A THESIS

Entitled

CONDENSATION OF HOMOPHTHALIC ESTERS WITH CARBONYL COMPOUNDS

"Stobbe condensation of aromatic aldehydes with dimethyl homophthalate"

Presented by

AFAF ABDEL MEGIED EL-BIEH
B.Sc.

In partial fulfilment of
the Degree of Master of Science

Faculty of Women
Ain Shams University

1971

[illegible]
FACULTY OF SCIENCE
CHEMISTRY DEPARTMENT

STOBBE CONDENSATION OF AROMATIC ALDEHYDES WITH DIMETHYL HOMOPHTHALATE

Thesis Adviser
Prof. A.M. El-Abbady

Approved
A.M. El Abbady
10/1/1972

W.I. Awad

Prof. W.I. Awad
Head of the Chemistry Department

بسم الله الرحمن الرحيم

[illegible]

Beside the work carried out in this thesis the candidate has attended post graduate course for two years in organic chemistry including the following topics:

1) Reaction mechanisms.
2) Spectroscopy of organic molecules.
3) Microanalysis.
4) Chemistry of heterocyclic compounds.
5) Organic reactions.

She has successfully passed an examination in these topics.

W. I. Awad.

Prof. W.I. Awad
Head of Chemistry Department

ACKNOWLEDGEMENT

The author wishes to express her thanks and deep gratitude to Professor [illegible] A[illegible]ad, D.Sc., Head of Chemistry Department, Faculty of Women, Ain Shams University, for the facilities he put at her disposal.

The author is grateful to Professor A.M. El-Abbday, Head of the Chemistry Department, Faculty of Science at Tanta, Alexandria University, for suggesting the problem for his invaluable guidance, helpful criticism and for revising this manuscript.

Thanks are also due to Dr. A.H. Moustafa, Faculty of Science, Ain Shams University, for his great help and discussions and to Dr. M. Wassof, Faculty of Women, for measuring the I.R. and U.V. spectra.

CONTENTS

Page

SUMMARY i

LIST OF NEW COMPOUNDS iii

INTRODUCTION

A- Stobbe Condensation:

I. General Character 1

II. Mechanism 2

III. Scope of the Reaction 5

1) Carbonyl compounds 6

(i) Aliphatic, aromatic and α,β-unsaturated aldehydes ... 6

(ii) Aliphatic, alicyclic and aromatic ketones 6

(iii) Diketones 8

(iv) Keto esters 9

(v) Cyanoketones 9

2) Succinic Esters and their derivatives 10

3) Condensing agents 10

B- Stobbe Type Condensation;

1) Condensation of tert-butyl acetate with o-benzoyl benzoic esters 11

2) Condensation involving carballylic esters 11

3) Condensation involving β-aroyl-propionic esters 12

4) Condensation involving glutaric and analogous esters 12

a- Glutaric esters 12

b- Thioglycolic esters 13

c- Methyl glutaconic esters ... 14

d- Homophthalic esters 14

C- Elucidation of Structures and Configurations :

1) Stereoisomeric half-esters from aromatic aldehydes 20
2) Stereoisomeric alkylidene succinic acids from alkyl aryl ketones ... 20
3) The double bond in the half-esters and diacids 21

D- Stobbe Condensation Products and Geometrical Isomerism

1) Geometrical isomerism 26
2) Determination of configuration of geometrical isomers 28
    (i) The formation of cyclic derivatives 28
    (ii) Chemical correlation 31
    (iii) Spectral properties 32
3) Relative proportions of the stereoisomeric products in Stobbe condensation 37

DISCUSSION 45

EXPERIMENTAL PART 67

REFERENCES 120

ARABIC SUMMARY

-oOo-

SUMMARY

Condensation of benzaldehyde, o-methoxy-, p-methoxy- and p-chlorobenzaldehyde with dimethyl homophthalate in presence of potassium *tert*-butoxide gave the corresponding half-esters methyl α-(o-carboxyphenyl) aryl cinnamate. Benzaldehyde and o-methoxy benzaldehyde gave each one half-estr in the cis-form, but two isomeric half-esters (cis and trans) were obtained in a good yield in case of p-methoxy and p-chlorobenzaldehyde.

The alkaline hydrolysis of all these half-esters gave the corresponding dibasic acids cis- and trans-α(o-carboxyphenyl)arylcinnamic acids.

On treatment these dibasic with acetyl chloride the corresponding anhydrides cis- and trans-α-(o-carboxyphenyl) arylcinnamic anhydrides were obtained, which on treatment with absolute methyl alcohol gave the corresponding isomeric half-ester cis- and trans-α-(o-carbomethoxyphenyl)-arylcinnamic acids.

The cis- half-esters on cyclisation using phosphorus oxychloride gave the corresponding 3-carboxy-2-arylinden-1-ones, which were decarboxylated very easily giving 2-aryl-inden-1-ones. Cyclisation of the cis-isomeric half-esters

gave the corresponding [illegible] cases, while trans-α-(o-[illegible]oxyphenyl)-[illegible] cinnamic acid gave back the anhydride.

Alkaline hydrolysis of the carbomethoxyphenyl-indenones gave in all cases an acidic product which differ from the cyclised products of the half-esters.

Cyclisation of α-(o-carboxyphenyl)aryl-cinnamic acids gave the corresponding anhydrides, but in case of the trans dibasic acid of p-methoxybenzaldehyde the cis-dibasic acid was obtained.

Lactonisation of the half-esters gave 4-carboxy-3-aryl-3,4-dihydroiso coumarin in all cases.

Reduction of the half-esters using sodium metal and absolute ethyl alcohol gave in all cases methyl aryl-2-(o-carboxyphenyl)propanoates in a good yield.

Alkaline hydrolysis of the reduced half-esters gave 2-(o-carboxyphenyl)-3(aryl)propanoic acids, which were then converted to anhydrides.

Treatment of these anhydrides with absolute methyl alcohol gave the corresponding isomeric half-esters, (2(o-carbomethoxyphenyl)-3-(aryl)propanoic acids.

LIST OF THE COMPOUNDS

1) cis-Methyl α-(o-carboxyphenyl)-o-methoxycinnamate.
2) cis-Methyl α-(o-carboxyphenyl)-p-methoxycinnamate.
3) trans-Methyl α-(o-carboxyphenyl)-p-methoxycinnamate.
4) cis-Methyl α-(o-carboxyphenyl)-p-chlorocinnamate.
5) trans-Methyl α-(o-carboxyphenyl)-p-chlorocinnamate.
6) cis α-(o-Carboxyphenyl)-p-methoxycinnamic acid.
7) trans α-(o-Carboxyphenyl)-p-methoxycinnamic acid.
8) cis-α-(o-Carboxyphenyl)-p-chlorocinnamic acid.
9) trans-α-(o-Carboxyphenyl)-p-chlorocinnamic acid.
10) cis-α-(o-Carboxyphenyl)-o-methoxycinnamic anhydride.
11) cis-α-(o-Carboxyphenyl)-p-methoxycinnamic anhydride.
12) trans-α-(o-Carboxyphenyl)-p-methoxycinnamic anhydride.
13) cis-α-(o-Carboxyphenyl)-p-chlorocinnamic anhydride.
14) trans-α-(o-Carboxyphenyl)-p-chlorocinnamic anhydride.
15) cis-α-(o-Carbomethoxyphenyl)cinnamic acid.
16) cis-α-(o-Carbomethoxyphenyl)-o-methoxycinnamic acid.
17) cis-α-(o-Carbomethoxyphenyl)-p-methoxycinnamic acid.
18) trans-α-(o-Carbomethoxyphenyl)-p-methoxycinnamic acid.
19) cis-α-(o-Carbomethoxyphenyl)-p-chlorocinnamic acid.
20) trans-α-(o-Carbomethoxyphenyl)-p-chlorocinnamic acid.
21) 3-Carboxy-2-phenylinden-1-one.

22) 3-Carboxy-2-(o-methoxyphenyl)inden-1-one.

23) 2-Anisyl-3-carboxy inden-1-one.

24) 3-Carboxy-2-(p-chlorophenyl)inden-1-one.

25) 2-Phenyl inden-1-one.

26) 2-(o-Methoxyphenyl)inden-1-one.

27) 2-Anisyl inden-1-one.

28) 2-Anisyl inden-1-one 2,4-dinitrophenyl hydrazone.

29) 2-(p-Chlorophenyl) inden-1-one.

30) 2-(p-Chlorophenyl) inden-1-one 2,4-dinitrophenyl hydrazone.

31) 2-(o-Carbomethoxyphenyl) inden-1-one.

32) 2-(o-Carbomethoxyphenyl)-4-methoxyinden-1-one.

33) 2-(o-Carbomethoxyphenyl)-6-methoxyinden-1-one.

34) 2-(o-Carboxyphenyl) inden-1-one.

35) 2-(o-Carboxyphenyl)-4-methoxyinden-1-one.

36) 2-(o-Carboxyphenyl)-6-methoxyinden-1-one.

37) 4-Carboxy-3-(o-methoxyphenyl)-3,4-dihydroisocoumarin.

38) 3-Anisyl-4-carboxy-3,4-dihydroisocoumarin.

39) 4-Carboxy-3-(p-chlorophenyl)-3,4-dihydroisocoumarin.

40) Methyl 2-(o-carboxyphenyl)-3-phenylpropanoate.

41) Methyl 2-(o-carboxyphenyl)-3-(o-methoxyphenyl)-propanoate.

42) Methyl 3-anisyl-2-(o-carboxyphenyl)-propanoate.

43) Methyl 2-(o-carboxyphenyl)-3-(p-chlorophenyl) propanoate.

44) 3-Anisyl-2-(o-carboxyphenyl) propionic acid.

45) 2-(o-Carboxyphenyl)-3-(p-chlorophenyl)-propionic acid.
46) 2-(o-Carboxyphenyl)-3-(o-methoxyphenyl)-propionic anhydride.
47) 3-Anisyl-2-(o-carboxyphenyl)propionic anhydride.
48) 2-(o-Carboxyphenyl)-3-(p-chlorophenyl)-propionic anhydride.
49) 2-(o-Carbomethoxyphenyl)-3-phenylpropionic acid.
50) 2-(o-Carbomethoxyphenyl)-3-(o-methoxyphenyl)propionic acid.
51) 3-Anisyl-2-(o-carbomethoxyphenyl)-propionic acid.
52) 2-(o-Carbomethoxyphenyl)-3-(p-chlorophenyl)propionic acid.

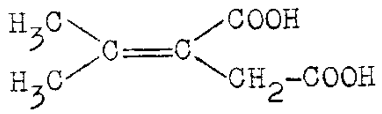
INTRODUCTION

A- THE STOBBE CONDENSATION

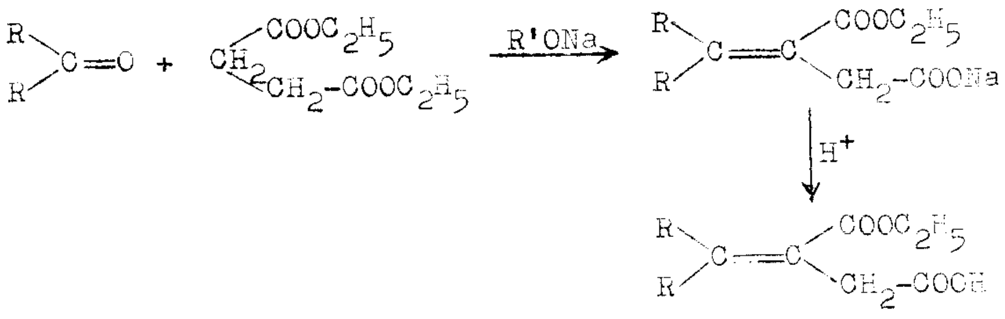
I- General Character

The condensation of aldehydes and ketones with succinic esters in presence of a basic catalyst to give alkylidene succinic acids (or its tautomers) is referred to as the Stobbe condensation.

Stobbe[1] in 1893 reported the first example and that was the reaction of acetone with diethyl succinate in presence of sodium ethoxide to form mainly teraconic acid.



One mole of a metal alkoxide is required per mole of each of the carbonyl compound and succinic ester. The primary product is the metal salt of the half-ester which by acidification liberates the half-ester or the dibasic acid produced by hydrolysis.



half-ester

II- Mechanism

The currently accepted mechanism of the Stobbe condensation was put forward by Johnson *et al.*[2] It involves the initial addition of the carbanion derived from succinic esters at the carbonyl group of the second reaction component. This is followed by a cyclisation step leading to the formation of an intermediate paraconic ester which could be subsequently cleaved by alkoxide ion to give the salt of the unsaturated half-ester as shown in the following reaction sequence. The irreversibility of the last step is the determining factor which drives the reaction to completion.