GREEN APPROACH TOWARDS THE SYNTHESIS OF 1-PHENYL NAPHTHALENE LIGNAN AND THEIR DERIVATIVES

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Abstract-The use of green chemistry technique reduces the chemical waste and reaction time. Recently, it has been proved in several organic synthesis and chemical transformation. In present work, synthesis of 1-phenyl naphthalene fromβ-Benzoyl propionic acid, aryl aldehyde, acetic anhydride and pyridine was carried out and it was cyclised with PPA and sulphamic acid, by using microwave irradiation. It is a three step reaction. In first step synthesis of α-arylidineγ-phenyl δ,β-butenolide by perkin reaction, in second step synthesis of α-arylidine, β-BenzoylPropionic acid by cleavage using alcoholic sodium carbonate and In third step synthesis of 1-phenyl naphthalene by cyclisation using PPA , H_2SO_4, Sulphamic acid has been carried out. It has been observed that microwave irradiation method produces better yield and reduces the time period compared with conventional method. The structure of 1-phenyl naphthalene was confirmed by spectral and elemental analysis.

Keywords:Microwave irradiation, 1-phenyl naphthalene, PPA, cyclisation, green chemistry

1. Introduction

In the recent years, microwave assisted organic reaction have emerged as a new tool in organic synthesis. Microwaves are a form of electromagnetic radiation that falls at lower frequency end of electromagnetic spectrum, and lie in the 0.3-300 GHz frequencies and wavelengths ranging between 1mm-1m. The magnetic field interaction does not normally compared to the typical energy required to cleave a bond (80-120 kcal/mol):thus microwave do not affect the structure of an organic molecule. Microwave dielectric heating is dependent on the ability of a solvent or matrix to absorb microwave energy to convert into heat. The matrix absorbs radiation by two mechanism: dipole polarization and conduction. Important advantages of this technique include highly accelerated rate of reaction, reduction in reaction time with improvement quality and yield of the product. Moreover the technique is considered as “Green approach “towards chemistry of its ecofriendly nature.

Conventional methods of organic synthesis usually need longer heating time,elaborate and tedious apparatus setup, which result in higher cost of process and the excessive use of solvent/reagents leads to environmental pollution. Microwave irradiation produces efficient internal heating (in situ condition), resulting in even heating through the sample, as compared with the wall heat transfer that occurs when an oil bath is applied as an energy source. Microwave assisted organic synthesis (MAOS) has attracted a considerable amount of attention in the recent years by not only reducing chemical reaction times from hours to minutes but reducing side reaction, increasing atom economy and improves reproducibility.

1-phenyl naphthalene has been subject to great interest as it versatile moieties in that pendent like skeleton exist in a number of pharmaceuticals and natural product. 1-phenyl naphthalene attracted special attention to organic researchers. They have been used in medicinal purpose dating back to many thousand years. It has been great importance with regards to their synthesis and studiesof their physiological activities like reverse transcriptase inhibition, anti HIV, antimalarial, etc.

The Perkin condensation is the straightest forward and atom economic route to the synthesis of 1-phenyl naphthalene system.

2. Experimental:

All the chemicals used were obtained from Aldrich(*Sigma-Aldrich, St.louis, MO, USA*), Lancaster (*Alfa Aesar Johnson Matthey company, Ward Hill, MA, USA*) while the reagents and solvents were of analytical grade. Reaction was monitored by TLC, performed on silica gel glass plates containing 60 GF-254 using chloroform: methanol (8:2/9:1) solvent system, and visualization on TLC was achieved by UV light or iodine indicator.^{1}H and ^{13}C spectra were recorded Bruker UXNMR/XWIN-NMR (300 MHz) instruments. Heating was done in a microwave (LG Smart chef MS-255r operating at 2450 MHz and 800W). Melting points were determined with an Electro thermal melting points apparatus.

2.1 Green synthesis of 1-Phenyl Naphthalene

2.1.1 Synthesis of α-Arylidine β-Benzoyl Propionic Acid

I Synthesis of β-Benzoyl Propionic acid

After suspending anhydrous aluminum chloride (0.15 mol) in dry benzene (50 ml) under anhydrous conditions. The content was refluxed on a water bath succinic anhydride (0.10 mol) was then added to the reaction mixture in small portions with continuous stirring was continued for 6 hrs after leaving overnight at room temperature. Ice cold solution of concentrated hydrochloric acid (2.5% v/v) was added for the reaction mixture which was then concentrated

to a small volume by heating on a water bath. The solid compound which separated out, was filtered. It was purified by dissolving in 5% w/v sodium bicarbonate solution, followed by extraction with ether. The aqueous layer on acidification with dilute hydrochloric acid gave β-Benzoyl Propionic Acid, crystallized from aqueous ethanol to give a colourless compound.[1-3]

II. Perkin condensation of β- Benzoyl Propionic Acid and aryl aldehyde

Conventional Method

β- Benzoyl Propionic Acid(1) and aryl aldehyde (2) were refluxed with acetic anhydride and a drop of pyridine for 3 hours. The hot reaction mixture was poured in cold water with stirring and then acidified with concentrated HCl. The yellow mass obtained was filtered and crystallized with benzene to give α-Arylidineγ-Phenylδ,β-Butenolide(3). Its IR showed absorption at 1765 cm^{-1}. Melting point 124^0 c

Table-1: Characterization and spectral analysis ofα-Arylidine-Phenyl δ, β-Butenolide (3).

Sr. No.	Aryl aldehyde β-Aroyl Propionic Acid	Butenolide (Mol. Formula)	Yield % (m.p.0^0c)	IR (cm^{-1})
1	Anisaldehyde β-Benzoyl Propionic Acid	3a ($C_{18}H_{14}O_3$)	82.7 (150)	1765
2	Vertraldehyde β-Benzoyl Propionic Acid	3b ($C_{19}H_{16}O_4$)	73.3 (125)	1762
3	Benzaldehyde β-Benzoyl Propionic Acid	3c ($C_{17}H_{12}O_2$)	75 (153)	1762
4	Vanillin β-Benzoyl Propionic Acid	3d ($C_{18}H_{14}O_4$)	85.6 (147)	1760

Microwave Method

β- Benzoyl Propionic Acid (1) and aryl aldehyde (2) Was taken in a beaker with a glass rod with an inverted funnel. It was irradiated with acetic anhydride and a drop of pyridine by radiations of microwave oven 800W for 20 minutes. After completion of the reaction the immediate temperature of the reaction, mixture was taken out by the thermometer which is recorded as 55^0c. The hot reaction mixture was poured in cold water with stirring. Further it was acidified with concentrated HCl. The yellow mass obtained was filtered and crystallized with benzene to give α-Arylidine-Phenyl δ,β-Butenolide (3). Its IR showed absorption at 1762 cm^{-1}. The Melting point 124^0 c.[4-5]

2.2 Synthesis of α-Arylidine β-Benzoyl Propionic Acid from α-Arylidine γ-Phenyl δ, β-Butenolide

Conventional Method

α-Arylidine γ-Phenyl δ, β-Butenolide(3) was refluxed for 5 hrs with alcoholic sodium carbonate solution (prepared by dissolving 1gm anhydrous sodium carbonate in 4 ml methanol and 6ml water).The resulting mixture was filtered, cooled and acidified with concentrated HCl to get brown precipitate which was crystallized with aqueous methanol and was identified as α-Arylidineβ-Benzoyl Propionic Acid (4). Its IR spectra showed absorption at 1681 cm^{-1}. Melting point-168^0c.

Microwave Method

α-Arylidineγ-Phenyl δ,β-Butenolide(3) and alcoholic sodium carbonate solution (prepared by dissolving 1 gm anhydrous sodium carbonate in 4 ml methanol and 6ml water). Was taken in a beaker with a glass rod with an inverted funnel. It was irradiated by radiations of microwave oven 800W for 19-20 minutes. After completion of the reaction the immediate temperature of the reaction, mixture was taken out by the thermometer which is recorded as 69^0c.The resulting mixture was filtered, cooled and acidified with concentrated HCl to get brown precipitate which was crystallized with aqueous methanol and was identified as α-Arylidineβ-Benzoyl Propionic Acid (4). Its IR spectra showed absorption at 1681 cm^{-1}. Melting point-167^0c.

Table-2: Characterization and spectral analysis ofα-Arylidineβ-Benzoyl Propionic Acid (4).

Sr. No.	α-Arylidineβ-Benzoyl Propionic Acid	Eq.Wt. Observed (Requiered)	m.p. ^{o}c m.f.	IR (cm^{-1})
1	4a	294 (296)	167 ($C_{18}H_{16}O_4$)	1685
2	4b	323 (326)	168 ($C_{19}H_{18}O_4$)	1681
3	4c	263 (265)	169 ($C_{17}H_{14}O_3$)	1680
4	4d	317 (312)	205 ($C_{18}H_{16}O_5$)	1681

2.3 Synthesis of 1-Phenyl Naphthoic Acid

Cyclization of α-Arylidine β-Benzoyl Propionic Acid to 1-Phenyl Naphthoic Acid using PPA

Conventional Method

α--Benzoyl Propionic Acid(4) was refluxed with polyphosphoric acid (PPA) at 100^0 for 1 hr . the mixture was poured on crushed ice when the solid precipitated. It was crystallized with aqueous ethanol and identified as 1-Phenyl Naphthoic Acid(5). Its IR showed absorption at 1680 cm^{-1}. Melting point-216^0c.

Table-3: Elemental and Spectral analysis of 1-phenyl naphthoic acid

Sr. No.	1-phenyl naphthoic acid	Eq.Wt. Observed (Requiered)	m.p (^{o}c) m.f.	IR (cm^{-1})
1	(5a) $R_1=R_2=R_4=R_5=H$ $R_3=OCH_3$	277 (278)	211 ($C_{18}H_{14}O_3$)	1682
2	5(b) $R_1=R_4=R_5=H$ $R_2=R_3=OCH_3$	305 (308)	217 ($C_{19}H_{16}O_4$)	1680
3	(5c) $R_1=R_2=R_3=R_4=R_5=H$	247 (249)	198 ($C_{17}H_{12}O_2$)	1680
4	(5d) $R_1=R_4=R_5=H$, $R_2=OCH_3$, $R_3=OH$	291 (294)	179 ($C_{18}H_{14}O_4$)	1681

Microwave Method

α-Arylidine β-Benzoyl Propionic Acid(4) was refluxed with polyphosphoric acid (PPA) was taken in a beaker with a glass rod with an inverted funnel. It was irradiated by radiations of microwave oven 800W for 4-5 minutes. After completion of the reaction the immediate temperature of the reaction, mixture was taken out by the thermometer which is recorded as 75^0c. The mixture was poured on crushed ice when the solid precipitated. It was crystallized with aqueous ethanol and identified as 1-Phenyl Naphthoic Acid(5). Its IR showed absorption at 1680 cm^{-1}. Melting point- 216^0c.

2.4 Synthesis of 1-Phenyl Naphthalene from α-Arylidine β-Benzoyl Propionic Acid

2.4.1 Preparation ofDiazomethane

Nitrosomethyl urea (3 gm) and sodium hydroxide (3) was taken in beaker and it was kept in ice bath to maintain its temperature at o^{o}c. it was kept the resulting mixture contain diazomethane (CH_2N_2).

2.4.2. Synthesis Methyl α-Arylidineβ-Benzoyl Propionate from α-Arylidineβ-Benzoyl Propionic Acid

To a suspension of α-Arylidineβ-Benzoyl Propionic Acid(4) in ether was added a solution of CH_2N_2 in the ether solution was washed with water sodium bicarbonate and dried (anhydrous) sodium sulphate. Evaporation of solvent leads to a yellow oil which was crystallized from methanol and identified as methyl α-Arylidineβ-Benzoyl Propionate(6). Its showed absorption at 1680 cm^{-1} .Melting point-94^0c.[6]

Table-4: Elemental and spectral analysis of 1-phenyl naphthoates.

Sr. No.	1-phenyl naphthoates	m.p (^{o}c) (m.f.)	IR (cm^{-1})	Percentage (%) yield
1	1-phenyl 3-carbomethoxy 6-methoxy naphthoate	123 (C19H18)	1721	89.2
2	1-phenyl carbomethoxy-6,7 methoxynaphthoate	122	1720	88.7
3	1-phenyl 3-carbomethoxy naphthoate	120	1722	88.5
4	1-phenyl 3-carbomethoxy 6-methoxy 7-hydroxy naphthoate	124	1720	85

2.4.3. Cyclization Methyl α-Arylidine β-Benzoyl Propionate to 1-Phenyl Naphthalene

Conventional Method

Methylα-Arylidineβ-Benzoyl Propionate(5) was refluxed with PPA at 100^0c for 1 hour. The mixture was poured in crushed ice when the solid precipitated. It was crystallized with aqueous ethanol and identified as 1-Phenyl 3-Carbomethoxy Naphthoate (6). Melting point-123^0c.[7]

Microwave Method

Methylα-Arylidineβ-Benzoyl Propionate(5) and PPA was taken in a beaker with a glass rod with an inverted funnel. It was irradiated by radiations of microwave oven 800W for 4-5 minutes. After completion of the reaction the immediate temperature of the reaction, mixture was taken out by the thermometer which is recorded as 73^0c. The mixture was poured in crushed ice when the solid precipitated. It was crystallized with aqueous ethanol and identified as 1-Phenyl 3-Carbomethoxy Naphthoate (6). Melting point-123^0c.[8]

Result and discussion

To Green synthesis of 1-Phenyl Naphthalene, β-Benzoyl Propionic Acid was used which has two reactive methylene group and a carboxylic functional group which could lead to the basic skeleton of lignan. The carbonyl group yield part of furan ring and the oxo group could be reduced.

In reported methods, Perkin condensation reactions were carried out by conventional heating mental for three hours refluxed using pyridine as a catalyst. The traditional heating techniques are however, rather slow and a temperature gradient can develop within the sample. In addition, local overheating can lead to product, substrate and reagent decomposition that is why we have turned towards microwave heating to overcome the above mentioned disadvantages as in

microwave dielectric radiation passes through the walls of the vessels and heat only the reactants and solvents, not the reaction vessel itself, which can lead to less by products and or decomposition products.[9] β-Benzoyl Propionic Acid underwent Perkin as well as Stobbe condensation due to the presence of two reactive methylene groups. The above condensation reactions are restricted to aldehyde having hydroxyl, methoxy or methylenedioxy groups in para position.

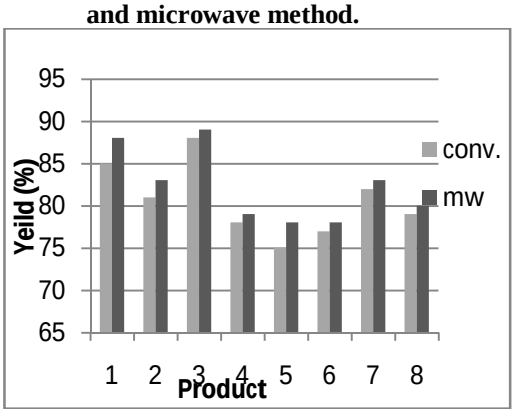
To extend the scope of reaction and to generalize the procedure, we carried out the reaction of β-Benzoyl Propionic Acid (1) with a series of aryl aldehyde like anisaldehyde(2a), varatraldehyde (2b), benzaldehyde (2c), vanillin (2d), to obtain the butenolide (3a-d) and corresponding α-Arylidineβ-Benzoyl Propionic Acid (4a-d).The lactone ring of butenolide was then opened with alcoholic sodium carbonate to give the keto acid which was identified as α-Arylidine β-Benzoyl Propionic Acid.

Encouraged the outcome of our Cyclization reactions by green chemistry, we next planned to investigate the effects of various reaction parameters.

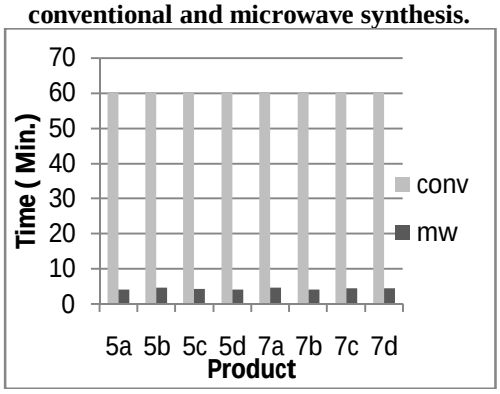
Table-5: Comparative data of conventional and microwave synthesis of 1- Phenyl naphthalene systems.

Sr. No.	Product	Time(min)		%yield		Melting Point (0^oc)
		PPA		PPA		
		CONV	MW	CONV	MW	
1	5a	60	4	85	88	216
2	5b	60	4.5	81	83	217
3	5c	60	4.2	88	89	176
4	5d	60	4	78	79	179
5	7a	60	4.5	75	78	171
6	7b	60	4.1	77	78	124
7	7c	60	4.4	82	83	132
8	7d	60	4.3	79	80	152

Graph-1: Comparison for %yield in conventional and microwave method.



Graph-2: Comparison for time required in conventional and microwave synthesis.



4. Conclusion

The classical Perkin reaction of β-Benzoyl Propionic Acid consists of heating with aromatic aldehyde, acetic anhydride and pyridine a catalyst. It takes long periods and the products are obtained in low yield. In this process, we have developed a newer route in which an efficient Perkin reaction is performed in this microwave method. Microwave irradiation provides a way for flash heating as an alternative to standard thermal heating in chemical reactions. This technology has been employed to drastically reduce reaction times to save energy and even modify selectivity. In addition to this feature. The use of microwave irradiation outperform conventional reaction conditions in other aspects, such as easier workup, reduction of the usual thermal degradation products. Thus the alternative MW-assisted method was found to be more convenient over that of conventional, to produce butenolide in terms of considerable reduction in reaction time, improved yields and facile nature of the reaction.

We are successful inn finding an analogous cyclization reaction which can be performed under natural and mild conditions in the presence of catalytic amount of PPA and Sulphamic acid under the cooperative effect of microwave irradiation. It is seen that due to drastic reaction conditions, the classical intermolecular cyclodehydration reaction has been plagued by a number of serious disadvantages. So, we are seeking a new method involving method involving factors such as reduced pollution low cost and simplicity in processing, which are beneficial to industry as well as to environment. That is why our procedure convenient and highly efficient since the titled compounds are produced in good to excellent yields after short reaction times. Consequently, our method can be a viable alternative to the presently existing procedures.

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