSTRACT

1,8-dioxooctahydroxanthene derivatives have received considerable attention due to their valuable biological and medicinal properties such as anticoagulant, antispasmodic, diuretic, and anti-cancer activities. 1,8-dioxooctahydroxanthene derivatives have strong relaxing activity on blood vessels, cardiac muscles, and smooth muscles. The present study reports the easy synthesis of 1,8-dioxooctahydroxanthene derivatives using aldehydes and dimedone in the presence of nano-TiO₂/ CNT as an efficient catalyst.



1. Introduction

Xanthenes are essential compounds, and researchers are still studying them several years after their discovery. Xanthenes are the basic structure of many natural products, medicines, dyes and insecticides. Various polycyclic compounds with xanthene structures, including xanthenes, are composed of natural sources. α -simamycins (4) are some examples of natural products with anti-tumor properties. Phenyl xanthenes, in which carbon number 9 of xanthene is attached to a phenyl group, have a basic chromophore structure and fluorescence properties, and they are used in the dyeing industry. 5-Bromo-methyl fluorescein (5), 5-Iodoacetamide Fluorescein (6), and rhodamine B7 (7) are some examples of xanthene derivatives with fluorescent properties. Halogenated xanthene paints are used as insecticides. In their mechanism, insects are killed in a few minutes by absorbing the light, but they will not die even after several days in the absence of light. fluvoxin B 8 (8) is an example of these insecticides with a xanthene structure. Spiro xanthene was synthesized by the ring-forming reaction of 1, 3 dipole nitrile imine and xanthene (9). These compounds have shown anti-inflammatory and analgesic activity against ibuprofen. Xanthene (10) has

been introduced as a compound that affects the central nervous system and has antifungal and antibacterial activities[1-7].

Following the discovery of the medicinal properties of these derivatives in recent years, the synthesis of these compounds has been considered. Here we evaluate the synthesis of these compounds using nano-TiO₂/ CNT as an efficient catalyst.

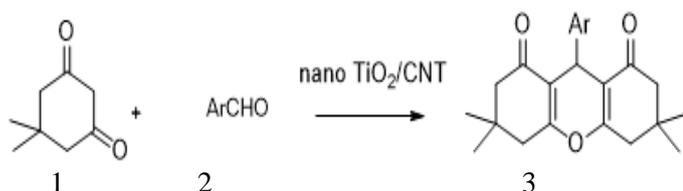
2.Result and Discussion

Xanthenes are three-ring heterocyclic compounds that have been highly considered for their color, antibacterial, and antiviral properties. They are also widely used in the food and textile industries. In addition, xanthenes are fluorescent materials and are used in the visualization of biomolecules and laser technology due to their properties. Due to the extraordinary applications mentioned above, xanthenes and their derivatives have been widely considered, and various synthetic methods have been developed for their preparation. In this regard, we tried to obtain several 1 and 8-dioxo-octa-hydra-xanthene derivatives under suitable conditions with small amounts of nano-TiO₂/ CNT.

A nanoparticle is a particle with dimensions of about 1 to 100 nanometers. Nanoparticles include insulators and semiconductors like composite nanoparticles such as layered core structures, In addition to the metal type. Also, Nano-spheres, Nano-rods and Nano-cups are only some forms of nanoparticles.

Due to the low affinity of carbon Nano-tubes, coating their surfaces increases the bonding probability between carbon Nano-tubes and other materials and thus expands the production of carbon Nano-composites. By creating a coating on Nano-tubes' surfaces and increasing the possibility of producing Nano-composites, their usage has been developed in various industries. There are few reports on the application and engineering of carbon Nano-tubes because of their novelty. Still, there are few articles and essays on titanium oxide and titanium due to the formation of a uniform Ti coating on carbon Nano-tubes and the buffering of Ti coating. In the industrial production of carbon Nano-tubes, its use in the industries of power and energy transmission lines, railway and train construction, automobiles, airplanes, space and missile industries, etc., can create a dramatic change. Today, these materials are used in small enterprises such as transistors, diodes, catalysts of chemical reactions, especially in the oil and gas industry (also used in Iran). Separators are used in the reactions (disperses), intelligent memory, Nano-sensors, etc. Carbon Nano-tubes are used in Nano-composites as a booster and a completely uniform fiber in metal, polymer, and ceramic fields. Carbon Nano-tubes can also be used as gas discharge tubes. Nano-tubes are used in Nano-sensors and intelligent electronic components, transistors, rectifier diodes, etc. nano-TiO₂/CNT are used in making batteries for the possibility of storing more energy on their surfaces. Fracture toughness and electrical conductivity of CNT Nano-composites with Aluminum background increases. CNT Nano-composites with a polymer background can be used to construct aircraft wings and fuselage [8].

We used nano-TiO₂/CNT as a catalyst for the synthesis of 1,8-dioxooctahydroxanthene derivatives from aldehyde, dimedone (Scheme 1).



Scheme 1. Synthesis of 1,8-dioxooctahydroxanthene using nano-TiO₂/CNT

3. Experimental

In this research, various materials and devices have been used, and they have the following characteristics: In measuring the melting points, the 9200-BranstedElectrothermal device was used. Reaction

improvement was followed by the TLC technique and UV lamp with two wavelengths of 254 and 356. IR spectra were prepared by the Tensor FT-IR device by the use of KBr tablets. ¹H-NMR spectra were obtained in DMSO-d₆ solvent by the use of TMS as an internal standard using the AvanceDRXDRX400 bruker.

Merck Company provides the solvents and chemicals in this project. The structure of obtained products has been compared and confirmed with the spectra and physical data recorded in the references.

3.1. Select CNTs for testing:

The molecular structure of CNTs(carbon nanotubes) has strong covalent bonds. Unique one-dimensional structure, nanometer size, yield stress and ultra-high jump rate, varying electronic properties from semiconductor to conductor, high capacity of electrical conduction and high thermal conductivity [9] led to the usage of CNTs with SWN(Single-wall carbon nanotubes) structure mixed with MWNTs(Multi-walled carbon nanotubes) for Ti coverage. However, if pure MWNTs or SWNTs are available, the experimental methods of this study can be generalized (Figure1).

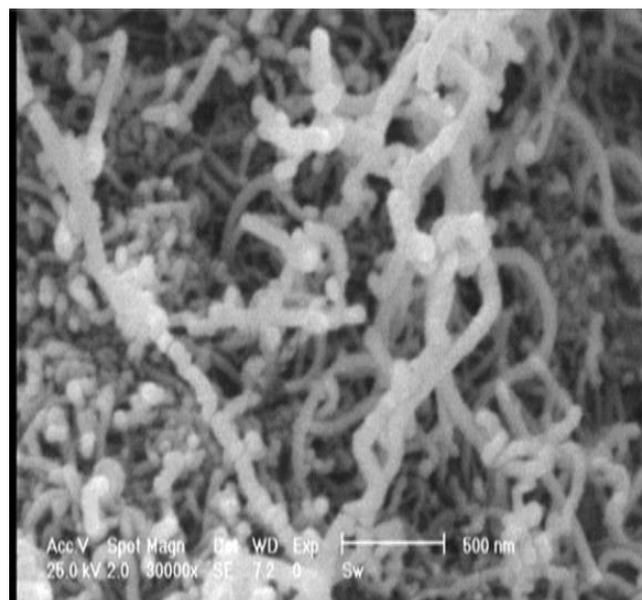


Figure 1. SEM image obtained from SWNTs with MWNTs in raw material with 30,000 magnification.

3.2. Activating CNTs surfaces:

First, 0.5 g of CNTs was poured into 40 ml of 3: 1 concentrated nitric acid/sulfuric acid solution with 2-propanol as a separator and it was subjected to sonication for 2 hours in an ultrasonic device. Before applying the ultrasonic force, CNTs were not dispersed in the solvent, but carbon Nano-tube particles were dispersed in the solvent and did not settle over months after using the ultrasonic force.

3.3. Separation of CNT powders dispersed in the acid medium by centrifugation:

After dispersing the CNTs, it was necessary to separate these materials from the acidic mixture to obtain functionalized CNTs powder and cover its surfaces in the following steps. In the first step, a centrifuge with 4500 Rpm was used to separate the powder, but the powder was not wholly separated inside the mixture. In the next step, after centrifugation, distilled water was added to the solution and the solution was stored for 24 hours at room temperature. The dispersed powders were deposited inside the test vessel.

3.4. Deposition of dispersed powders in solution without using a centrifuge:

At this stage, before the centrifugation, the acid concentration was reduced by adding distilled water, and it was observed that the dispersed particles were gradually deposited at the bottom of the container.

3.5. Separating the precipitated powders:

The precipitated particles were passed through filter paper from section 3-2-3, and to de-acidify the powder in the filter paper, it was washed with distilled water in several steps. The pH increased to about 7. After this step, the filter paper was washed in a beaker, and the resulting mixture was placed in a glass for 24 hours to dry at room temperature. Then the activated carbon nano-tube powder was obtained.

3.6. Dispersion of activated carbon Nano-tubes in water:

CNTs powders were dispersed in water before and after activation, and as it can be seen in Figures 2 (a) and (b), it was observed that before activation, CNTs particles formed as agglomerates and lumps on the surface or underwater, but after activation, the characteristic of wettability will appear and they will be dispersed in water.

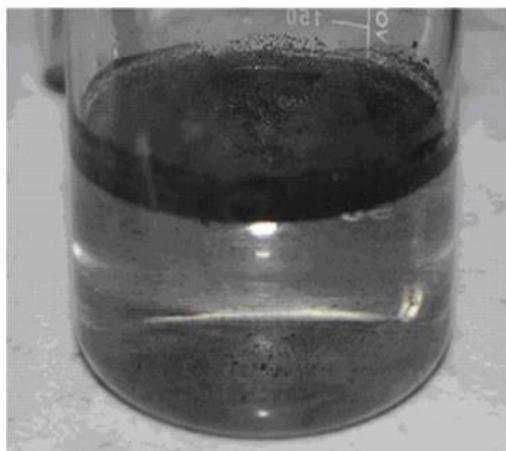


Figure 2 (a): The image of CNTs before activation in which the Nano-tube particles are not dispersed in water and are present on the surface or underwater as agglomerates.

3.7. Test by FTIR device:

The FTIR spectrum was used to prove the activation of carbon nano-tubes, which clearly showed the spectral differences between the nano-tubes before and after the

activation. Figure 3 (a) shows the FTIR spectra of carbon nano-tubes before, and Figure 4 (b) shows these spectra after activation.



Figure 2 (b): The image of CNTs after activation is dispersed in water and suspended as fine particles.

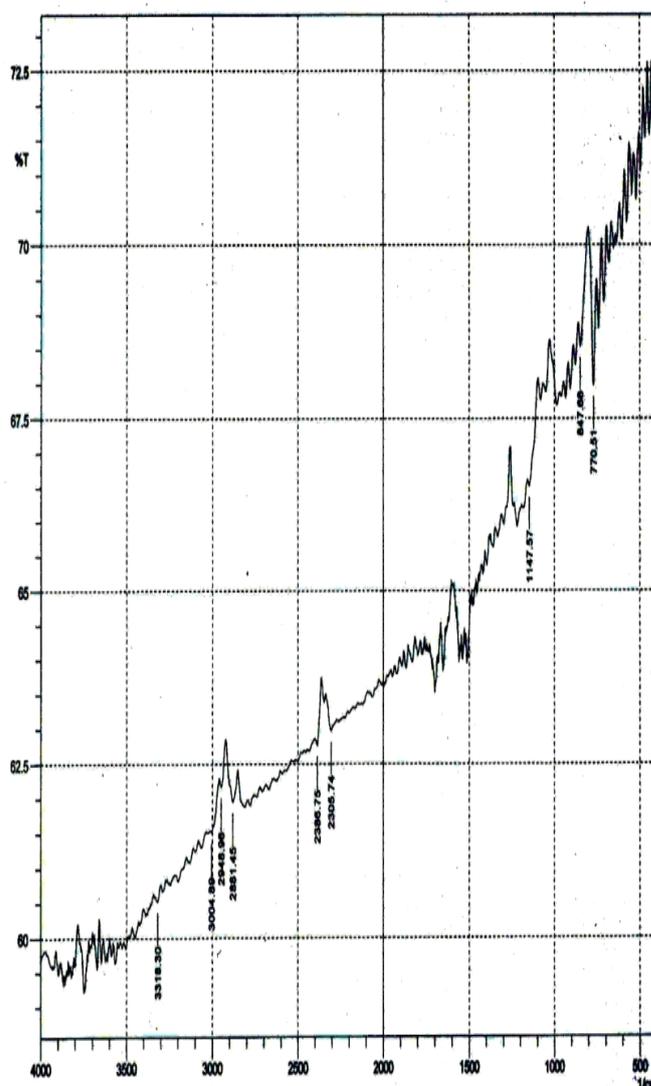


Figure 3 (a) FTIR spectrum for carbon nanotubes before activation.

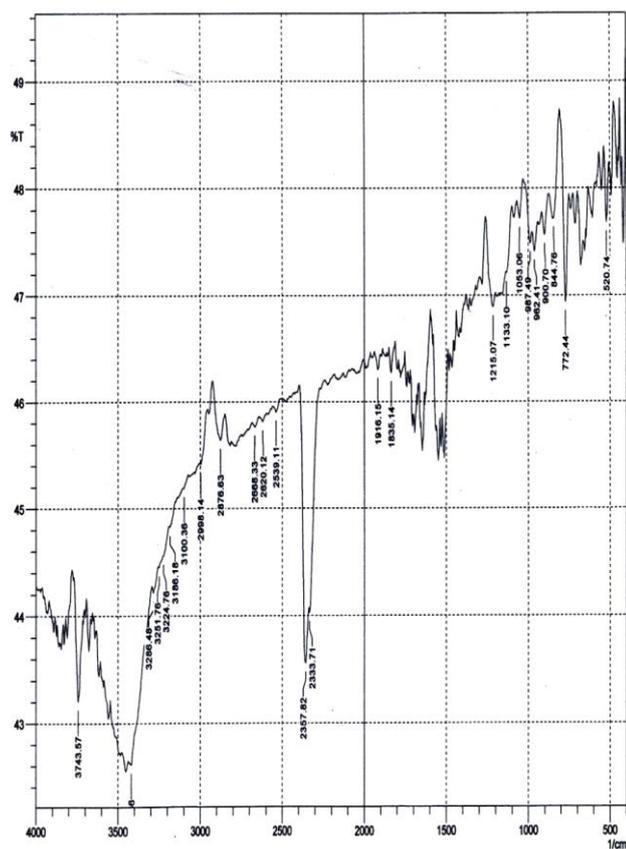


Figure 3 (b) FTIR spectrum for carbon nanotubes after activation.

3.8. SEM test of different activation steps:

SEM imaged products and raw materials in three stages to study and compare the structure of carbon nano-tubes before and after activation; figure 3-1 shows the SEM image of the primary CNTs before any operation. Carbon nano-tubes with different diameters can be seen in this image. Figure 4 shows the SEM image of the active powders separated from the solution without using a centrifuge, and Figure 5 shows the SEM image of the CNTs powders affected by the centrifuge.



Figure 4 - SEM image after the activation of CNTs and the separation of Nano-tube powder without the use of centrifuge with an x30,000 magnification.

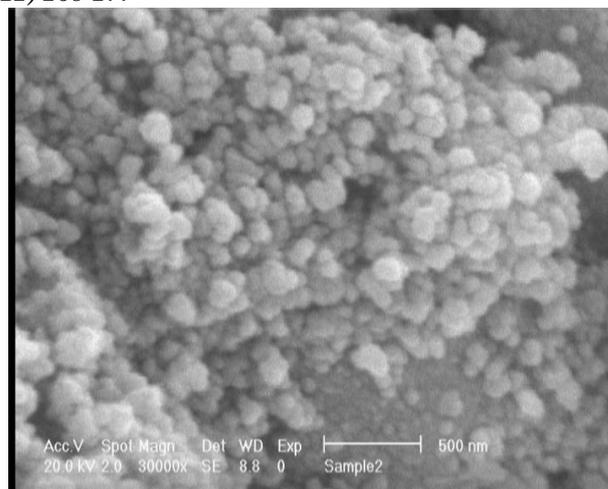


Figure 5- The SEM image is taken after the CNTs activation and the separation Nano-tube powder by using a centrifuge and a magnification of x30,000, which shows the CNTs agglomeration.

3.9. Making a coating solution:

10 ml of concentrated HCl was dissolved in 220 ml of distilled water, and then 100 ml of TiO₂ solution was slowly added to it. The reaction was done by high heat energy, and many toxic fumes were produced, which required a strong fan and mask and observance of other safety points. The container containing the test material was placed in the presence of dry ice or plenty of ordinary ice to reduce the high temperature of the reaction. A tiny amount of polyethylene amine was added to the test vessel in a few drops as a disperse. The container containing the test materials was wrapped in an aluminum foil after the noisy reactions, and it was kept at 70 ° C for one hour. After 24 hours, TiO₂ white powder was deposited at the bottom of the container. The powder was separated from the mixture by a filter paper. Then the contents of the filter paper were washed several times with distilled water to remove the acids associated with these nanoparticles, and its pH reached near 7. The mixed particles with distilled water were dried at room temperature for 24 hours. The obtained XRD particles proved the presence of TiO₂ (Figure 4) and the obtained TiO₂ powder was imaged by SEM to show that titanium oxide was formed as nanoparticles (Figure 6).

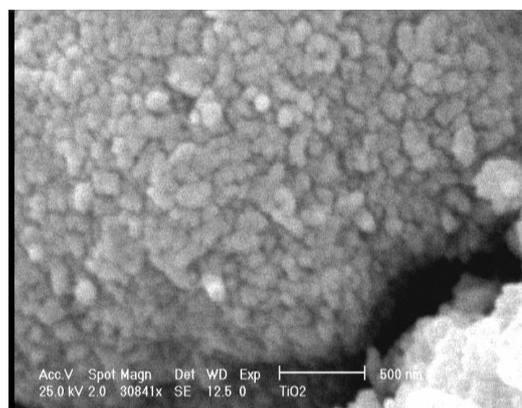


Figure 6 - SEM image of TiO₂ powder produced by mixing TiCl₄ and HCl

3.9. Apply a Coating on Carbon Nano-tubes:

At this stage, TiO₂ coating was first formed on the surfaces of carbon Nano-tubes. Then the generated titanium oxide was reduced to obtain titanium coating on the surfaces of carbon Nano-tubes. To perform this step, the amount of 100 mg activated SWNTs was first poured into the obtained suspension from previous test and then it was mixed at 70 °C for 2 hours with a magnetic stirrer. After this period, there was no trace of SWNTs, but gray colored particles were formed, indicating the presence of TiO₂ coating on the surfaces of SWNTs. By diluting the acid solution with distilled water, these particles were deposited at the bottom of the container. The residue was passed from the filter paper, and the filter paper content was washed in several steps with distilled water to reduce the acid concentration and pH to about 7. The powder in the filter paper was then soaked in a beaker, and the obtained mixture was dried by a drier for 24 hours at

room temperature. The resulting powder is carbon Nano-tubes with a TiO₂ coating.

XRD tests before and after applying TiO₂ coating on the surface of carbon Nano-tubes:

After applying the coating on the Nano-tubes by TiO₂ a test was performed on the powders of the three XRD stages, the results of which can be seen in Figures 3, 4 and 5. In figure 3, XRD was taken from the TiO₂ powder produced in previous, in which a rutile allotrope of TiO₂ crystal was observed, and proved that the produced material was titanium oxide, then the XRD was taken from single-walled carbon Nano-tubes, which were available as raw materials, and the results are shown in figure 4. After coating the carbon nano-tubes with TiO₂, XRD was taken from the resulting powder for the comparison of XRD in figure 7 and 8, and the results of this comparison can be seen in figure 9 which showed that TiO₂ and C did not react chemically and they co-exist without any chemical reaction or compound.

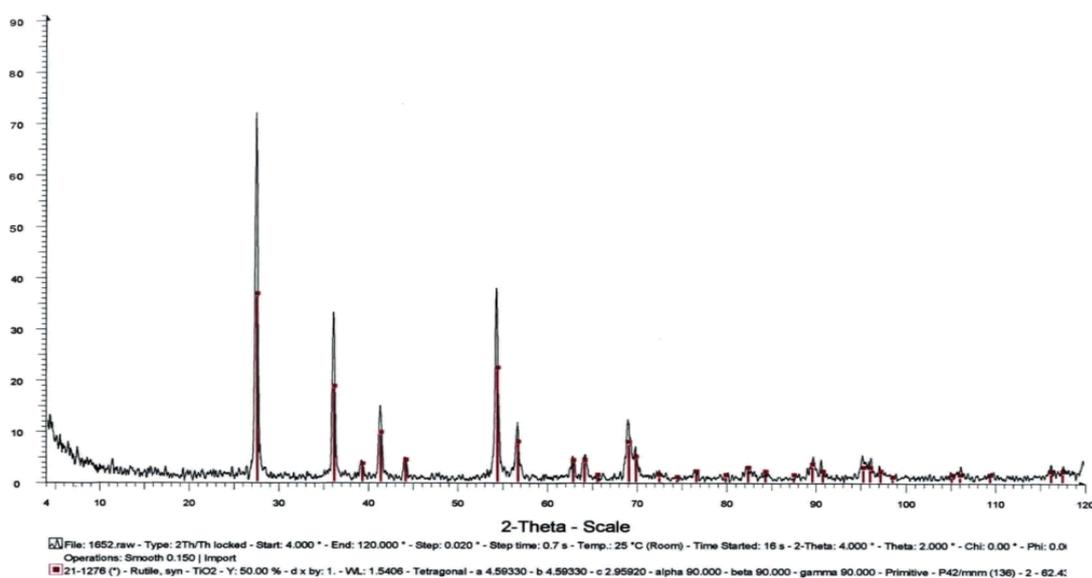


Figure 7 - XRD test that proves the presence of TiO₂.

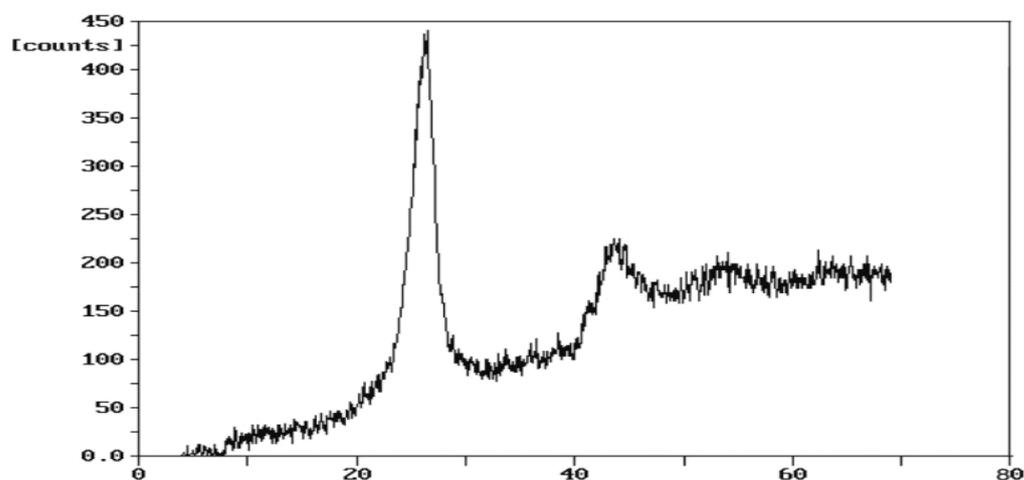


Figure 8. XRD test confirmed the presence of carbon nanotubes (CNTs) in the test sample.

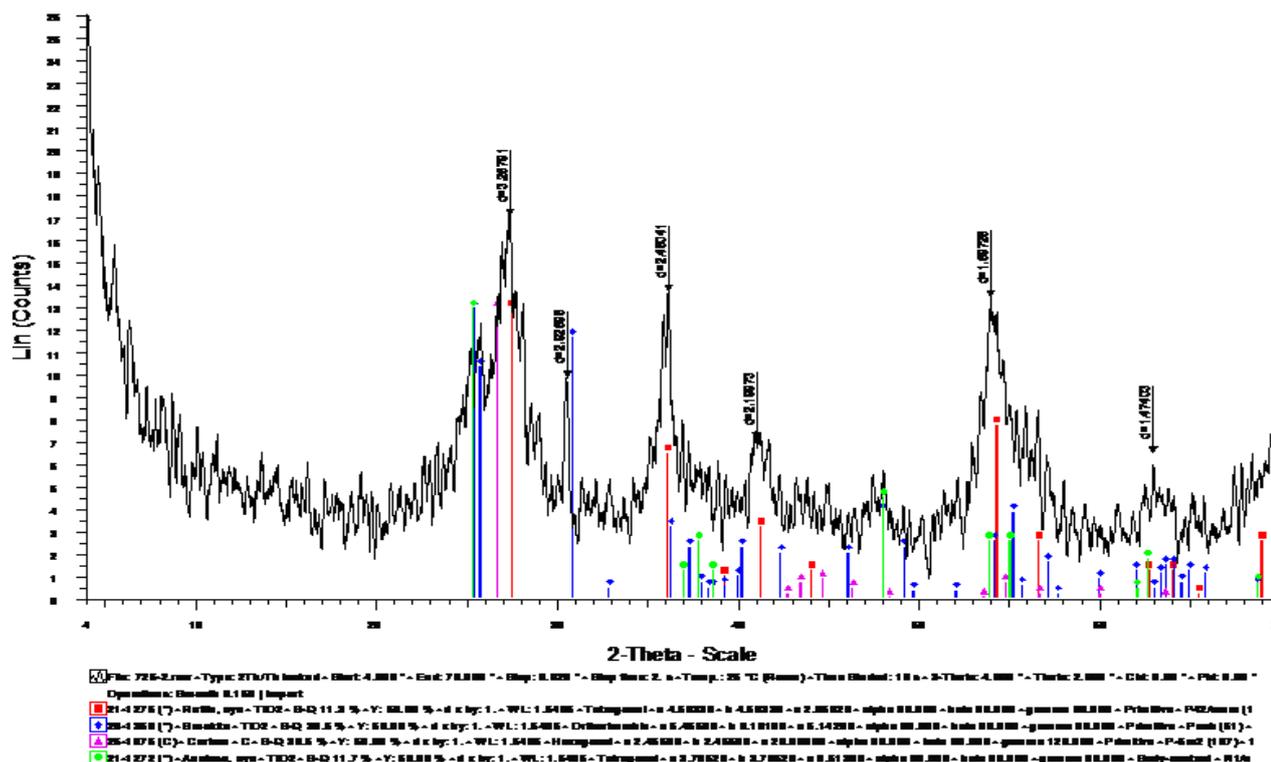


Figure 9- XRD test shows the presence of carbon nanotubes and TiO₂ without reacting together.

3.10. SEM test after TiO₂ formation:

The centrifuge could not precipitate all of the suspended Nano-tube particles in the acidic medium. Still, they slowly precipitated with the addition of distilled water. It was separated by centrifugation and the SEM image was taken from the stage where the powder was precipitated without centrifugation and only with the addition of distilled water. Figures 10 illustrates the granulation of Nano-tubes during centrifugation, and Figure 11 shows the TiO₂ coating on carbon Nano-tubes which are obtained without centrifugation.

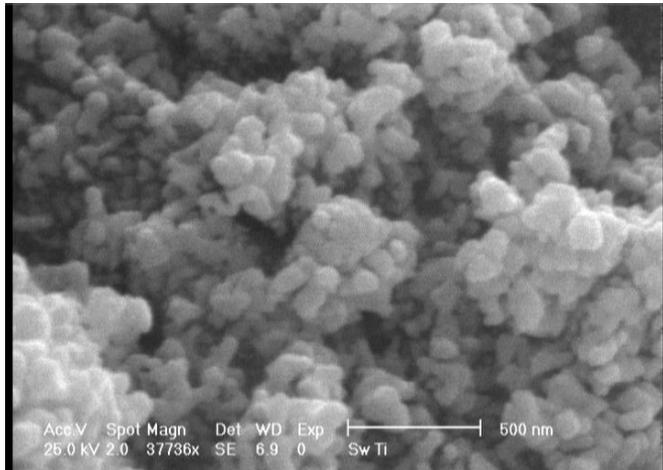


Figure 11 - SEM image of carbon Nano-tubes coated with TiO₂, and the Nano-tubes were separated from the solution without centrifugation, which seems to have lost the shape of the Nano-tubes.

According to Figure 11, while the centrifuge was not used when precipitating the suspended powder in the mixture, the carbon Nano-tube particles were again broken; this error was solved by repeating the experiment.

Repeating the test:

The test was repeated from the step of mixing the TiO₂suspension with the functionalized carbon Nano-tubes to eliminate the breakage of the carbon Nano-tubes shown in Figure 12, and a low-speed vane stirrer was

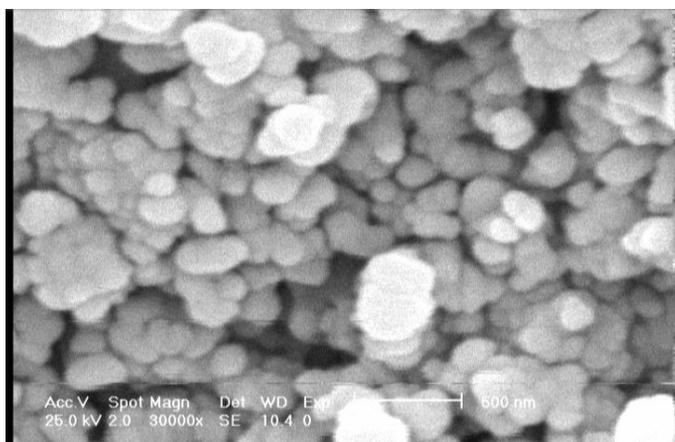


Figure 10- SEM image shows that after coating TiO₂ on carbon Nano-tubes, the shape of the Nano-tubes is lost because the powder is separated from the acid mixture by centrifugation.

used instead of the magnetic stirrer. In Figure 8, the non-breaking of SWNTs is visible.

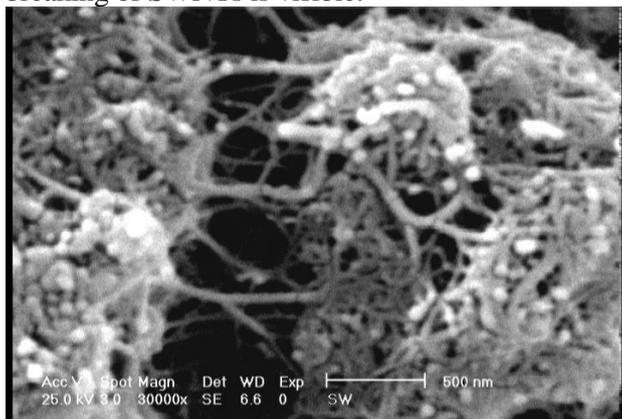


Figure 12. SEM image of carbon nanotubes coated with TiO₂.

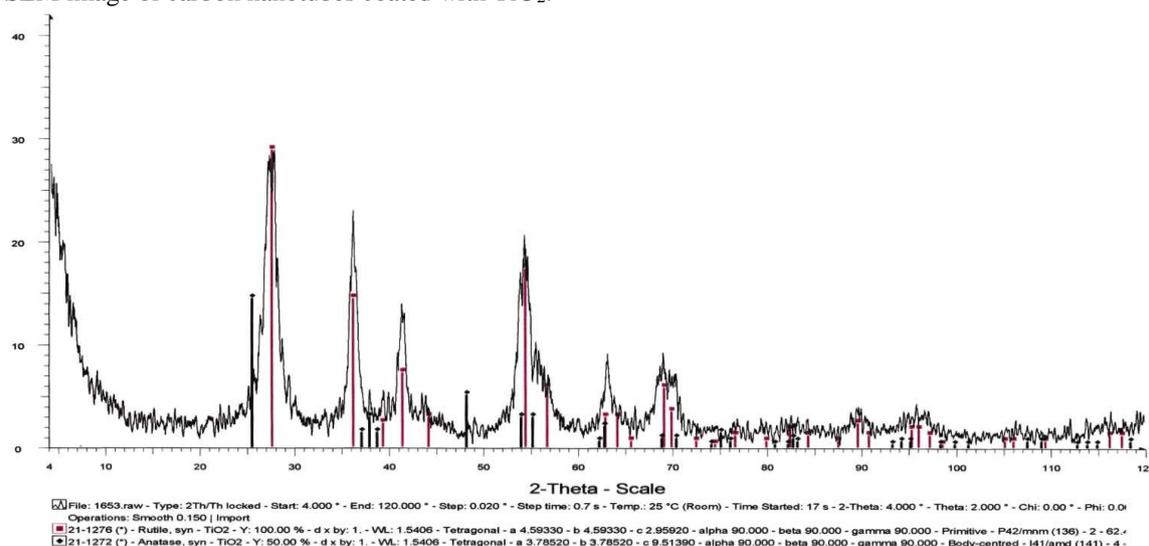


Figure 13. The XRD test showed that at temperatures above 700 ° C, the allotropy of anatase was formed from crystals.

3.12. Reduction of TiO₂ by hydrogen gas in TPR (Temperature program reduction) device:

At this stage, a device called TPR (Temperature program reduction) was used to reduce TiO₂. In this device, a gas containing 5.1% H₂ in argon medium passed over the TiO₂ coating on the surfaces of carbon Nano-tubes. Ambient temperature was increased at 50 NCC / min for 40 min, and titanium oxide was converted to Ti at 850 ° C. The results are shown in Figure 14.

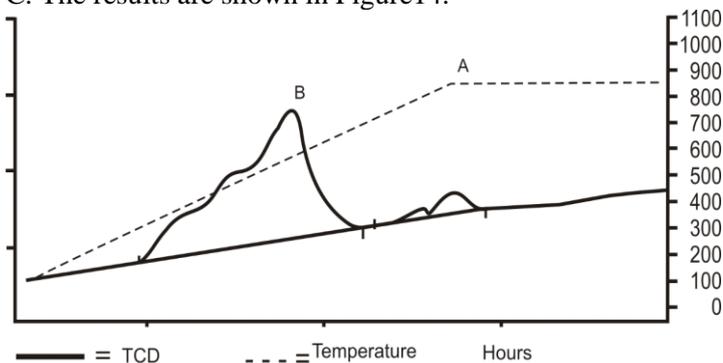


Figure 14- TPR curve showing TiO₂ reduction conditions.

3.11. Reduction of TiO₂ by hydrogen gas:

Reducing TiO₂ can be done by passing a suitable gas through a reduction reactor. First, it passed over the TiO₂ powders of hydrogen gas, by test and error in a reactor for 2 hours at a pressure of 3 bars, a speed of 20 ml per minute and a temperature of 700 ° C, but the final result indicated the formation of anatase which is another allotropy of TiO₂ crystal. Its effects are shown in Figure 13.

3.13. Reduction of TiO₂ by hydrogen gas and by applying the obtained conditions from TPR in the reduction reactor:

After obtaining the reduction conditions of TiO₂ by the TPR device, the Nano-tube coated with TiO₂ was placed inside the reduction reactor and the TiO₂ coating was converted to Ti by applying the obtained conditions from the TPR curves.

3.14. EDAX analysis to prove the presence of Ti:

After the reduction of TiO₂ by hydrogen gas, EDAX analysis was used to prove the presence of Ti coating on SWNTs. The results are shown in Figure 15.

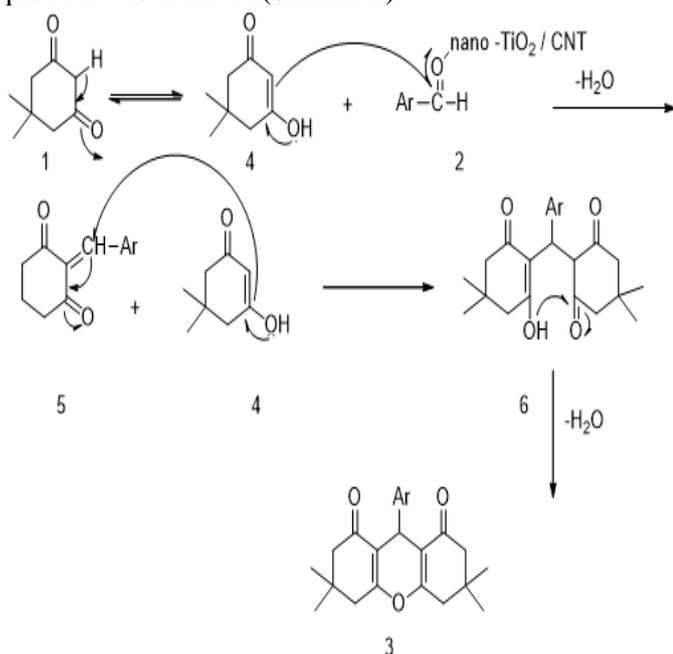
•		3g	1	95	244 - 245	246- 248 ^[11] 01
•		3h	1	96	233	230- 232 ^[11] 01
•		3i	1	97	231	228- 230 ^[11] 01

a) Yields refer to isolated products.

4. Reaction mechanism

The proposed mechanism for performing the reaction is as follow:

Initially, a neonatal response occurs between Dimedone and aryl aldehyde, and an intermediate is formed. Then the second Dimedone is added, and it creates the desired product after removing the water in the last step and the product was achieved (Scheme 2).



Scheme 2. Mechanism of synthesis of 1,8-dioxooctahydroxanthene

5. Result and Discussion

In this reaction, optimization was performed by changing the solvent. The best solvent for the reaction was found to be the ethanol solvent. (Table 2)

Table 2. Synthesis of 3a in the presence of different solvents using nano-TiO₂/CNT as a catalyst

Entry	Solvent	Yield (%) ^a
1	THF	68

2	C ₂ H ₅ OH	96
3	CH ₃ CN	85
4	CHCl ₃	71
5	water	90
6	Solvent-free	92

^aYields were analyzed by GC

6. Reusability of nano-TiO₂/CNT

After the reaction, 10 ml of ethyl acetate was added to the compounds on filter paper containing catalyst. The mixture was stirred at room temperature for 5 minutes using a magnetic stirrer. The reaction mixture was filtered, and the catalyst remained on filter paper due to its insolubility in ethyl acetate solvent. Then, in order to reuse the catalyst, the filter material was washed several times with acetone. After drying, the reaction was repeated to check the potency of the catalyst (Table 3).

Table 3. Reuse of the nano-TiO₂/CNT for synthesis of (3a)

Entry	run	Yield(%) ^a
1	first	96
2	second	93
3	third	90
4	fourth	88
5	fifth	85

Isolated yields

7. Comparison of the performance of nano-TiO₂/CNT with a number of different catalysts in the synthesis of xanthene derivatives

By comparing the reaction results with other methods, we found that the nano-TiO₂/CNT performed the reaction in a shorter time and with higher efficiency (Table 4).

Table 4. Comparison of various catalysts for the synthesis of 3a

Ent ry	Catalyst	Yiel d (%)	Time(h)	Ref
1	Selecfleur	93	1.5	[11]
2	SaSA(Saccharin sulfonic acid)	90	1	[12]
3	DABCO(1,4-diazabicyclo[2.2.2]octane) – bromine	80	2.5	[13]
4	TCCA(Trichloroisocyanuric acid)	89	1	[14]
7	SiO ₂	95	3	[15]
8	nano-TiO ₂ /CNT	96	1	Present study

To optimize the amount of catalyst, various amounts (0.01, 0.02, 0.03, 0.05, and 0.08 g) of nano-TiO₂/ CNT were used. Table 5 represents the test results performed to optimize the amount of catalyst in the presence of different amounts of nano-TiO₂/ CNT. The results presented in the table show that the amount of 0.05 g of nano-TiO₂/ CNT had the best efficiency.

Table 5. Comparison of amount of catalysts for the synthesis of 3a

Entry	Solvent	Yield (%) ^a
1	0.02g	80
2	0.03g	89
3	0.05g	96
4	0.08g	96

^aYields were analyzed by GC

8. Conclusion:

In this research study, we developed a novel, simple and efficient method for the synthesis of 1, 8-dioxooctahydro xanthene derivatives by using nano-TiO₂/ CNT as a catalyst with high efficiency and short time reaction. Nano-TiO₂/ CNT catalysts are recyclable, heterogeneous, environmentally benign solid catalysts possessing desirable properties such as high thermal and hydrothermal stability. There are some remarkable properties which are playing noticeable roles, such as: mildness of the conversion, simple experimental part, and also ability of compatible with various functional groups, impressive and efficient yields, short reaction times, and the easy workup procedure. Finally, these features make target procedure more attractive to synthesize a variety of these derivatives. As shown in Table 5, the highest efficiency (96%) in a short time (1h) was obtained in this study, which is very important compared to other previous methods presented.

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