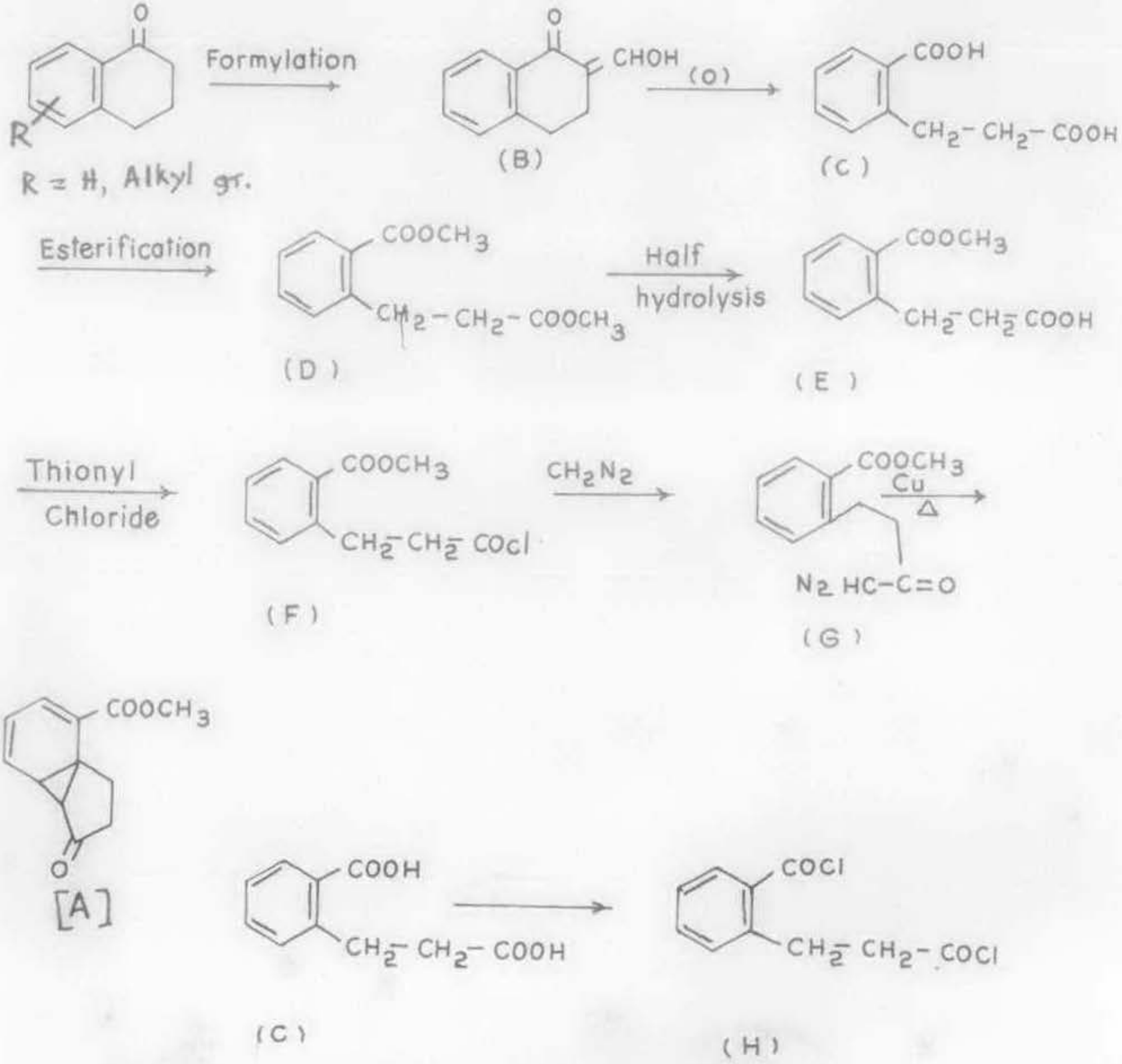
CHAPTER - V

Intra molecular ketocarbene addition to aromatic system.

Section-A : Aims and Objects

With a view to study the carbene addition in the intramolecular sense to benzylic hydrogen, the following course of reactions was contemplated.



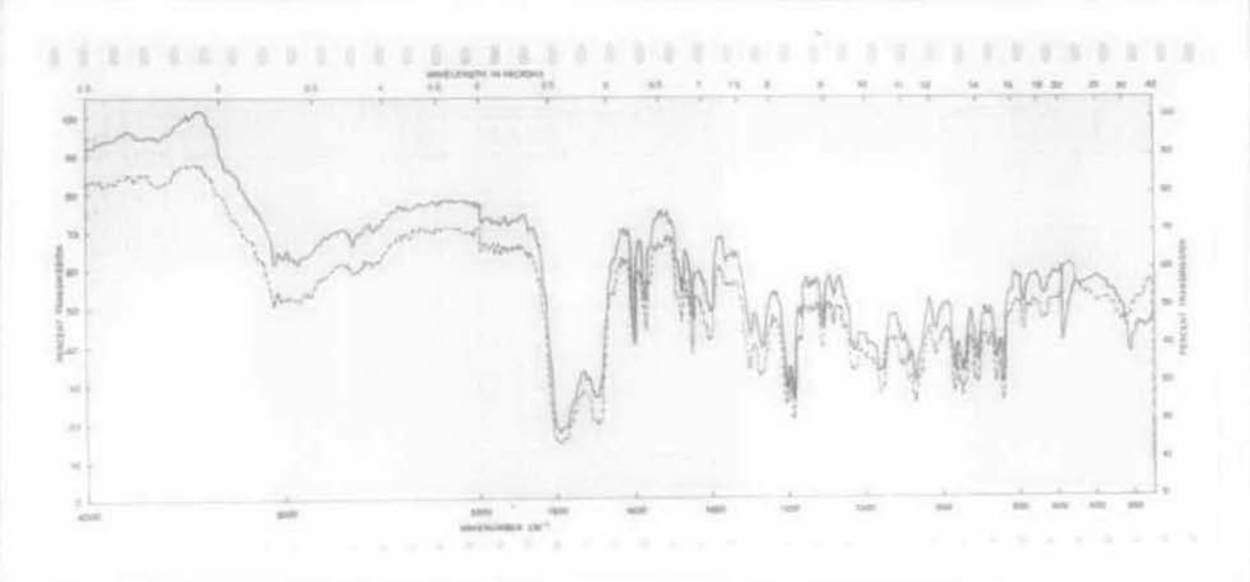


Fig. P.12. I.R. spectrum comparison of acid chlorides

... I.R. spectrum of the acid chloride obtained from O-carboxy dihydrocinnamic acid.

—— I.R. spectrum of the acid chloride obtained from O-carbomethoxy dihydro cinnamic acid.

Section-B: Results and discussions.

In order to prepare the product [A] and others via carbene α-tetralone was chosen first as the starting material. Formylation was done resulting [B]. This on oxidation by potassium periodate and potassium permanganate gave [C] named o-carboxy dihydro cinnamic acid. This is also prepared by another route i.e. by the oxidation and thereby hydrogenation of β-naphthol. This diacid on esterification by methanol and conc. sulphuric acid gave diester [D]. This diester on half-hydrolysis compound [E] was resulted. On treatment of thionyl chloride on [E] instead of giving compound [F] our desired product, diacid chloride [H] of the acid was isolated. We attempted to prepare F with other reagent of preparing acid chloride; but in all cases we were able to isolate only [H]. Some other alternatives were tried which led to more complications.

The structure of [F] was confirmed to be the structure of the diacid chloride [H] of the diacid by comparison of I.R. spectra Fig-P.12. The identification of the other compounds was done by chemical analysis and I.R. spectra.

Some cursory work to prepare [G] by alternative synthetic procedures have not as yet yielded fruitful results. So we could not complete our scheme.

Section-C: Experimental.

Melting points and boiling points are uncorrected. Dry solvents were used where necessary. I.R. spectra were recorded in a Beckmann IR-20 Spectrophotometer.

1. α-tetralone (161):

(a) 2-Benzoyl propionic acid: In a 1 litre three-necked flask, which was fitted with a mechanical stirrer and two efficient reflux condensers, was taken 200 c.c. sodium dried benzene (A.R) and 34 gm of succinic anhydride. The reaction mixture was stirred and in it 100 gm powdered anhydrous aluminium chloride was added at a time. The reaction had started immediately and then the reaction mixture was allowed to reflux gently. On an oilbath with continued stirring for half an hour. The flask was cooled, placed in an ice bath and 150 ml of water was added from a separatory funnel inserted into the top of one of the condensors followed by 50 ml of conc. Hydrochloric acid. Benzene was removed by steam distillation. The hot mixture was transferred to a beaker; The 2-benzoyl propionic acid separate as a colourless oil, which soon solidified. It was cooled and the acid filtered at the pump and washed first with 100 ml of cooled dilute. Hydrochloric acid (1:3)v/v and then with 100 ml of cold water. The crude acid was dissolved in a solution of 50 gm anhydrous sodium carbonate in 275 ml of water. The solution was filtered. The coloured filtrate decoloured with active charcoal. The hot filtrate was acidified with 80 ml of concentrated hydrochloric acid and the mixture was cooled to 0°. The acid filtered and washed thoroughly with cold water and air dried. The m.p. 115°C (Lit. 115°C) Yield-

(b) γ-phenyl butyric acid: Amalgamated zinc from 120 gm of zinc was prepared in a 1 lit. round bottomed flask. In it 75 ml of water, 180 ml of concentrated Hydrochloric acid, 100 ml of pure toluene and 50 gm of 2-benzoyl propionic acid were taken. The flask was fitted with a reflux condenser connected to a gas absorption device. The reaction mixture was refluxed vigorously for 30 hours and during this period, 50 ml of concentrated Hydrochloric acid was added to the reaction mixture of approximately six hours intervals to maintain the concentration of the acid. It was then allowed to cool to room temperature and the two layers separated. The acquous layer diluted with about 200 ml of water and extracted with three 100 ml portions of ether. Toluence layer an ether extracts were combined and washed with water till neutral and dried over anhydrous sodium sulphate. Solvents were removed under diminished pressure on a water bath and the liquid residue was distilled at the vacuum pump. The colourless distillate solidified on cooling which melts at 48°C (Lit. 48°).

(c) <u>α-tetralone</u>: In a 500 ml R.B. flask which fitted with a reflux condenser, and a calcium chloride guard tube which was connected with a tube leading to gas absorption trap, were taken 32 gm of pure and redistilled thionyl chloride and 32 gm of n-phenyl butyric acid. The reaction mixture was heated continuously on a water bath until the acid melts, and it was kept aside. After when hydrogen chloride no longer evolved, the reactions was completed by heating on a water bath for 10 minutes. Excess thionyl chloride was removed completely by distilling on water bath under reduced pressure. The resulting γ-phenyl butyryl chloride used as such for the subsequent step.

To the cold acid chloride, 175 ml of pure carbon disulphide added. The flask cooled in an ice-salt bath. To it, 30 gm of powdered anhydrous aluminium chloride added in one lot, and immediately a reflux condenser with a calcium chloride guard tube fitted to the flask. When the evolution of hydrogen chloride ceased, the reaction mixture warmed slowly to its boiling point on a water bath. It was refluxed for 10 minutes with shaking. The reaction mixture was then cooled to 0°C and the aluminium complex decomposed by the cautious addition with shaking 100 gm of crushed ice and 25 ml of conc. Hydrochloric acid. The mixture was transferred to a R.B. flask and then steam distilled (calcium chloride) first and then tetralone. Oil was separated; and the aqueous layer extracted thrice with 100 ml portions of benzene. Oil and benzene extract combined and dried over anhydrous sodium sulphate. Solvent removed, liquid residue distilled at the pump at 140-45°/15 mm. (Lit. 117-20/10 mm).

2. <u>2-hydroxy methylene tetralone (162)</u>:

A mixture of 4.7 gm molecularised sodium 400 ml of dry benzene, 29.2 gm of 1-tetralone, and 22 gm (-24 ml) of redistilled ethyl formate was placed in a 1 lit. three-necked flask equipped with a mechanical stirrer, stopper and a bent tube. The reaction was initiated by the addition of 1.3 ml of ethyl alcohol. The flask was then placed in a cold water bath and stirred for 6 hrs. After standing over night, 5 ml of ethyl alcohol added and the mixture was stirred for an additional hour. After addition of 40 ml of water, the mixture was shaken in a 1 lit. separatory funnel. The benzene layer washed with 20 ml of water and the combined aqueous layer was extracted with 25 ml of benzene. The aqueous layer acidified with 33 ml of 6N hydrochloric acid, and the mixture was extracted with 100 ml of benzene. The benzene solution washed with 5 ml of saturated sodium chloride solution was dried over anhydrous Na_2SO_4. Solvent was removed at reduced pressure on a water bath. The liquid residue distilled at the pump at 140/10 mm. Yield-15 gm.

The 2:4 dinitro phenyl hydrozone derivative of the above compound prepared which was crystallised from chloroformmethanol solvent mixture. Methanol solvent m.p. 218-20°.

Analysis found:	C, 57.34%; H, 4.00%
Calculated	C, 57.6%; H, 3.99%.

3. Oxidation of 2-hydroxy methylene tetralone (163):

To a solution of 1.74 gm 2-hydroxy methylene tetralone and 10 ml water solution 0.5 gm NaOH, a solution of 1 gm $KMNO_4$ and 15 gm Na 10_4 (700 ml water) was added. The mixture was agitated for 5 hours at room temperature.

The oxidants were destroyed with SO_4 and the solution rendered acidic with aqueous HCl. The products were extracted with ethyl acetate. Removal of the solvent after washing of the combined extracts left light yellow crystals. Traces of elemental S were eliminated by dissolving the material in a dil. $NaHCO_3$ aq. and filtering and recovering of the organic acid. This was crystallised from benzene. Yield-450 mg (25%) m.p. 165°C.

4. Preparation of o-carboxy dihydro cinnamic acid (155):

In an open 1 lit. wide mounted R.B. flask were placed 189 (0.094 mole) of o-carboxy cinnamic acid and 550 ml of 10% sodium hydroxide solution. The mixture was warmed to 90° on a steam bath and stirred mechanically. The steam bath was then removed while 54 gm of Nickel Aluminium alloy powder was added through the open neck of the flask in small portions at frequent

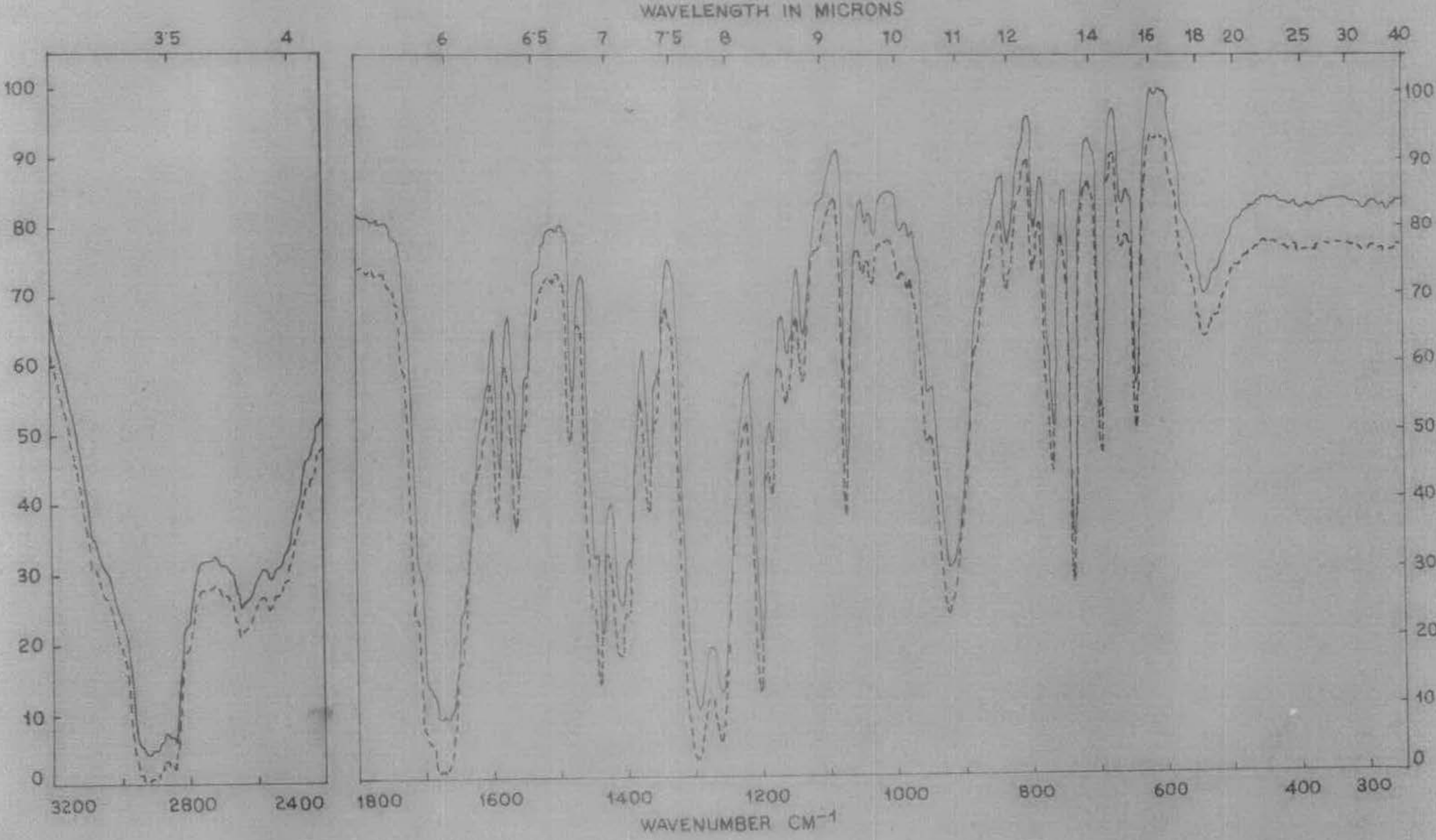


Fig- 44. o- Carboxy dihydro cinnamic acid.

intervals. When the addition of the alloy was complete, the mixture was stirred and maintained at 90°-95°C for 1 hour by warming on a steam bath. Distilled water was added as needed to maintain the total volume at approximately 550 ml. The hot mixture was filtered with suction, and the metallic residue was washed with 50 ml portions of hot water in such a manner that the solid residue was never exposed to air. The cooled filtrate and washings were added dropwise with mechanically stirring to 300 ml of conc. Hydrochloric acid in a beaker at such a rate that the temperature did not exceed 80-85°C. Separation of crystals started immediately when the contents of beaker cooled. The o-carboxy dihydro cinnamic acid was separated by filtration, washed with water and air dried. Yield 14 gm, m.p. 164° (Lit. 165.5 - 167°C).

Gave no depression in melting point on mixed melting point determination with above sample i.e. Oxidation product of 2-hydroxy methylene tetralone. I.R. of this acids prepared from the two route is identical. Fig. 44.

5. <u>Dimethyl o-carboxy dihydro cinnamate</u>:

4.3 gm of acid was dissolved in 100 ml of dry methanol and then adding 5 to 6 drops of conc. Sulphuric Acid, the reaction mixture was refluxed for 6 hrs. It was cooled and methanol was removed completely. The liquid residue was treated with 200 ml solvent ether and washed with 5% sodium bicarbonate

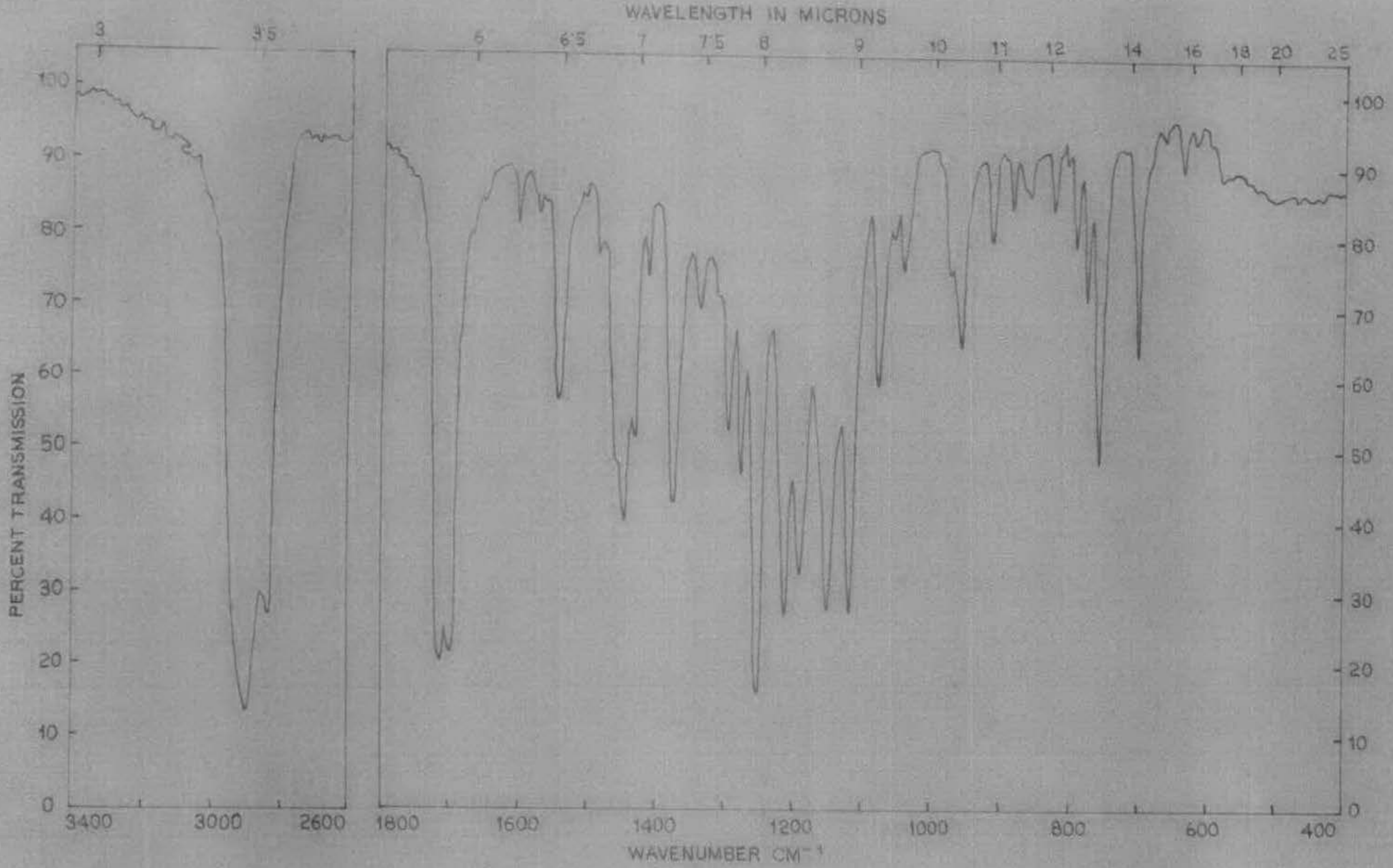


Fig- 45. o- Carbomethoxy dihydro cinnamic acid.

solution and then with water till the solution became neutral to pH paper. It was dried on anhydrous sodium sulphate and it was filtered. Ether was removed completely when a liquid product remained. I.R. peak - at 1710 cm^{-1} which showed ester function. Yield-4 gm. B.P. 180/2 mm.

6. o-carbomethoxy - dihydro cinnamic acid (Half hydrolysis):

3 gm of the ester was treated 5% 16 ml methanolic potassium hydroxide and the reaction mixture was kept overnight. Then the reaction mixture was neutrallised with 5 ml hydrochloric acid and the excess methanol was removed at low temperature. The liquid residue was treated with 100 ml ether and washed with water to remove any free acid. When washing was found to be neutral, to pH paper, the ether solution was dried on anhydrous sodium sulphate and filtered. A liquid residue left behind which solidified on cooling. m.p. 68°C (Crude). This was recrystallised from pet-ether m.p. 74°C. Yield- 1.8 gm I.R. peak at 1710 cm^{-1} and 1680 cm^{-1} showed one ester function and one acid function. (Fig. 45).

Analysis found: C, 63.48%; H, 5.78%
Calculated for $C_1H_{12}O_4$: C, 63.51%; H, 5.82%.

This was identified as o-carbomethoxy-dihydromethyl cinnamic acid.

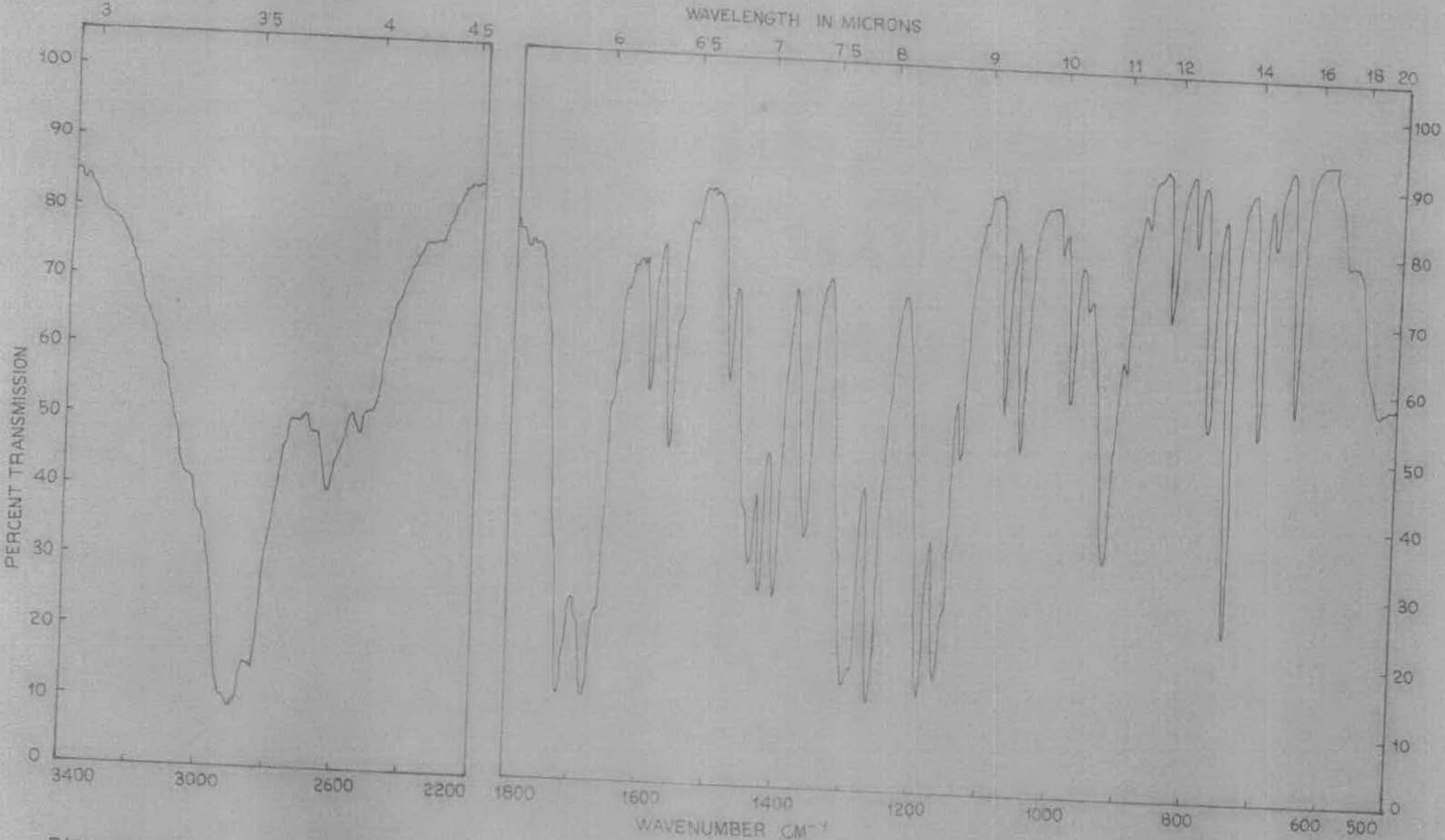


Fig- 46 o- Carboxy di hydro methyl cinnamate

7. Preparation of o-carboxy dihydro methyl cinnamate from o-carboxy dihydro cinnamic acid (141):

A mixture of 0.5 gm diacid in excess dry methanol and 3 drops of conc. sulphuric acid was kept overnight at room temperature. Then excess methanol was removed at 30°. Residue was treated with ether and washed with water to free the mineral acid. The organic layer dried on anhydrous sodium sulphate and filtered. Ether was removed. Residue recrystallised from pet-ether. Colourless needle shaped crystals. m.p. 86°C. Yield - 0.3 gm.

I.R. peak at 1710 cm^{-1} and 1680 cm^{-1} showed that this compound contains one ester and acid group. Fig. 46.

Gave a depression in melting point on mixed melting point determination with the above half ester (6). So these two compounds were different.

Analysis found:	C, 63.45%; H, 5.71%
Calculated for $C_1H_{12}O_4$	C, 63.51%; H, 5.82%.

8. α-methyl 3,4 dihydro naphthalene ( ):

4.15 gm of clean magnesium fillings dried in vacuum covered with 25 c.c. dry ether in a three necked R.B. flask, then 15 c.c. Methyl Iodide in 100 c.c. ether added dropwise; first lot rapidly, while the condenser was cooled with ice-cooled water and addition of the methyl iodide slowed down to maintain refluxing. The flask was warmed on steam bath for 5-6 hrs when all magnesium dissolved. The flask was placed in a ice-bath. 20 gm of 1-tetralone in 70 c.c. ether was added dropwise. After standing 1.5 hr. (first in ice-bath, then at room temperature) the flask was heated on water for half an hour. Reaction mixture was kept overnight. The reaction product decomposed with 17 ml conc. sulphuric acid in 70 c.c. water in the cold. The aqueous layer washed with ether and combined extract dried on anhydrous sodium sulphate and ether was removed and distilled at 115°/10 mm. The distillate was then taken in 200 c.c. ether and washed with 10% hyposolution and washed with water till neutral. Ether was removed and the residue was distilled at 110-15°/10 mm. Yield-10 gm. I.R. of this product showed no carbonyl band.

9. Preparation of trans-o-chloro-(α-naphthyl) cinnamic acid (182):

A mixture of 14 gms (0.1 mole) of o-chlorobenzaldehyde 28 gms (0.15 mole) of 1-naphthyl acetic acid, 50 ml (0.54 mole) of acetic anhydride and 10 gms (0.1 mole) of trimethyl amine was refluxed for 30 minutes in a 250 ml flask. The solution was cooled to 90°C, and 50 ml of cold water was added over a period of 5 mins, at a rate that maintained the temperature above 90°C. Trans-o-chloro-(1-naphthyl) cinnamic acid precipitated out. It was separated by filtration and washed with

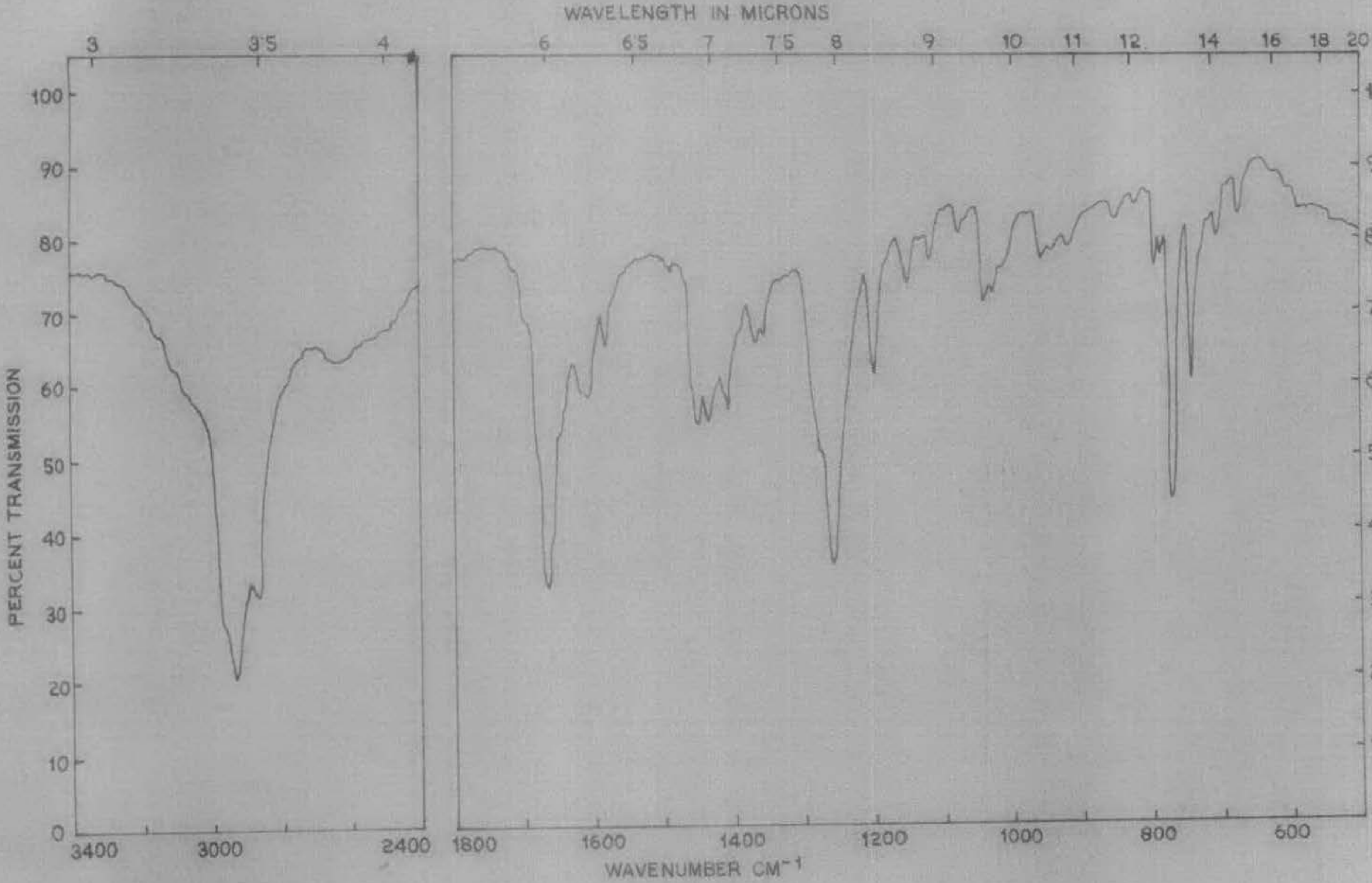


Fig- 47. Trans-o- chloro-α naphthyl cinnamic acid.

30 ml of 50% acetic acid and with water. It was air dried and recrystallised from methanol several times giving a light yellow coloured crystals of m.p. 160-161°C. I.R. peak at 1680 cm^{-1} showed that this is a conjugated acid and also gave positive test for an acid function. Yield-18 gms.

Analysis found: C, 73.28%; H, 4.13%
Calculated for $C_{19}H_{13}O_2Cl$ C, 73.91%; H, 4.24%
I.R. (neat) Fig. 47.