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A Simple, Solvent Free Synthesis of 3-(Bis(4-Chlorophenyl) Metheylene) - Ethoxy-5-Oxopentanoic Acid and its Antimicrobial Activity

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ABSTRACT

A Simple and solvent free synthesis of alkylidene acid esters by using a mixture of 4, 4 -dichloro-benzophenone and Diethyl succinate was treated with tert.potassium butoxide at room temperature. The synthesis of alkylidene acid esters and their different compounds are very popular in the world of synthetic organic chemistry due to their activities such as antibacterial, antiviral and anti-inflammatory. The reaction remained ignored almost for a century, but with the confirmation that alkylidene acid esters possess diverse and important biological properties, the intrest in their synthesis has been greatly increased from last decade. In the conclusion, we have developed a simple and solvent free method for the synthesis of compounds containing benzophenone moieties were successfully synthesized in excellent yield and their structures are elucided using elemental analysis and FTIR, 1H-NMR spectral analysis. The result of antimicrobial activity reveals that the newly synthesized compound found to have moderate to outstanding antimicrobial effect against various bacteria at all concentrations analyzed.

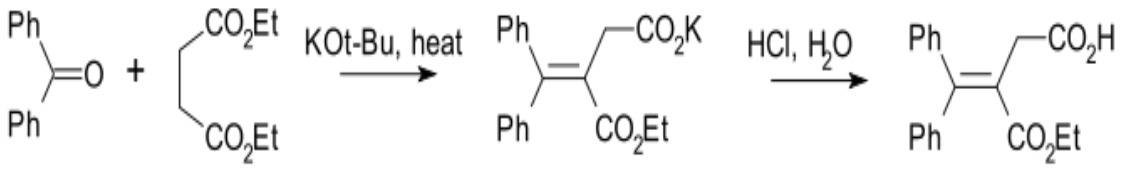
Keywords: Benzophenone, tert. potassium butaoxide, diethyl succinate, 4,4 dichlorobenzophenone, antimicrobial activities etc.

I. INTRODUCTION

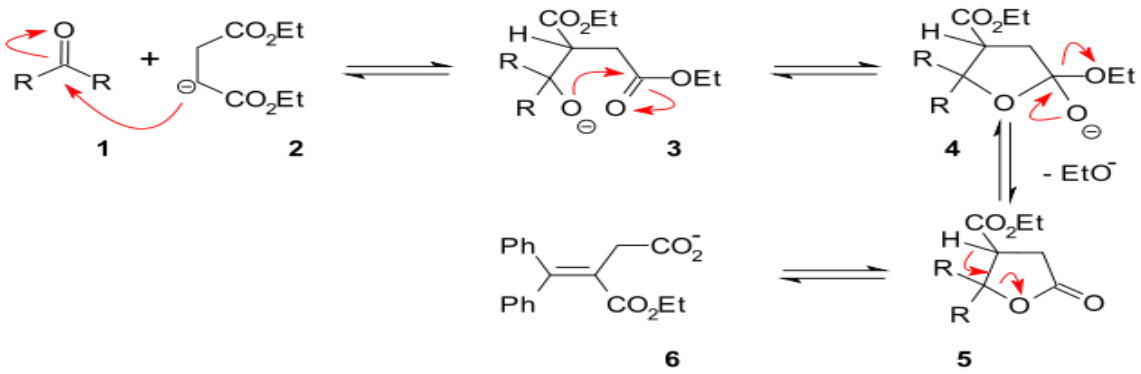
In 1893 Hans Stobbe[1] demonstrated that when a mixture of acetone and diethyl succinate was treated with sodium ethoxide the expected acetoacetic ester type of condensation to give a 3-diketo compound, which do not take place; but the main reaction product was Teraconic acid, formed by an aldol type of condensation between the carbonyl group of the ketone and a methylene group of the ester. This reaction was indeed surprising in view of the numerous precedents from the work of Claisen for the former type of behavior. It is striking that this facile aldol type of condensation of esters with ketones is limited to succinic and substituted succinic esteia, with few exceptions. Benzophenone condenses with diethyl succinate to give pure 3-

carbethoxy-7,substitued-diphenyl-vinyl-acetic acid[2] in under the same conditions this ketone in contrast fails altogether to react with ethyl or t-butyl acetate[3].

1) The Stobbe condensation is the reaction in which diethyl ester of succinic acid requiring less strong bases. For example, its reaction with benzophenone as follows:



2) A reaction mechanism that explains the formation of both an ester group and a carboxylic acid group is centered on a lactones intermediate:



Benzophenone is widely used as photo initiator for inks and lacquers that are cured with ultraviolet light. In the area of food packaging UV-cure inks and lacquers are used without solvent and they contain typically 5–10% photo initiator. UV-cure lacquers are commonly employed either as varnishes for UV-cure printing or as varnishes for materials printed by other processes. Benzophenone is not completely used up or removed during or after the printing process, nor is it bound irreversibly into the print film layer.

In these reaction systems, good to excellent yields (up to 97%) of acylation products were obtained in a short reaction time. This method features high yield, a simple product isolation procedure, ILs reusability and reduced waste discharge, thus rendering this catalytic system both efficient and environment friendly.

K. Amimoto and etals studied photochromism of organic compound and found Fulgides are important for their photochromic properties[4-5]stobbe condensation[6-7] S. Banerjee &etalsstadied green synthesis of acid ester they reacted different substituted carbonyl compound including aldehyde, aromatic and alicyclic, aliphatic ketones and an active methylene group namely dimethyl succinate were condensed in anhydrous condition and found the reaction is feasible in a dry agate mortar at room temperature, avoiding hazards of using solvent[8].

Yadav Hanumansingh *et al*[9] synthesized by greener chemical reaction strategy managed to synthesize Fulgenic acid successfully by simple and efficient means with improved yield.

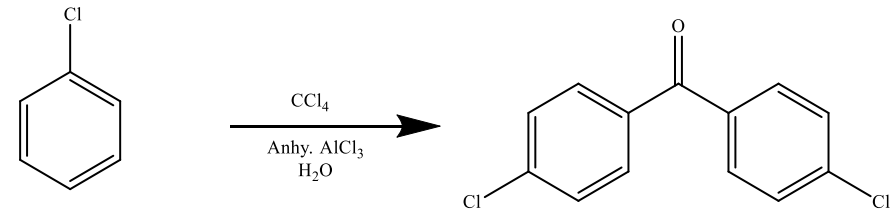
II. EXPERIMENTAL METHOD

i) Synthesis of dichloro benzophenone and its derivatives

A mixture of chlorobenzene react with of carbon tetrachloride in presence of alluminiumchloride .This mixture was refluxed for 3-4 hours, after cooling the reaction mixture poured in ice-cold water with stirring till precipitation was complete.Melting point of compound - 139°CPercentage of yield is 41%

Reaction

PRG 1



chlorobenzene

bis(4-chlorophenyl)methanone

Properties of compound:

1) Element detection: Presence of halogen :Sodium extract + dilute H_2SO_4 + boil + dilute HNO_3+ 1% $AgNO_3$, a heavy curdy white ppt of silver chloride is obtained.

2) Group detection: ***Test for –CO of ketone.*** Dissolve a small quantity of sodium nitroprusside in about of 1 ml of distilled water in a clean test tube and then add a small quantity of given compound. Shake the test tube well and add sodium hydroxide solution drop wise. Appearance of red colour confirmed the presence of ketonic group.

3) Percentage of elements:

%C	%H	% Cl	%O
62.18	3.21	28.24	6.37

4) Spectral analysis:IR spectral Study

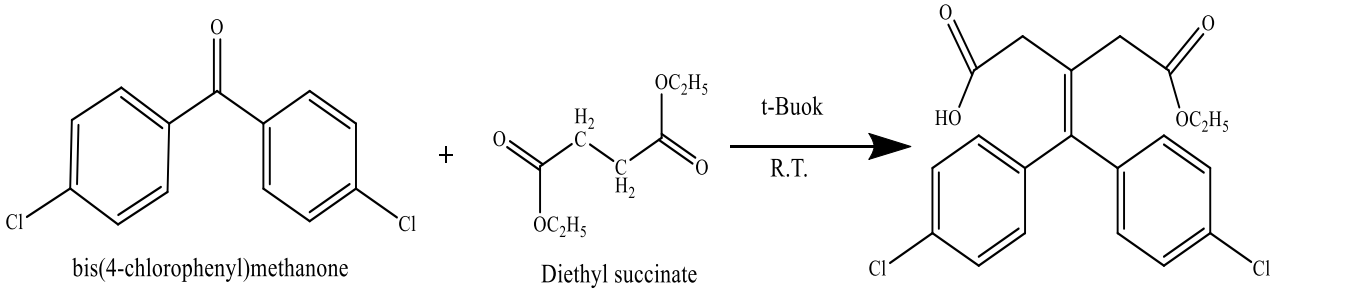
The main absorption bands observed in IR spectrum of compound are shown below.

Abs. Observed (cm^{-1})	Assignment	Absorption expected
1485 cm^{-1} 1734 cm^{-1}	C=C Ringstretch C=O stretch	1600 – 1475 1715-1810

ii) Synthesis of derivative of 4,4 dichloro benzophenone.

A mixture of 4, 4 dichlorobenzophenone and Diethyl succinate was treated with tert.potassim butoxide at room temperature.

Reaction :



bis(4-chlorophenyl)methanone

Diethyl succinate

3-(bis(4-chlorophenyl)methylene)-5-ethoxy-5-oxopentanoic acid

Properties of compound:

1) Element detection: Presence of halogen:Sodium extract + dilute H_2SO_4 + boil + dilute HNO_3+ 1% $AgNO_3$, a heavy curdy white ppt of silver chloride is obtained.

b) Presence of halogen: Sodium extract + dilute H_2SO_4 + boil + dilute HNO_3+ 1% $AgNO_3$, a heavy curdy white ppt of silver chloride is obtained.

2) Group detection: *Test for –CO of ketone.*Dissolve a small quantity of sodium nitroprusside in about of 1 ml of distilled water in a clean test tube and then add a small quantity of given compound. Shake the test tube well and add sodium hydroxide solution drop wise. Appearance of red colour confirmed the presence of ketonic group.

3)Percentage of elements

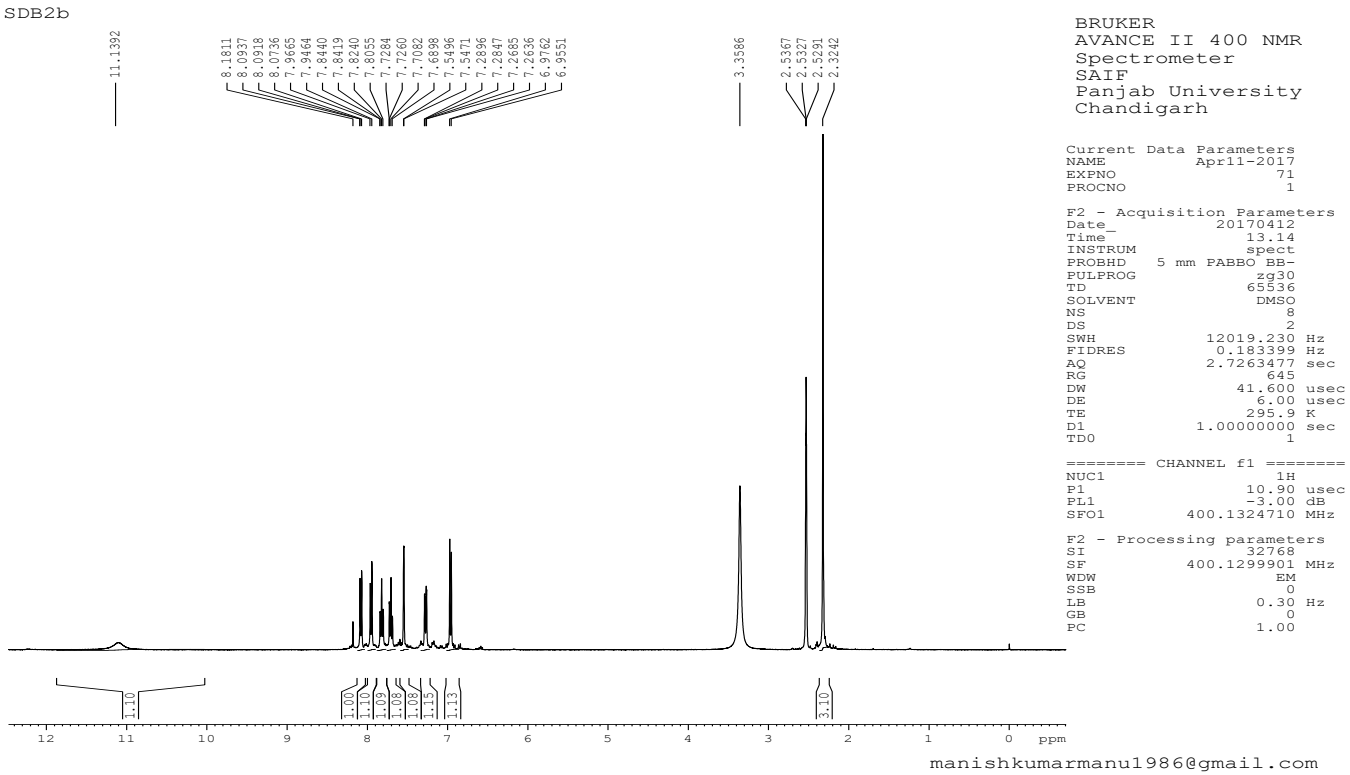
%C	%H	% Cl	%O
61.08	4.61	18.03	16.27

4) Spectral analysis:IR spectral Study:

The main absorption bands observed in IR spectrum of compound are shown below.

Abs.Obs. (cm^{-1})	Assignment	Abs. expected
1494cm^{-1}	C=C Ring stretch	1600 -1475
1719cm^{-1}	C=O stretch of -COOH	1700-1725
1749cm^{-1}	C=O stretch of Ester	1735-1750

NMR spectral study:*[1]NMR spectrum shows signals due to three C-H proton of ester at δ 3.35 ppm, singlet due to one hydrogen atom of –COOH at δ 11.13 ppm and aromatic eight protons multiplate at δ6.95-8.18 ppm.*



III. ANTIMICROBIAL ACTIVITY OF SYNTHESISED COMPOUND

In the 20thcentury antibiotics are undeniably one of the most imperative therapeutic discovery that improved or alleviate in human beings that had been effective against serious bacterial infections. The advancement in science and technology occurs in four decades so remarkable progress had been made in the field of medicine with the discoveries of many natural and synthetic drugs[10]. However, only one third of the infectious diseases known have been treated from these synthetic products[11]. This is because of the emergence of resistant pathogens that is beyond doubt the consequence of years of widespread indiscriminate incessant and misuse of antibiotics[12-13].The antibacterial activities of the compounds synthesized in were tested to evaluate their efficiencies against pathogenic organisms.

i) First the substance to be evaluated must be brought in an intimate contact with the test organisms against which activity is to be estimated.
ii) Secondly, favourable conditions (nutritional, environmental etc.) must be provided to offer a maximum opportunity for optimum growth of the organisms in absence of antimicrobial agent and
iii) Thirdly, there should be a method for measuring antibacterial response obtained by antimicrobial agent[14].

The antimicrobial activities of the synthesized compounds against *Escherichia coli*is highly remarkable, synthesized compound was highly active than*, Staphylococcus aureus, E.Aerogenes*and *Salmonella typhi.* The synthesized drugs can be used the alternative drugs for the treatment of diseases caused by*E.coli*.

E. Coli	*S. Typhi*	*S. Aureus*	*E. Aerogenes*
Active	Active	Active	Active

IV. RESULTS AND DISCUSSION

In the present work substituted -benzophenone viz. 4, 4 dichloro-benzophenone by reacting them with diethyl succinate. Reaction was carried out in the presence of tertiary potassium butoxide. The reaction mixture stirred for 50 – 60 minutes at the room temperature. The product so obtained is filtered washed with water and crude product were recrystallized from 80% ethanol. The structure of these compounds was confirmed by FT-IR, 1H-NMR, and elemental analysis techniques. Spectral data were in good agreement with the composition of the synthesized compounds.

V. CONCLUSION

Compound containing benzophenone moiety was successfully synthesized in excellent yield; their structureis elucidated using elemental analysis, FTIR, 1HNMR spectral analysis. The result of antimicrobial activity reveals that all newly synthesized compound found to have moderate to outstanding antimicrobial effect against *E.coli, S.aureus, E.aerogenes*and *Salomonella typhi* at all the concentrations analysed. Thus it is concluded that these newly synthesized alkylidene acid ester can be usedfor the development of new antibacterial drugs to cure many disorders caused by different bacterial species.

VI. ACKNOWLEDGMENT

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