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SYNTHESIS OF 1-(4-NITROPHENYL)-3-PHENYLPROPANE-1,3-DIONE AND STUDYING SOME OF ITS BIOLOGICAL AND PHYSICAL PROPERTIES

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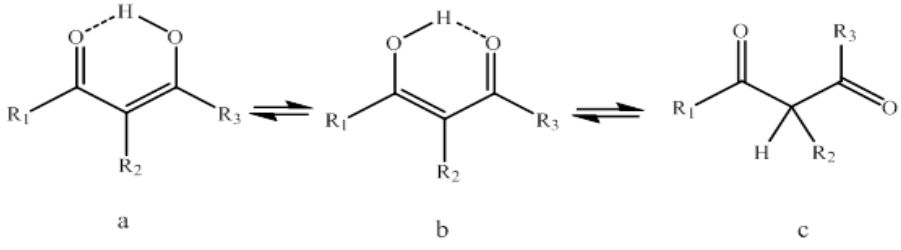
ABSTRACT

In this paper the reaction of propyl 4-nitrobenzoate with acetophenone to prepare 1-(4-nitrophenyl)-3-phenylpropane-1,3-dione was carried out using appropriate conditions, where a homogeneous basic catalyst (tetrabutyl ammonium hydroxide) was used with a molar ratio (1:1) (propyl 4-nitrobenzoate: Acetophenone), at a temperature of 45°C and a reaction time of 14 hours. The desired product was obtained with high selectivity and high yield (76%). After that, some physical properties of the reaction product were determined by measuring the turbidity and density of the aqueous solution. After that, the biological activity of the product was studied on two types of bacteria "positive and negative gram" and compared it with a reference substance "gentamicin", The results of the study show an average ability to inhibit the growth of negative bacteria and a better ability to inhibit the growth of positive bacteria at the concentrations studied compared to the reference substance (gentamycin). The product was separated and purified, the molecular structures have determinate by spectroscopy methods FT–IR, ^{1}H–NMR, ^{13}C–NMR.

KEYWORDS: β-diketones, propyl 4-nitrobenzoate, acetophenone, 1-(4-nitrophenyl)-3-phenylpropane-1,3-dione.

1. INTRODUCTION

The **β-diketones** organic compounds that contain two carbonyl groups in their structure separated by one carbon atom, the carbon separating these groups is denoted as the α-carbon[1] the hydrogen atoms on the α carbon are acidic and have a typical pK_a of approximately 13 in DMSO solvent.[2] linear β-diketones are also characterized by the presence of enolic and ketone displacement (tautomeric) isomers[3] as shown in the (scheme 1).



Scheme 1: Tautomerism of β-diketones.

It has several distinct and highly interesting properties due to its structure (having two carbonyl groups separated with one carbon atom), one of these properties is the conversion between two forms known as enolic and ketogenic tautomerism, as the enolic form is more stable than the ketogenic one and the tautomeric equilibrium can be affected Depending on various factors such as solvent polarity,[4] substitution groups[5,6] and environmental stimulation such as pH values and UV light irradiation.[7]

Due to the properties of β-diketones and their complexes, they have been widely used in both science and industry. these compounds are commonly employed in polymer technology, for example they serve as substrates for the production of both homogeneous and heterogeneous

catalysts, as well as polymerisation catalysts (metal complexes) and substances which modify the properties of resulting polymers, such as oxygen resistance and UV resistance, β-diketone complexes, particularly with transition metals, are commonly employed as catalysts of reactions, for example olygomerisation, ans olefin oxidation, and epoxidation.[8,9,10]

β-Diketones are widely utilized in analytical chemistry as a group of spectroscopic reagents due to their remarkable ability to form complexes. In addition, derivatives of these compounds play a pivotal role in the treatment of inflammatory diseases with antioxidant and antiviral properties.[11]

Many natural products, such as vanilla beans, [12] eucalyptus leaves,[13] sunflower pollen,[14] or licorice roots,[15] contain 1,3-diketones, also known as β-diketones. These compounds are known to exhibit a broad range of biological activities. Among the examples of 1,3-diketones, dibenzoylmethane and n-tritriacontane-16,18-dione are typical examples of this type of compounds.

Furthermore, β-diketones are frequently found as major components in plant skin waxes, which form an intriguing class of molecules present in wheat straw extracts. They are not limited to wheat, as β-diketones can also be found in various other grain crops, including barley, oats, and flax.[16]

2. MATERIALS AND METHODS

2.1. Materials

4-nitrobenzoic acid, propanol-1, sulfuric acid concentrated by the German company Merck, acetophenone, tetrabutyl ammonium hydroxide, dichloromethane, ethyl acetate, hexane, hydrochloric acid.

2.2. Apparatus

Spectrum NMR proton and carbon device 400 MHz model Bruker by Switzerland company. Optical absorption spectrum infrared device model FT-IR-4100 from the Japanese company Jasco.

2.3. Methods

Synthesis of propyl 4-nitrobenzoate

To a three-necked flask equipped with a mechanical stirrer, reflux condenser, and drying tube, (2 g, 1.2 mmol) of 4-nitrobenzoic acid is added. Then, (7.2 g,12 mmol) of propanol-1 is added in a molar ratio of (10:1). Next, (5% mol) of the acid catalyst "sulfuric acid" is added. The reaction mixture is stirred at a temperature of 110 °C. After stirring, the mixture is allowed to cool, Once the completion of the reaction. the solution was added NaOH (100 mL, 0.5 N) and extracted with ethyl acetate (2 x 50 mL). The organic layer was thoroughly washed with water (2 x 100 mL) and dried with anhydrous sodium sulfate. The solvent is evaporated sing a rotary evaporator under vacuum. An oily product is obtained with a yield of 81%.

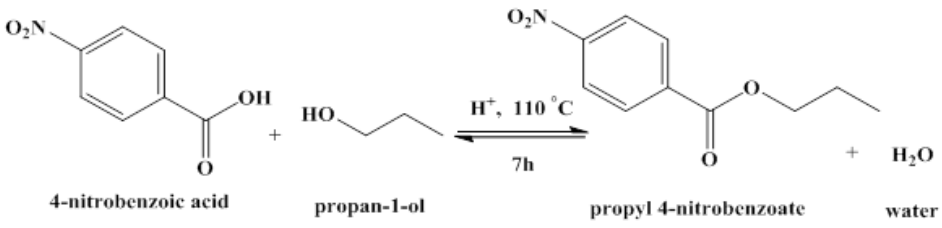
Synthesis of 1-(4-nitrophenyl)-3-phenylpropane-1,3-dione general procedure

To a three-necked flask equipped with a mechanical stirrer, reflux condenser, and drying tube, the mixture of tetrabutyl ammonium hydroxide (10% mol) and acetophenone (0.4 gr, 3 mmol) in CH_2CL_2 (30 mL) was placed. Then (0.68 g, 3 mmol) of propyl 4-nitrobenzoate was added. The reaction mixture was stirred at 45°C for about 14 hours, The progress of the reaction was monitored by TLC, Once the completion of the reaction, The reaction mixture is then left to cool to grade 5 and added to it 10ml of distilled water and 2 drops of concentrated hydrochloric acid is extracted using a dichloromethane solvent, and finally the organic phase is collected The solvent is evaporated sing a rotary evaporator under vacuum.The product was purified using Glass Plate Chromatography Yield: 76%.

3. RESULTS AND DISCUSSION

3.1. Preparation propyl 4-nitrobenzoate

The compound β-diketones were prepared in two stages. In the first stage, propyl 4-nitrobenzoate was synthesized by reacting 4-nitrobenzoic acid with Propanol-1 in the presence of a strong acid catalyst such as concentrated sulfuric acid, according to the following equation:



Scheme 2: Esterification of propanol-1 with 4-nitrobenzoic acid.

In order to confirm the reaction product, the infrared spectrum of the reaction product was recorded. The sample was prepared by mixing KBr powder well with the sample powder and then pressing it forcefully to obtain tablets. The infrared spectrum was then measured. Figure 1 displays the infrared spectrum of the prepared ester.

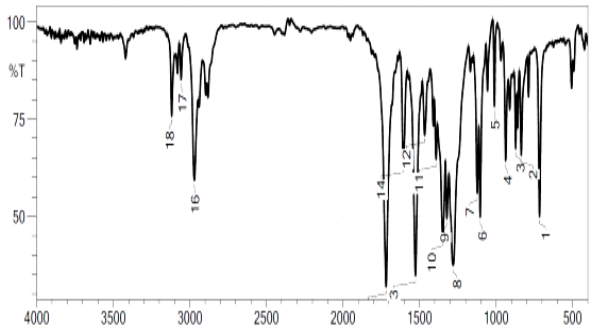
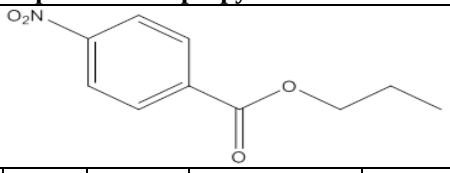


Figure 1 :The infrared spectrum of "propyl 4-nitrobenzoate".

In Table 1 we show the most important wavenumber values for the resulting ester.

Table 1: Interpretation of the infrared spectrum of "propyl 4-nitrobenzoate".



C-H Aromatic bent	CH_2 Bent	C-O-C	C=O	Csp^2–H	Csp^3–H	Functional group
716	1466	1280	1719	3119	2970	Wave number, cm^{-1}

Comparing the spectra of both 4-nitrobenzoic acid and the resulting ester, it is observed that the absorption band belonging to the carbonyl group in the product 1719 cm^{-1} shifts towards the larger wavenumbers compared to the acid 1693 cm^{-1}, which indicates the formation of the compound (see Figure 2).

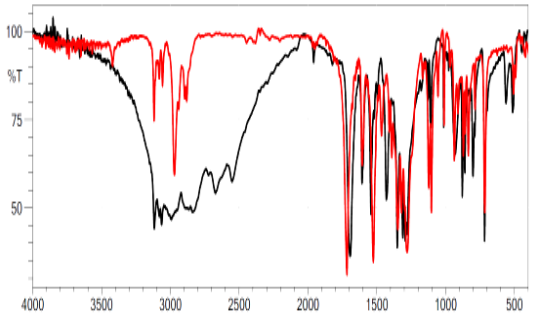
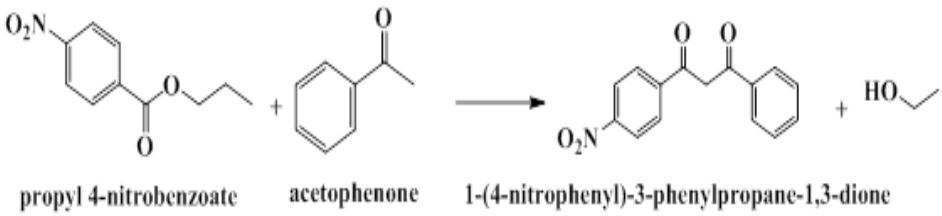


Figure 2: Overlay spectrum of 4-nitrobenzoic Acid and The product.

3.2. Preparation of β-Diketone derivative (DNM)

In the second stage of the reaction, a **DNM** was obtained by reacting propyl 4-nitrobenzoate with acetophenone in the presence of a suitable basic catalyst according to the following equation:



Scheme 3: Reaction of propyl 4-nitrobenzoate with acetophenone.

The structure of the resulting compound was determined by appropriate spectroscopic methods: (^{13}C–NMR, ^{1}H–NMR, FT–IR).

A. Infrared Spectroscopy FT-IR

The infrared spectrum of compound DNM (Figure 3) was recorded, showing distinct absorption attributed to the carbonyl group (C=O) at 1730 cm^{-1}.

Table 2 illustrates the corresponding wavenumber values for the infrared absorption bands of DNM compound.

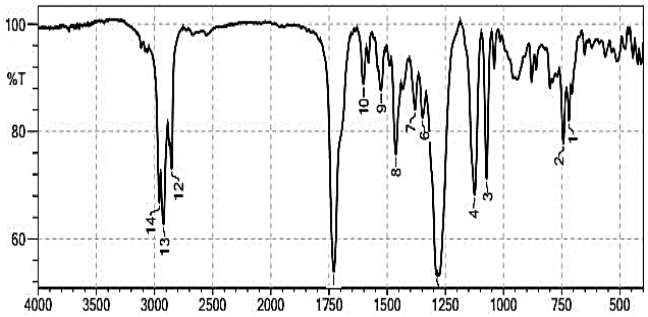
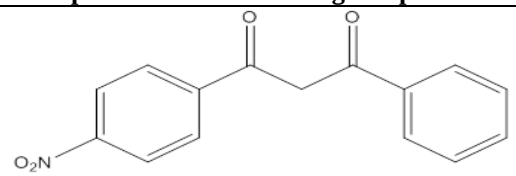


Figure 3: Infrared spectrum for DNM.

In Table 2 we show the most important absorption values for the resulting β-diketone.

Table 2: Interpretation of the infrared spectrum of the resulting compound.



C-H aromatic bent	CH_2 Bent	C=O	Csp^2–H	Csp^3–H	Functional group
719	1462	1730	3051	2922	Wave number, cm^{-1}

Comparing the spectra of both propyl 4-nitrobenzoate (**Figure 1**) and the resulting β-diketone (**Figure 3)**, it is observed that the absorption band belonging to the carbonyl group in the product shifts towards the larger wavenumbers compared to the ester, indicating the formation of the compound.

B. Proton nuclear magnetic resonance spectrum ^{1}H–NMR

The nuclear magnetic resonance ^{1}H–NMR spectrum of DNM was recorded using the diluted chloroform solvent, where a singlet signal for the protons of the methylene group is observed in the strong field, and in the weak field (δ_c = 7.54–8.35 ppm) it is observed that there are shifts due to the protons of the aromatic ring present in the compound.

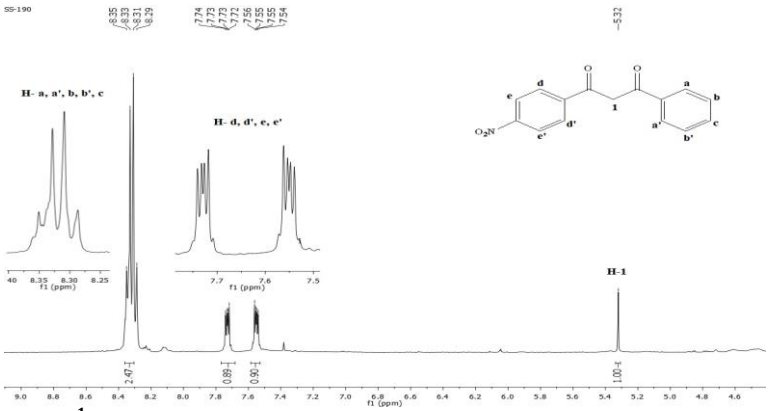


Figure 4: ^{1}H–NMR spectrum of DNM (400 MHz, $CDCl_3$, δTMS = 0 ppm).

Table 3: Interpretation of the proton nuclear magnetic resonance spectrum of the resulting compound.

Type of hydrogen atom	^{1}H-NMR, ppm	№
Aliphatic	5.32 (s, 2H)	1
Aromatic	7.54 -7.56 (q, 2H)	d,d′
Aromatic	7.72 – 7.74 (q, 2H)	e,e′
Aromatic	8.29 – 8.35 (q, 5H)	a,a′, b,b′,c

4. Study of Characteristics and Applications

A dichloromethane solution was prepared from the product of the previous reaction of the prepared product at a concentration of 0.05 gr/10mL, after which some physical properties were determined. The degree of density was measured by determining the weight of a precisely specified volume of the previous solution using a Pycnometer, in addition to determining the degree of turbidity using a device. Turbidity measurement, as Table 4 shows the values of some of the physical properties that were identified.

4.1. Measuring the degree of turbidity[17]

It is done using a turbidity measuring device, where 10ml of the solution is placed in a designated container and placed within the device, and the degree of turbidity of the prepared concentration is measured.

4.2. Density measurement[18]

This is done using a density meter and then applying the density relationship:

d=m/v

m: weight of solution (gr)

v: volume of solution (ml)

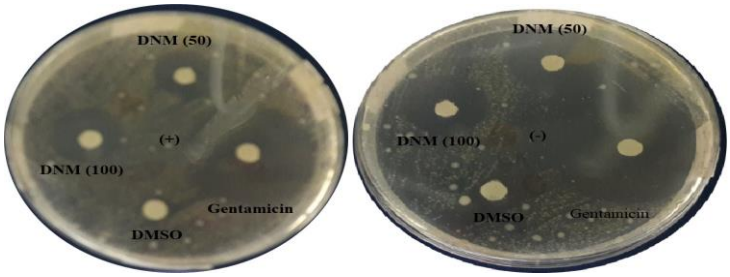
Table 4: Shows the results of studying the physical properties of the resulting compound and dichloromethane.

Degree of turbidity (FNU)	Density gr/ml	The sample
0	1.32	**CH_2Cl_2**
1.65	1.36	**DNM**

4.3. Study of biological properties

In this research, the effectiveness of the prepared compounds against two types of bacteria was studied (Gram-positive Staphylococcus aureus[19] and Gram-negative Escherichia coli[20]).

Solutions of the prepared product were prepared at a concentration of: (100,50) $\mu g \cdot ml^{-1}$ by dissolving it in a dimethyl sulfoxide solvent in order to determine the biological activity against E.coli and St.aureus bacteria, then a solution of TSB (Tryptic soy broth) was prepared This is done by dissolving (1.5 gr of it in (50 ml) distilled water, then heating it until the boiling point and leaving it until its temperature becomes (50–45 ºC). After the growth of the microorganisms, the culture medium is prepared using Nutrient Agar (NA) by dissolving (5.6 gr) of it in (200 ml) distilled water to obtain a concentration of 0.028 gr/l by heating the solution until it boils, then leaving it until it cools to (40–45 ºC), then pouring the solution into two Petri dishes and leaving it until it turns into gelatin, and then it is etched. Four wells in each dish, culture the bacteria, and then inject 10 µl of the compounds into the wells separately. After that, the length of the corona formed is measured after incubation for twenty-four hours at a temperature of 37 °C. The Figure 5 shows how the diameter of inhibition is formed.



St aureus (+) **E coli (-)**

Figure 5: The results of the biological tests for the product compared to the reference material.

Table 5 shows the value of the diameter of inhibition for each product prepared at the prepared concentrations and its comparison with the reference compound (gentamycin), where an average ability to inhibit the growth of negative bacteria and a better ability to inhibit the growth of positive bacteria is observed at the concentrations studied compared to the reference substance (gentamycin).

Table 5: Values of the damping diameters of the product compared to the reference material.

Compound		Concentration, C µg/ml	Damping diameter, mm
Bacteria (+)	Gyn	100	26
	DNM	100	13
		50	11
Bacteria (-)	Gyn	100	25
	DNM	100	12
		50	11

5. CONCLUSION

An aromatic derivative of β-diketones was synthesized in two stages. the first stage involved the esterification reaction of 4-nitrobenzoic acid 1-propanol, and the second stage involved the reaction of the resulting ester with acetophenone. the structures of the products were determined by modern spectroscopic methods. some physical properties, such as the degree of turbidity and density, were also determined, in addition, the biological properties of the resulting β-diketone were studied on two types of bacteria: gram-positive (Staphylococcus aureus) and gram-negative (Escherichia coli).

6. REFERACES

1. Smith L. Sensitization of Lanthanide Ions by Triarylboron Functionalized B-Diketones (Doctoral dissertation).
2. Olmstead WN, Bordwell FG. Ion-pair association constants in dimethyl sulfoxide. The Journal of Organic Chemistry, 1980; 45(16): 3299-305.
3. Hansen PE. Tautomerism of β-Diketones and β-Thioxoketones. Encyclopedia, 2023; 30, 3(1): 182-201.
4. Tumambac GE, Francis CJ, Wolf C. Configurational stability of 2-benzoylcyclohexanone: Unexpected solvent effects on the rate of racemization. Chirality: The Pharmacological, Biological, and Chemical Consequences of Molecular Asymmetry, 2005; 17(4): 171-6.
5. Jaafari A, Ouzeau V, Ely M, Rodriguez F, Chane-Ching K, Yassar A, Aaron JJ. Synthesis and optical properties of novel 1, 3-propanedione bearing oligothiophene substituents. Synthetic metals, 2004; 7, 147(1-3): 183-9.
6. Godsi O, Turner B, Suwinska K, Peskin U, Eichen Y. Enol− enamine tautomerism in crystals of 1, 3-Bis (pyridin-2-yl) propan-2-one: A combined crystallographic and quantum-chemical investigation of the effect of packing on tautomerization processes. Journal of the American Chemical Society, 2004; 20, 126(41): 13519-25.
7. Zhang X, Li ZC, Xu N, Li KB, Lin S, Lu FZ, Du FS, Li FM. β-Diketones bearing electron-donating chromophores and a novel β-triketone: synthesis and reversible fluorescence behavior. Tetrahedron letters, 2006; 10, 47(15): 2623-6.
8. Cullen WR, Wickenheiser EB. Rhodium (I) complexes of β-diketonates and related ligands as hydrosilylation catalysts. Journal of organometallic chemistry, 1989; 11, 370(1-3): 141-54.
9. Rao CD, Rase HF. Exchange-coupled clusters as catalyst precursors: comparison of monomeric and trimeric acetylacetonates. Industrial & Engineering Chemistry Product Research and Development, 1981; 20(1): 95-101.
10. Lewis FD, Miller AM, Salvi GD. Spectroscopy and Photochemistry of Nickel (II), Palladium (II), and Platinum (II). beta.-Diketonates. Inorganic chemistry, 1995; 34(12): 3173-81.
11. Kurbanova MM, Maharramov AM, Sadigova AZ, Gurbanova FZ, Mali SN, Al-Salahi R, El Bakri Y, Lai CH. Synthesis, Characterization, DFT, and In Silico Investigation of Two Newly Synthesized β-Diketone Derivatives as Potent COX-2 Inhibitors. Bioengineering, 2023; 27, 10(12): 1361.
12. Brunschwig C, Collard FX, Bianchini JP, Raharivelomanana P. Evaluation of chemical variability of cured vanilla beans (Vanilla tahitensis and Vanilla planifolia). Natural Product Communications, 2009; 4(10): 1934578X0900401016.
13. Gominho J, Lourenço A, Marques AV, Pereira H. An extensive study on the chemical diversity of lipophilic extractives from Eucalyptus globulus wood. Phytochemistry, 2020; 1, 180: 112520.
14. Schulz S, Arsene C, Tauber M, McNeil JN. Composition of lipids from sunflower pollen (Helianthus annuus). Phytochemistry, 2000; 1, 54(3): 325-36.
15. Mancia MD, Reid ME, DuBose ES, Campbell JA, Jackson KM. Qualitative identification of dibenzoylmethane in licorice root (Glycyrrhiza glabra) using gas chromatography-triple quadrupole mass spectrometry. Natural Product Communications, 2014; 9(1): 1934578X1400900127.
16. Noppawan P, Sangon S, Chatsiri P, Khunmood N, Aintharabunya S, Supanchaiyamat N, Hunt AJ. Sustainable solvents for β-diketone extraction from wheat straw wax and their molecular self-assembly into nano-structured tubules for hydrophobic coatings. RSC advances, 2023; 13(4): 2427-37.
17. Gillett D, Marchiori A. A low-cost continuous turbidity monitor. Sensors, 2019; 10, 19(14): 3039.
18. Viana M, Jouannin P, Pontier C, Chulia D. About pycnometric density measurements. Talanta, 2002; 24, 57(3): 583-93.
19. Taylor TA, Unakal CG. Staphylococcus Aureus. StatPearls. Publishing: Treasure Island, FL, USA. 2017.
20. Wu W, Jin Y, Bai F, Jin S. Pseudomonas aeruginosa. InMolecular medical microbiology, 2015; 1: 753-767. Academic Press.