Chapter – II

CHAPTER - 2

STUDIES IN DIELS-ALDER REACTION

INTRODUCTION

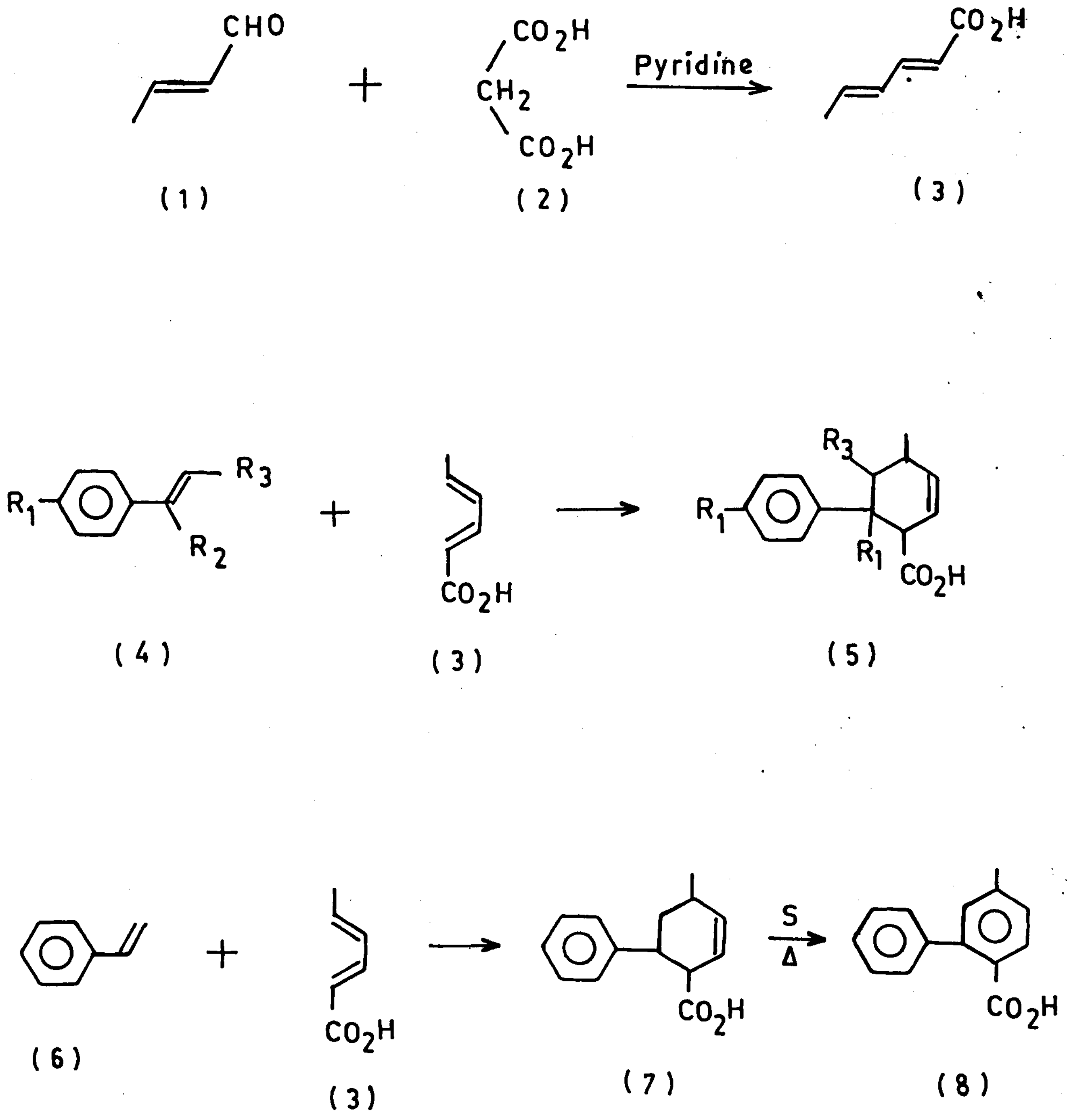
The Diels-Alder reaction is one of the most versatile reactions used in organic synthesis. Several important and complicated natural products have been synthesized using this reaction. We have studied a few reactions of sorbic acid and 1- acetoxy - 1, 3-butadiene with various dienophiles.

PRESENT WORK

DIELS-ALDER REACTIONS OF SORBIC ACID

Sorbic acid (1.3) is an interesting diene for the Diels-Alder reaction. This can be easily prepared by Knoevengel condensation of crotonaldehyde with malonic acid. Some of the reactions of sorbic acid have been studied earlier[1-5]. Sorbic acid (1.3) reacts with various styrenes[1] (1.4) to give substituted cyclohexenes (1.5, possible double bond isomers). For example styrene (1.6) reacted with (1.3) to give the product (1.7 - possible double bond isomers) which was dehydrogenated by sulphur to 2-phenyl-4-methyl benzoic acid (1.8). The position of double bond in the product is

CHART—1


CHO
CO2H
CH2
CO2H
Pyridine
CO2H
(1)
(2)
(3)
R1
R3
R2
CO2H
R3
R1
R1
CO2H
(4)
(3)
(5)
CO2H
CO2H
S
Δ
CO2H
(6)
(3)
(7)
(8)

not certain. Diels-Alder studied[2] the condensation of sorbic acid (2.1) with maleic anhydride (2.2) without solvent in which they had problems in getting the desired product (2.3) in pure form and good yield. It was found[3] that the product formed at high temperature is quite different (2.6 or 2.7) and arises due to the decarboxylation of cycloaddition product (2.3) as depicted in chart-2.

Farmer and Warren[4] have carried out the cycloaddition reaction of sorbic acid and maleic anhydride. On the basis of partial oxidation they suggested structure (2.4) for the adduct. However, Wicks[3] has suggested structure (2.3).

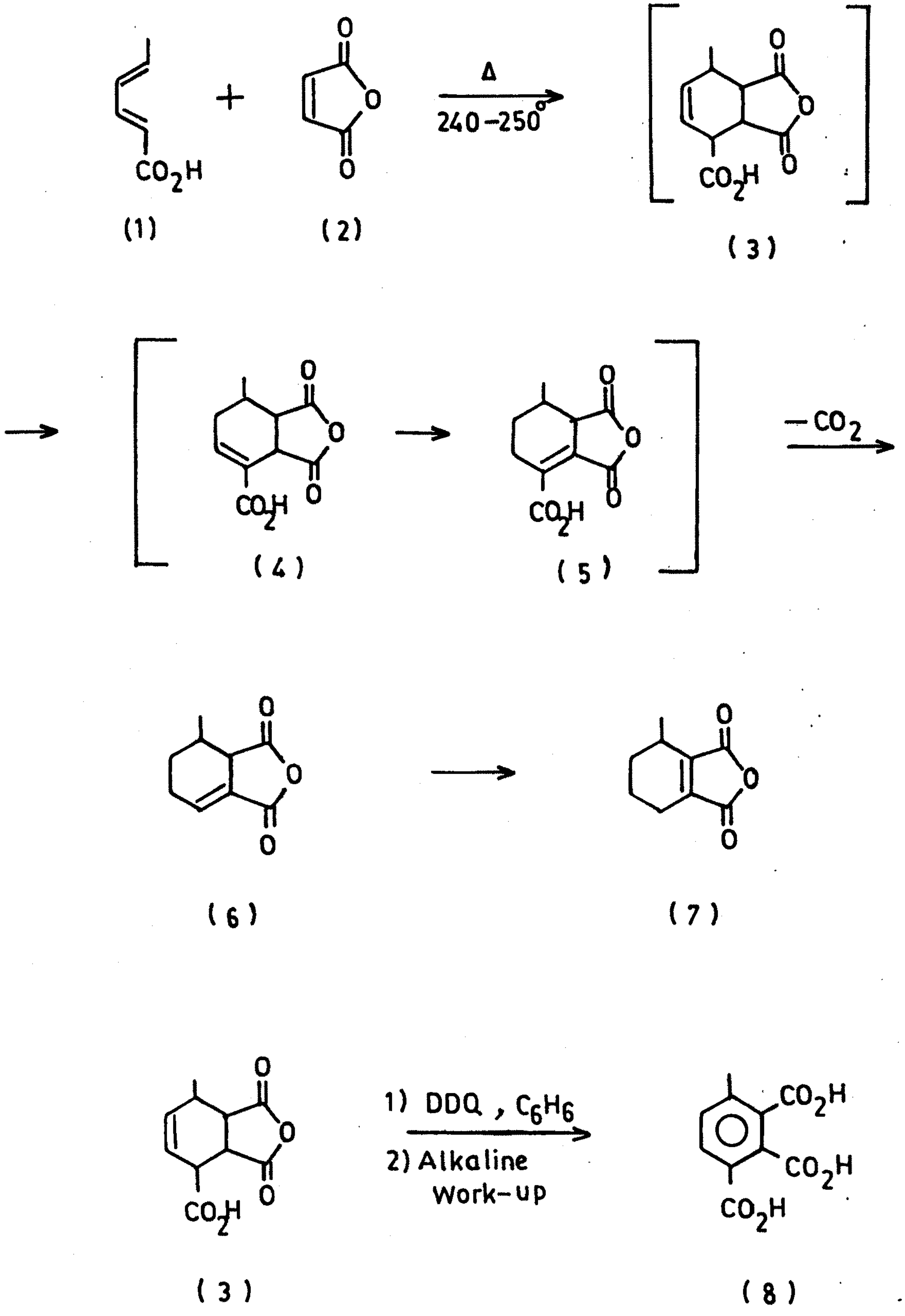
In view of formation of different products under different condition by Diels-Alder reaction of sorbic acid and maleic anhydride, we undertook the study of this reaction to begin with.

1) Reaction of sorbic acid with maleic anhydride :

Reaction of sorbic acid (2.1) with maleic anhydride (2.2) in dry benzene at reflux temperature gave quantitative yield of 6- carboxy - 3 - methyl - 1, 2, 3, 6 - tetrahydrophthalic anhydride (2.3). The I.R. spectrum (Fig.1) indicated bands due to anhydride carbonyls at 1845 and 1780 cm^{-1} (more intense than 1845 cm^{-1} band indicating cyclic anhydride) and a acid carbonyl at 1720 cm^{-1} (looks like two peaks at 1725 and 1710 cm^{-1}). A broad band from 3500 to 3000 cm^{-1} is indicative of carboxyl OH group. The I.R. spectrum confirms the cyclic saturated nature of anhydride. The acid carbonyl absorption indicates the possibility of the presence of isomer such as (2.4) which has conjugated acid group. The reported work on sorbic acid[3,4] points to the fact that one can get double bond isomers in these reactions. The PMR spectrum in $CDCl_3$ showed a doublet for the methyl group at 1.3, a broad multiplet for methine protons between 3.0 and 4.6 and multiplet for the olefinic protons between 5.9 to 7.0. The reaction was also carried out in toluene without any significant change.

The Diels-Alder product (2.3) undergoes decarboxylation at high temperature to yield (2.6) and (2.7) which has been dehydrogenated with sulphur to give 3- methyl - phthalic acid. In order to gain further insight into the structure we carried out the dehydrogenation of (2.3) with dichlorodicyanobenzoquinone (DDQ), a powerful dehydrogenating agent under milder conditions. The product obtained is 3- carboxy-4-methylphthalic acid (2.8), obtained without

CHART–2

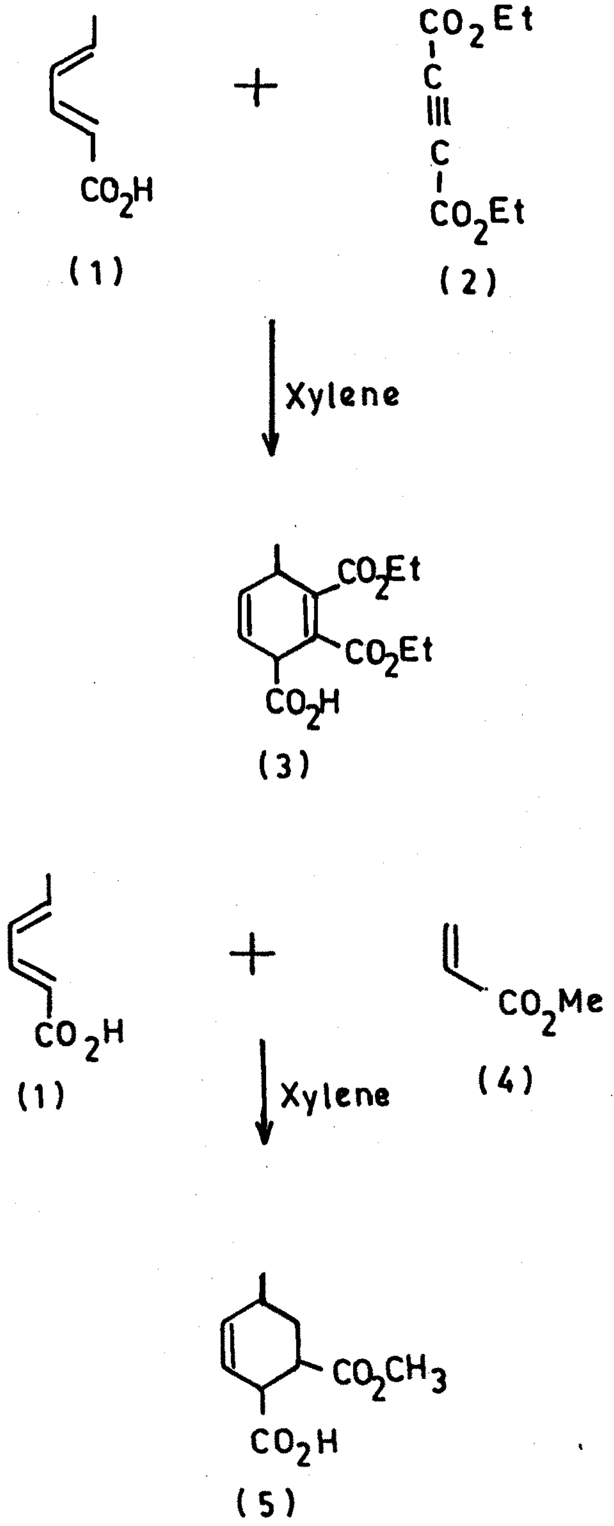


decarboxylation. The I.R. spectrum of this product indicated a broad signal characteristic of carboxyl group between 3500 and 3100 cm^{-1}. The carbonyl group appeared at 1695 cm^{-1} (aryl acid). The PMR spectrum of the product which was sparingly soluble in $CDCl_3$ was recorded using F.T. NMR. It indicated characteristic aromatic methyl singlet at 2.3 and a multiplet for two aromatic protons at 7.8.

2) **Reaction of sorbic acid with diethyl acetylene dicarboxylate :**

Diethyl acetylene dicarboxylate (3.2) serves as a good symmetrical dienophile in Diels-Alder reactions. Reaction of (3.2) with sorbic acid (3.1) gave a product (3.3). 2,3- dicarbethoxy-4-methyl- 2,5- cyclohexa- 2,4-diene-1-carboxylic acid, which showed following spectral characteristics. The PMR spectrum(fig.2) showed a broad multiplet at 1.25 for two ester methyl groups and secondary methyl group, a broad quartet for the methylene protons at 4.3, methine protons appeared between 3.2 to 4.8 and olefinic protons between 6.0 and 6.8. The I.R. spectrum (fig.3) showed broad band for the ester and acid carbonyl between 1715 and 1740 cm^{-1}.

CHART-3


CO2H
(1)
CO2Et
C
C
CO2Et
(2)
Xylene
CO2Et
CO2Et
CO2H
(3)
CO2H
(1)
CO2Me
(4)
Xylene
CO2CH3
CO2H
(5)

3) Reaction of sorbic acid with methyl acrylate :

Diels-Alder reaction of sorbic acid with methylacrylate (3.4) in refluxing xylene gave (3.5)- 2-carbomethoxy-4- methyl-cyclohex-5- ene-1-carboxylic acid. Its PMR spectrum showed a doublet for the methyl group at 1.1, multiplet for methylene and methine protons between 1.8 to 3.6, a singlet for the ester methyl at 3.9 and multiplet for the olefinic protons between 5.9 and 6.8. The I.R. spectrum indicated the presence of ester carbonyl at 1740 cm^{-1} and acid carbonyl at 1715 cm^{-1}. The orientation is as predicted by the FMO theory.[6]

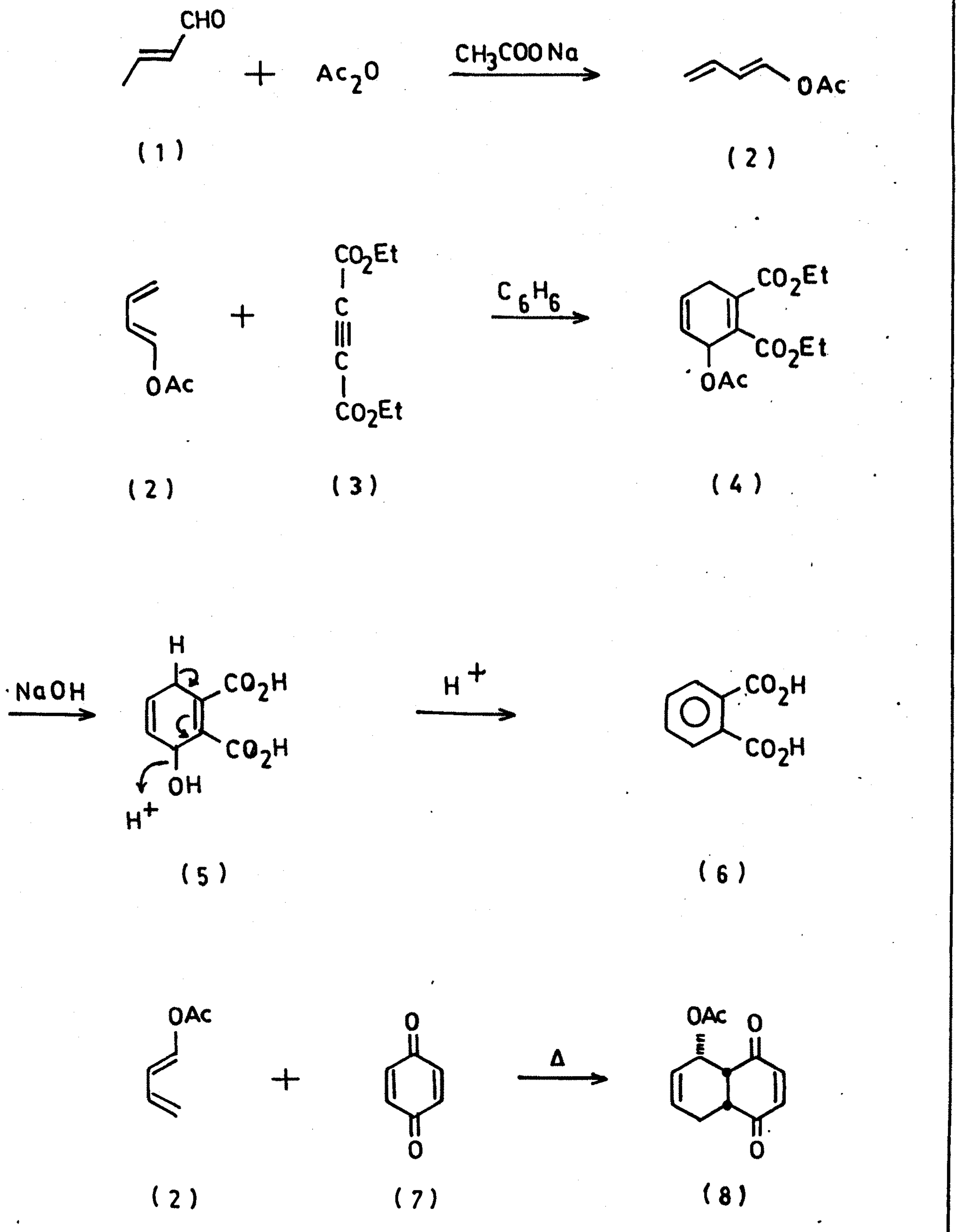
DIELS-ALDER REACTIONS OF 1-ACETOXY-1, 3-BUTADIENE

1-Acetoxy-1, 3-butadiene serves as a good diene in Diels-Alder reactions as the products could be suitably elaborated into complicated natural products. It is conveniently prepared[7] by the reaction of crotonaldehyde (4.1) with acetic anhydride in presence of sodium acetate , careful fractional distillation is required to get the pure product.

1) Reaction with diethyl acetylene dicarboxylate :

The cycloaddition reaction of 1- acetoxy-1, 3-butadiene (4.2) with diethyl acetylene dicarboxylate (4.3) was carried out in benzne to yield (4.4), 2, 3-

CHART–4


CHO
+
Ac_2O
CH_3COONa
OAc
(1)
(2)
+
CO_2Et
C
C
CO_2Et
C_6H_6
CO_2Et
CO_2Et
OAc
(2)
(3)
(4)
NaOH
H
CO_2H
CO_2H
OH
H^+
H^+
CO_2H
CO_2H
(5)
(6)
OAc
+
O
O
Δ
OAc
O
O
(2)
(7)
(8)

dicarbethoxy cyclohexa- 2, 5- diene - 1 - ol- acetate. The product was hydrolyzed with sodium hydroxide and treated with acid to give phthalic acid. The aromatization is facile as the hydroxyacid (4.5) undergoes dehydration easily to give phthalic acid. The m.p. and I.R. spectrum of this product matched well with authentic phthalic acid sample.

2) **Reaction with p-benzoquinone** :

Kaye and Matthews[8] have reported the reaction of 1- acetoxy- 1, 3- butadiene (4.2) with p-benzoquinone (4.7) in isopropyl ether and carbon tetrachloride to yield hexahydronaphthalene- 5α-ol-1, 4- dione acetate (4.8). We carried out the above reaction in xylene and toluene to yield (4.8). The I.R. spectrum of the product (fig.4) showed acetate carbonyl band at 1755 cm^{-1} and the carbonyl of ketone at 1670 cm^{-1}.

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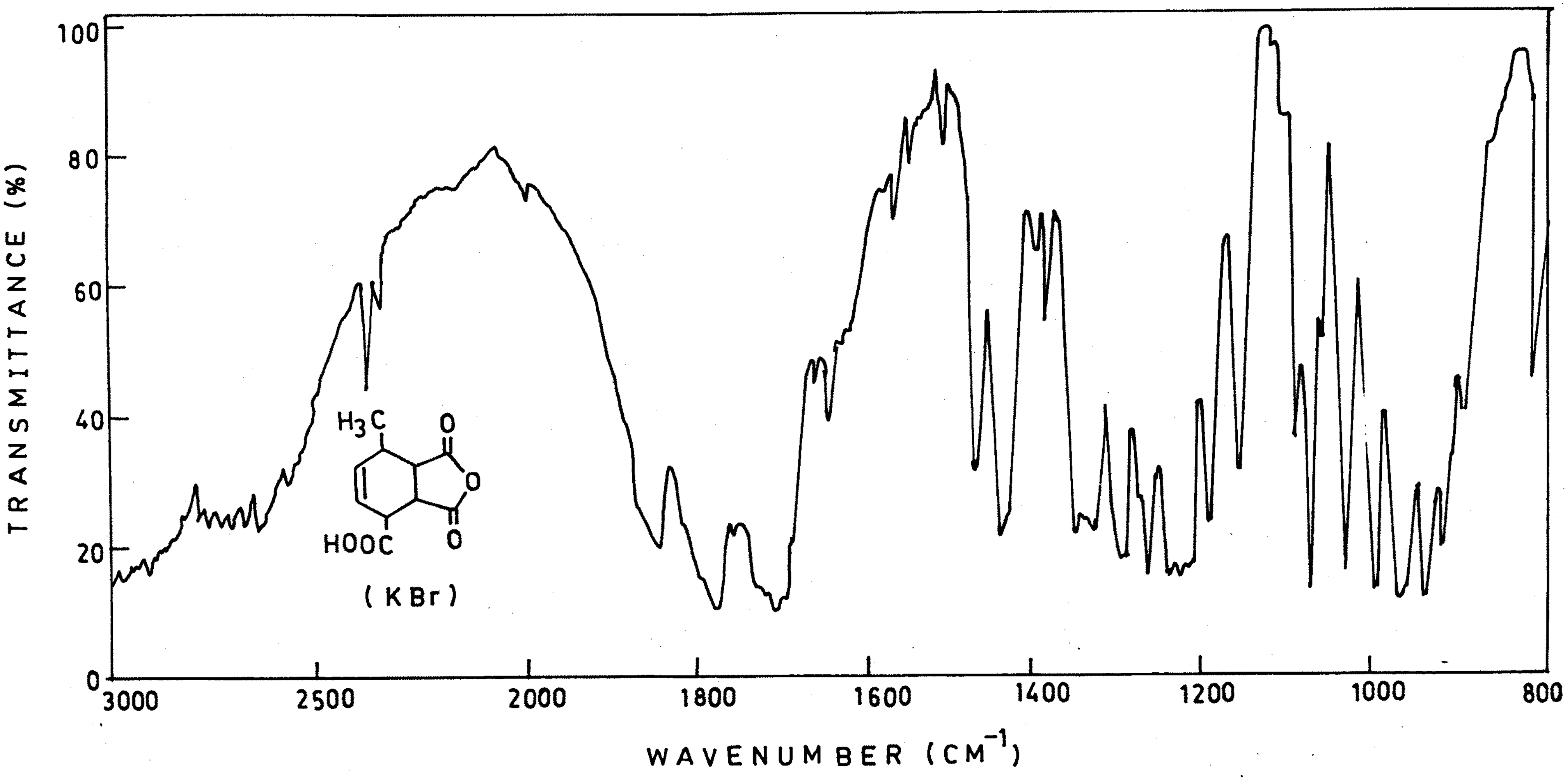
TRANSMITTANCE (%)
100
80
60
40
20
0
3000
2500
2000
1800
1600
1400
1200
1000
800
WAVENUMBER (CM^{-1})
H_3C
HOOC
O
O
O
(KBr)

FIG. 1

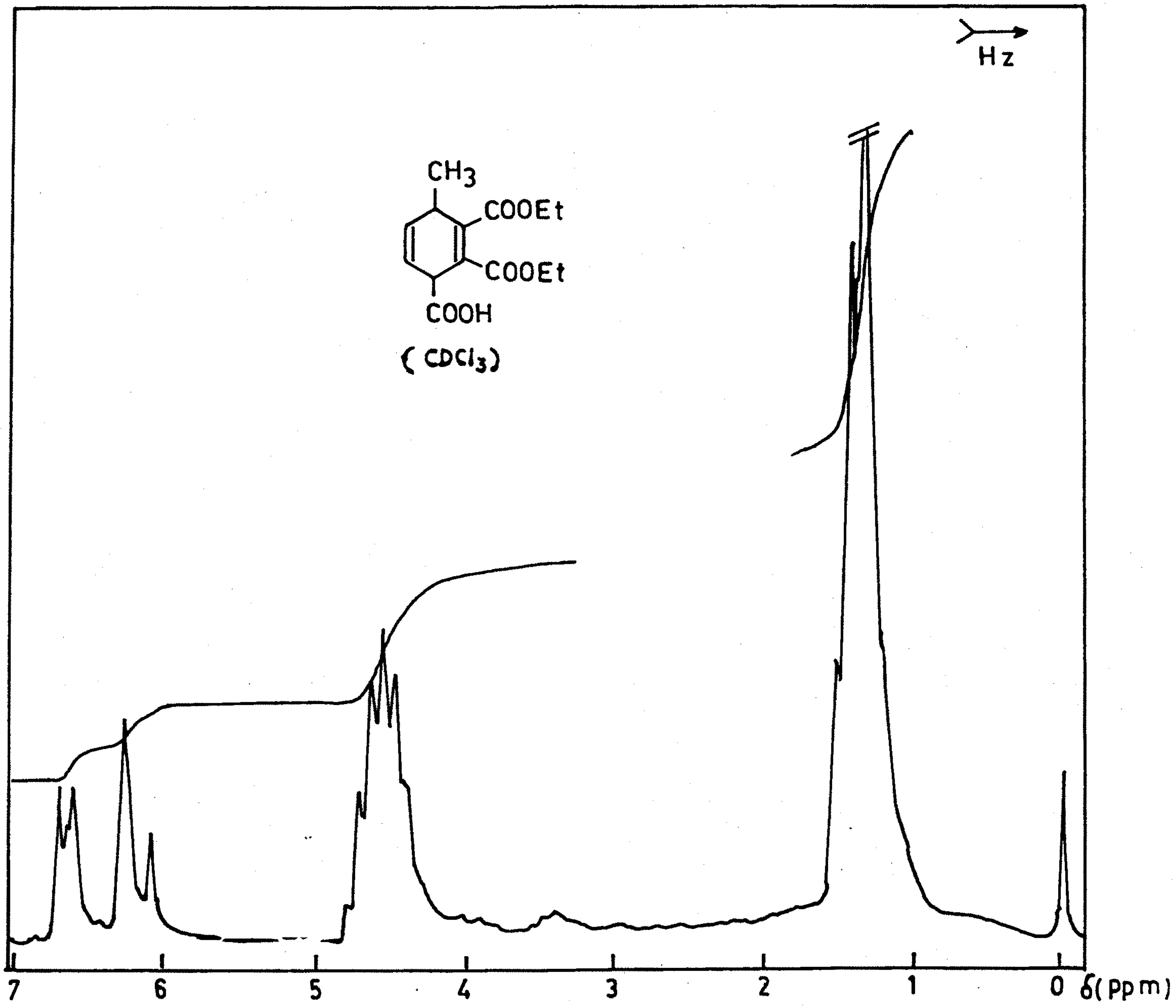

FIG. 7

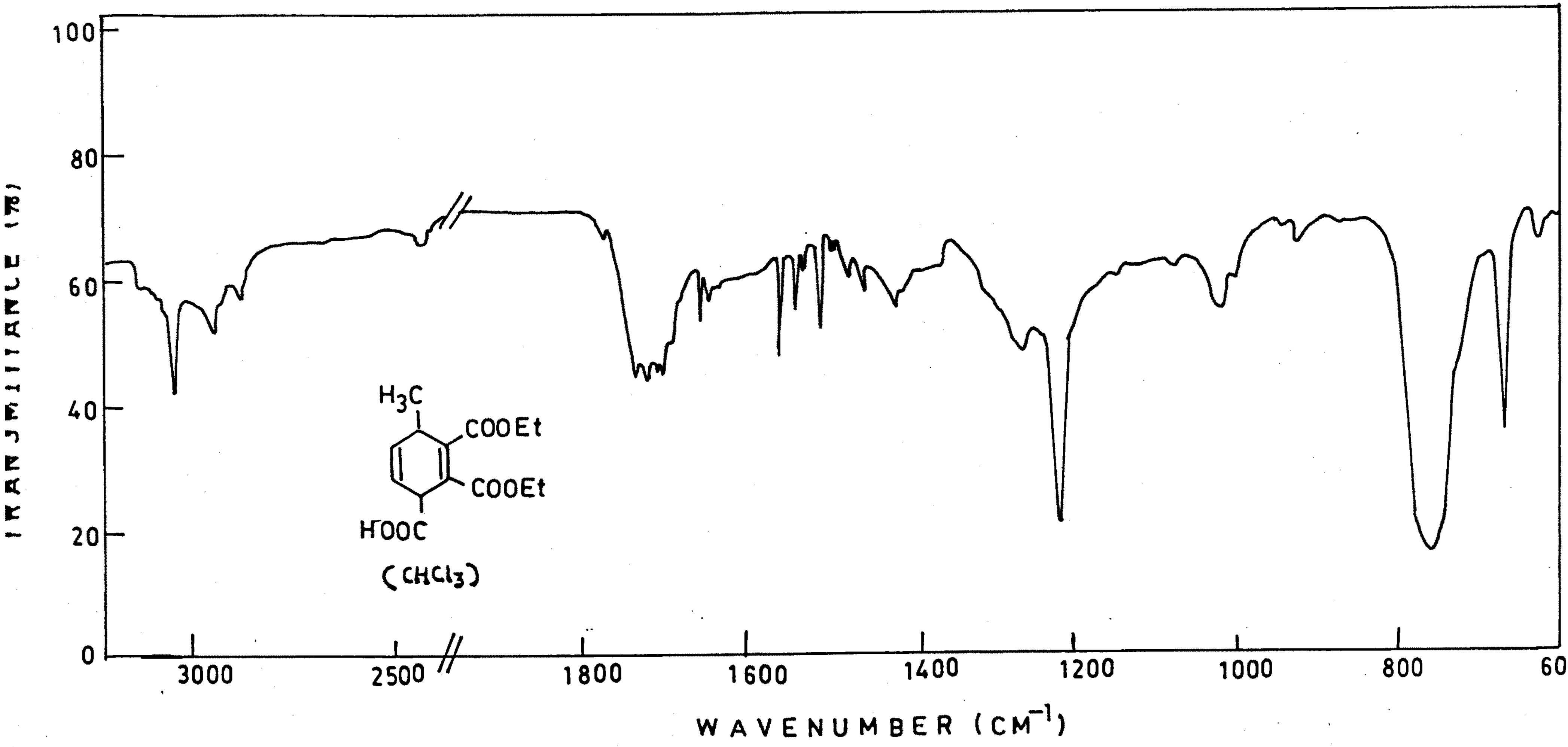
TRANSMITTANCE (%)
100
80
60
40
20
0
3000
2500
1800
1600
1400
1200
1000
800
600
WAVENUMBER (CM^{-1})
H$_3$C
COOEt
COOEt
HOOC
(CHCl$_3$)

FIG. 3

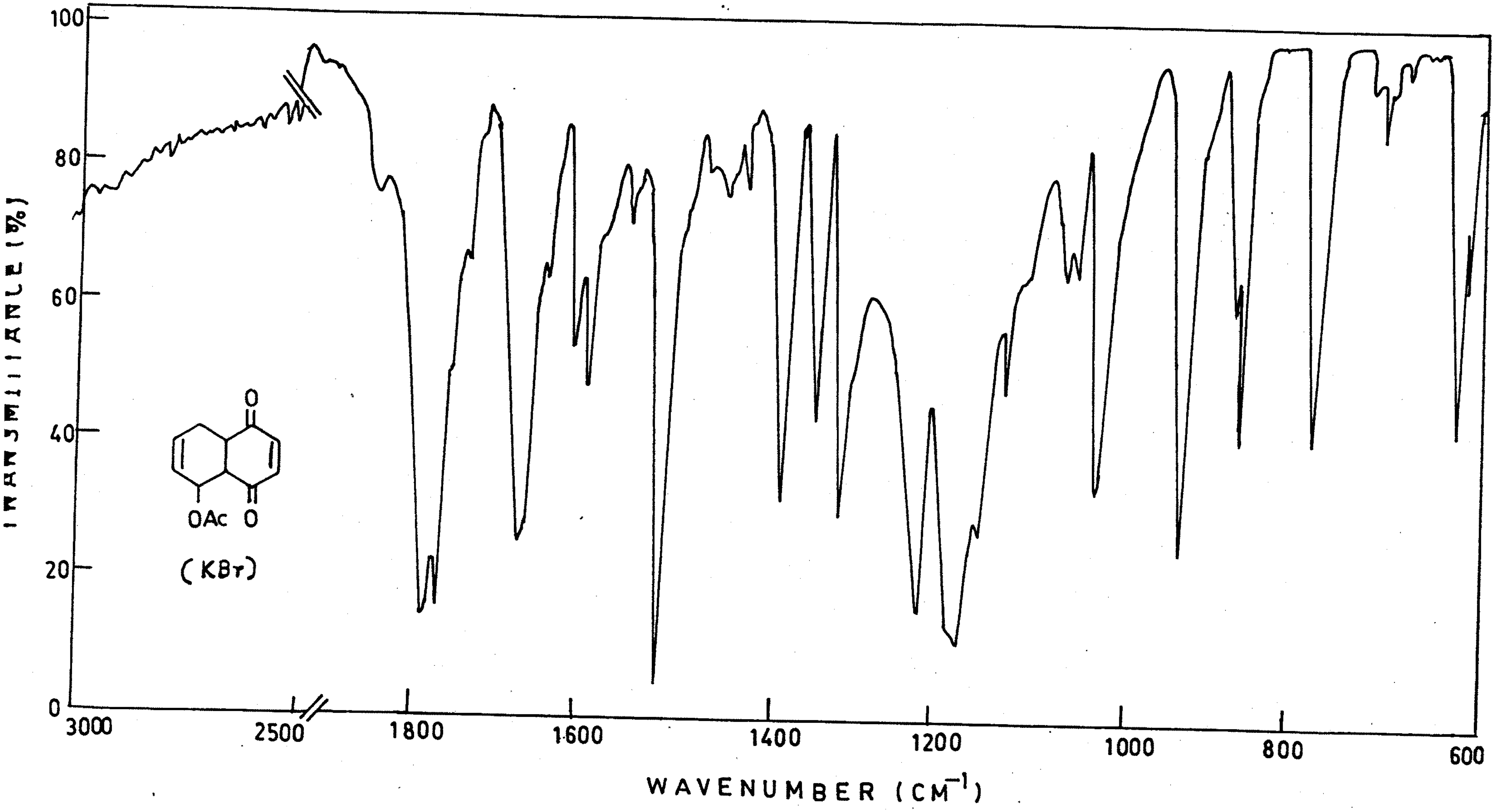
TRANSMITTANCE (%)
100
80
60
40
20
0
3000
2500
1800
1600
1400
1200
1000
800
600
WAVENUMBER (CM^{-1})
O
OAc
O
(KBr)

FIG. 4

EXPERIMENTAL

General remark :

All boiling points and melting points recorded are uncorrected. Distilled solvents are used in all cases. Pet. ether refers to the petroleum fraction boiling between 60-5°C. Dry benzene was prepared by preliminary drying on fused calcium chloride following by sodium wire drying, distillation and final storage on sodium wire.

Dry xylene was also prepared by distillation and storage on sodium wire. All liquid reagents were distilled and stored under anhydrous conditions. Silica gel used for TLC was of greater than 200 mesh grade.

The IR spectra were recorded on a Perkin-Elmer spectrometer. The IR data are presented in wavenumbers. The PMR spectra were recorded on Jeol FX 90 (90 MHz) model with TMS as internal standard.

The PMR data using standard notations, are presented in the following order - Chemical shift (δ ppm) /splitting pattern/assignment.

Preparation of sorbic acid[9] (Hexa-2, 4-dienoic acid)(1.3) :

A mixture of 40.0 g (46.5 ml, 0.57 mol) of crotonaldehyde. 70.0 g of malonic acid and 60.0 g (61.0 ml, 0.76 mol) of dry pyridine was heated on water bath for 3 hours. At the end of this period vigorous evolution of carbon dioxide ceased. The mixture was cooled in ice and cautiously acidified by the addition of dil. Sulphuric acid. Most of the sorbic acid separated out immediately, a more complete separation was obtained by cooling the solution in ice for 3-4 hours. The acid was filtered and washed with a little ice-cold water. Recrystallisation from boiling water gave pure acid. The yield of sorbic acid was 20.0 g (31%), m.p. 134°C (Lit. m.p. 135°C).

Diels-Alder reaction of sorbic acid with maleic anhydride to give 6--carboxy-3 -methyl - 1,2,3,6 - tetrahydrophthalic anhydride (2.3) :

A mixture of sorbic acid (1.12 g. 0.01 mol) and maleic anhydride (0.98 g, 0.01 mol) and 10.0 ml of dry benzene was heated under reflux in an oil bath for 4 hours. Crystals were separated in the flask. The completion of reaction was checked by TLC using pet. ether and ethyl acetate (70:30) as solvent system. This solid was filtered to get the white crystalline compound.

The yield was (2.00 g) m.p. 177-180°C.

The reaction was also carried out in boiling toluene without much change.

I.R. : (Fig.1, KBr pellet) 1845 cm^{-1} 1780 cm^{-1} (intense) (anhydride carbonyl bands), 1720 cm^{-1} (carbonyl of acid), 3500 to 3000 cm^{-1} (hydroxy of carboxylic acid group).

P.M.R. : (in $CDCl_3$, 90 MHz, δ units) : 1.3 (3H, d, methyl group), 3.0 to 4.6 (4H, broad multiplet, methyl protons), 5.9 to 7.0 (2H, multiplet, olefinic protons).

Dehydrogenation of (2.3) using DDQ to give 3-carboxy- 4-methyl phthalic acid (2.8) :

A mixture of 0.222 g (0.00125 mol) DDQ in dry benzene was refluxed for 30 hours. Then the reaction mixture was filtered, ether was added and the ether layer washed with saturated $NaHCO_3$ solution. The aqueous layer was acidified with dil. HCl and again extracted with ether. On evaporation of ether layer, solid was obtained with yield 71.42%, m.p. 228-232°C.

I.R. : 3500 to 3100 cm^{-1} (broad OH of carboxyl group), 1695 cm^{-1} (carbonyl of aryl acid).

P.M.R.: (in $CDCl_3$), 2.3 (3H, S, aromatic methyl protons) and 7.8 (2H, multiplet, aromatic protons.)

Analysis Found % : C, 53.57 H, 3.57

$C_{10}H_8O_6$ requires : C, 53.80 H, 3.74

Diels-Alder reaction of sorbic acid with diethyl acetylene dicarboxylate to give 2, 3- dicarbethoxy-4 -methyl-2, 5- cyclohexa-2, 4- diene - 1 - carboxylic acid (3.3):

A mixture of (1.12 g, 0.01 mol) of sorbic acid and (1.7 ml, 0.01 mol) of diethyl acetylene dicarboxylate was taken in dry xylene and a pinch of hydroquinone was added. It was heated at 140°C for 10 hrs. The reaction was monitored by TLC. The reaction mixture was extracted with ether and washed with saturated $NaHCO_3$. Ether layer gave some unreacted diethyl acetylene dicarboxylate. The aqueous layer was acidified with dil. HCl and extracted with ether. On removal of ether, solid was obtained. The crude product was washed with dist. water several times to get the pure adduct and to separate the unreacted sorbic acid. The product was purified by preparative TLC (silica gel, chloroform- pet. ether). The yield was 40% with m.p. 108-110°C.

I.R. : (Fig.3, $CHCl_3$), 1750-1740 cm^{-1} (broad band for ester and acid carbonyl groups).

P.M.R.: (Fig.2, $CDCl_3$) 1.25 (9H, broad multiplet, two ester methyl protons and secondary methyl group); 4.3 (4H, multiplet, methylene protons of ester group), 3.2-4.8 (2H, ^{S},methine protons), 6.0 to 6.8 (2H, multiplet,olefinic protons).

Analysis	Found % :	C,	59.57	H,	6.38
$C_{14}H_{18}O_6$	requires:	C,	59.38	H,	6.27

Diels-Alder reaction of sorbic acid with methyl acrylate to give 2- carbomethoxy-4-methyl - cyclohex-5-ene carboxylic acid (3.5) :

A mixture of (1.12 g. 0.01 mol) sorbic acid and (0.86 g, 0.01 mol) of methyl acrylate was taken in dry xylene and a pinch of hydroquinone was added to it. It was heated at 140°C for 15 hrs. The reaction was monitored by TLC. The reaction mixture was extracted with ether and washed with sat. $NaHCO_3$. The aqueous layer was acidified with dil. HCl and extracted with ether. On removal of ether solid was obtained. The crude product was washed with dist. water several times to get the pure product and to separate the unreacted sorbic acid. The product was purified by preparative

TLC (silica gel, chloroform- pet. ether). It was recrystallised from chloroform with 50% yield. m.p. 114-116°C.

I.R. : ($CHCl_3$), 1740 cm^{-1} (ester carbonyl), 1715 cm^{-1} (acid carbonyl).

P.M.R.: ($CDCL_3$), 1.1 (3H, d, secondary methyl protons), 1.8-3.6 (5H, multiplet, methylene and methine protons), 5.9-6.8 (2H, multiplet, olefinic protons).

Preparation of 1-Acetoxy-1, 3-butadiene[7] (4.2) :

Crotonaldehyde (70.0 ml, 1 mol), acetic anhydride (176.0 ml, 1.6 mol) and fused sodium acetate (50.0 g, 0.6 mol) were thoroughly mixed and then heated at 150°C in an oil bath for 10 hrs. Fractional distillation of the product under reduced pressure from the same flask yielded fraction boiling between 42 to 45°C at 10 mm Hg in 54% yield. It was collected and used for reactions.

Diels-Alder reaction of 1-acetoxy- 1, 3-butadiene with diethyl acetylene dicarboxylate to give 2, 3-dicarboethoxy cyclohexa - 2,5 - diene - 1 - 01 acetate (4.4) :

A benzene solution of (0.765 ml, 0.1 mol) diethyl acetylene dicarboxylate and (1.008 ml, 0.2 mol) of 1-acetoxy- 1, 3-butadiene was refluxed for 50 hrs. The reaction was monitored by TLC. After distillation of benzene a liquid was obtained (4.4) which could not be crystallised. So hydrolysis of the product was carried out. Reaction in toluene also gave the same product.

Hydrolysis of (4.4) to phthalic acid (4.6) :

To the reaction mixture, (8.0 ml) 10% NaOH and (20.0 ml) distilled ethanol was added. It was refluxed for 8 hrs. The ethanol was removed. It was diluted with dist. water and extracted with ether. The aqueous layer was acidified with dil. Hcl. The product obtained was extracted with ether and dried. The ether layer was distilled. A viscous compound was obtained which after 24 hrs. gave yellow crystals melting at 197-200°C. On recrystallisation from ether white crystalline compound was obtained with m.p. 204-206°C (Lit. m.p. 206-210°C). The I.R. spectrum of this product matches with that of phthalic acid.

Diels-Alder reaction of 1-acetoxy-1, 3-butadiene with p-benzoquinone to give hexahydronaphthalene - 5α- ol - 1, 4- dione acetate (4.8) :

A mixture of (2.0 ml, 0.017 mol) 1-acetoxy-1, 3-butadiene and (0.5 g. 0.0046 mol) of p-benzoquinone[9] in dry xylene with a pinch of hydroquinone was heated in an oil bath at 120°C for 8 hrs. The xylene was removed under vacuum. The solid obtained was recrystallised from pet. ether - chloroform. Pet. ether extract gives the fine yellow crystals with 80% yield, m.p. 64-66°C.

I.R. : (Fig.4, KBr pellet), 1755 cm^{-1} (carbonyl of acetate), 1670 cm^{-1} (carbonyl of ketone).

###

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