

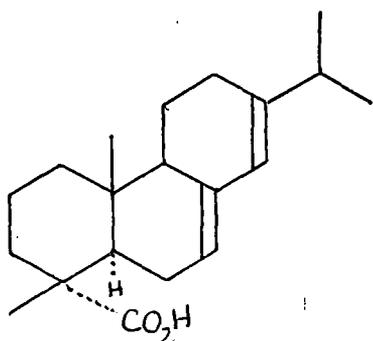
PART - III

Attempted Synthesis of C₁₁ -acid - a
degraded product of abietic acid.

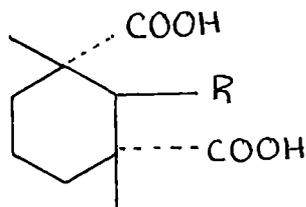
CHAPTER - I

Section A: Introduction

Abietic acid (1) on energetic oxidation with potassium permanganate or vigorous ozonolysis^{1,2} and on oxidation with nitric acid³, gives two homologous tricarboxylic acids $C_{11}H_{16}O_6$ of m.p. 219° and $C_{12}H_{18}O_6$ of m.p. 213° which have been assigned structures 2 and 3 respectively⁴⁻⁷.



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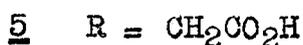
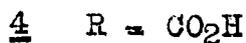
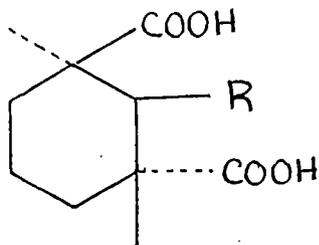
2) R = COOH

3) R = CH₂COOH

The important part played by these acids in the elucidation of the structure and stereochemistry of A/B ring junction of abietic acid and other related resin acids is well known. The fact that these acids are optically inactive⁸ settled the relative configuration of the two asymmetric carbon atoms (C-1 and C-3) substituted by methyl and carboxyl groups.

Determination of the configuration of the substituents at the carbon atom C-2 in the C₁₁- and C₁₂ - acids offered considerable difficulty. However, Barton and Schmeidler⁷ from a study of the thermodynamic dissociation constants of the C₁₁-acid and its mono and dimethyl esters arrived at the conclusion that the C₁₁ -acid has trans meso structure.

Mention should also be made of optically active C₁₁- and C₁₂- acids which were obtained by Ruzicka and Bernold⁹ as mixture, by the oxidation of agathene dicarboxylic acid. Although these acids were not obtained in a pure state, the very fact that their ester mixture showed optical activity, along with the evidence that the stereochemistry of agathene dicarboxylic acid is the same as that of abietic acid, led Ruzicka to assign the stereostructures 4 and 5 for the active C₁₁ - and C₁₂ acids respectively.



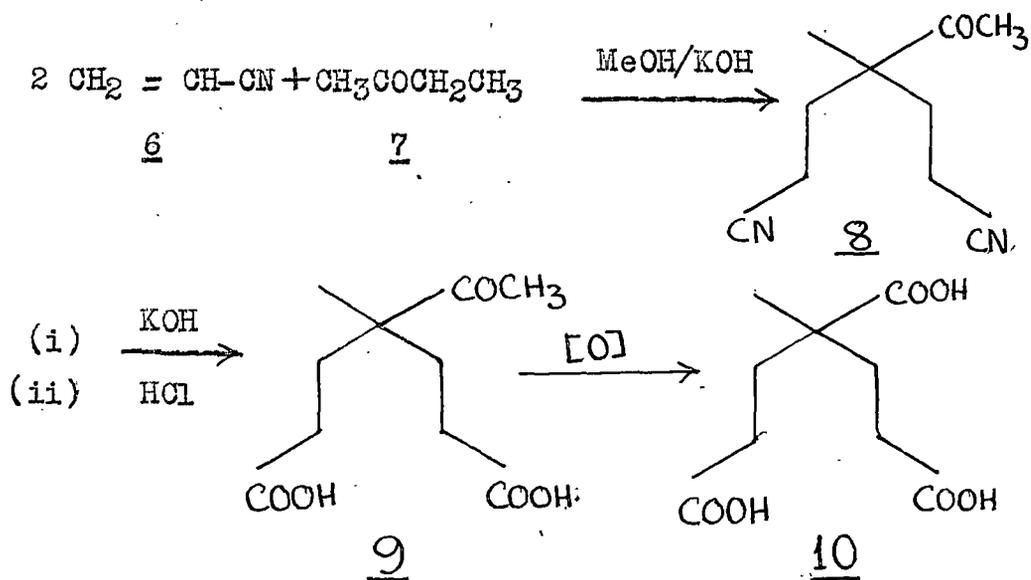
In view of the important part played by the C₁₁- and C₁₂- acids in the elucidation of the structures of diterpenoid resin acids, there have been attempts to provide confirmation of their structures by synthesis.

Mention may be made of the unsuccessful attempts by Arbusov and Schapschinskaja¹⁰, for the synthesis of C₁₁- and of Mukherjee¹¹, Banerjee¹² and Rao et al¹³ for the synthesis of C₁₂- acids (degraded product from naturally occurring abietic acid). Mukherjee¹¹ as well as Banerjee¹² and Rao et al¹³ synthesised the stereo isomers.

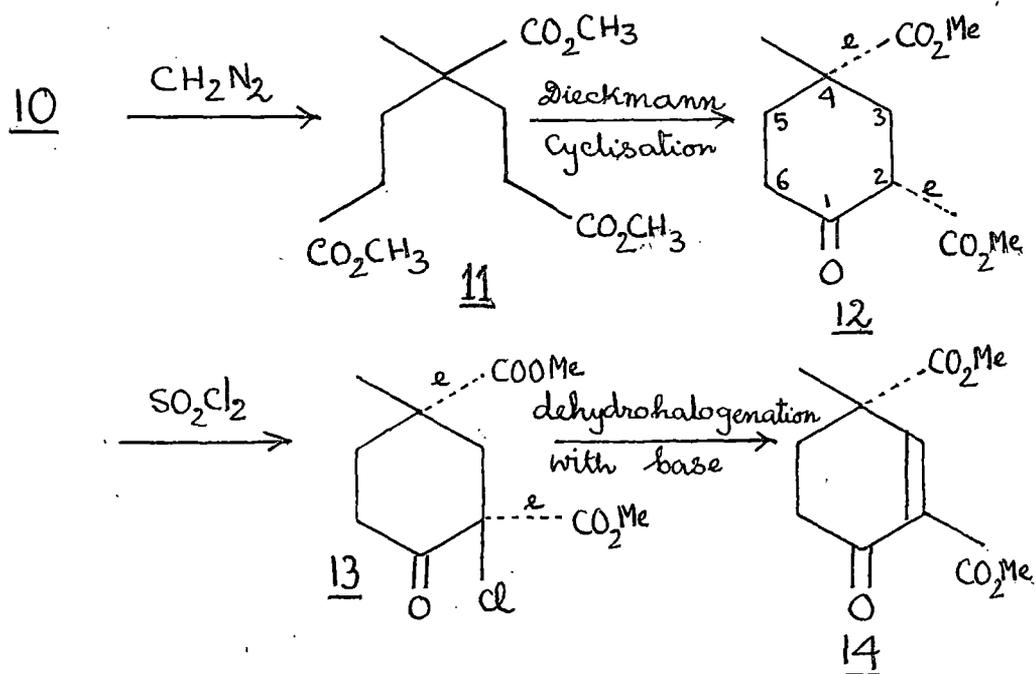
Section B: Scope of the present work

As no successful method for the synthesis of C₁₁- acid which is identical with the C₁₁ acid derived from abietic acid has yet been achieved we proposed a route for its total synthesis which is outlined as follows:

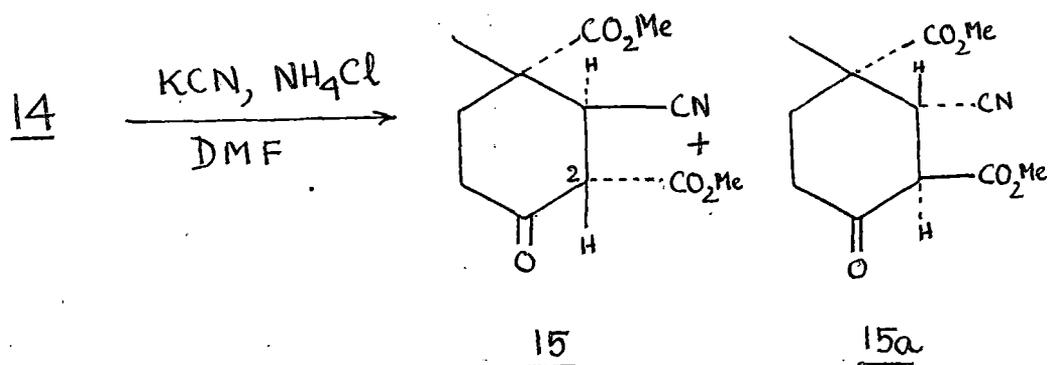
Bruson and Reiner^{14a} cyanoethylated ethyl methyl ketone 7 (1 mole) with acrylonitrile 6 (2 moles) in presence of base (methanolic potassium hydroxide), thereby they obtained 4-acetyl 4-methyl pimelonitrile 8 which on hydrolysis gave the diacid i.e. γ -methyl γ -acetyl pimelic acid 9. The latter on oxidation with calcium hypochlorite (H.T.H quality) containing 80% available chlorine afforded the triacid i.e. γ -methyl γ -carboxy pimelic acid 10.



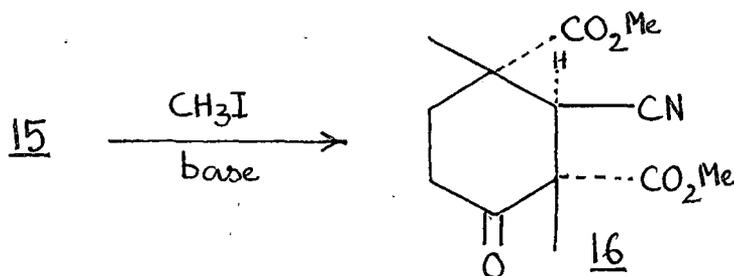
In view to esterify completely the carboxyl groups of γ -methyl γ -carboxy pimelic acid 10, we proposed to esterify the same with excess of diazomethane. Thus a triester i.e. γ -methyl γ -carbomethoxy dimethyl pimelate 11 would be obtained. The latter on Dieckmann cyclisation is expected to yield the β -keto ester 12. Inspection of Drieding model favours the orientation of the substituents at the asymmetric centres C-2 and C-4 of the β -keto ester as indicated in its structure i.e. two carbomethoxy groups are cis oriented in equatorial conformation. Then we intended to introduce a double bond between C-2 and C-3 from the β -keto ester by reaction with sulfonyl chloride (the halogen atom is expected to be linked with the more substituted carbon atom α to carbonyl group i.e. attachment at C-2 is preferred to C-6) followed by dehydrohalogenation with a base.



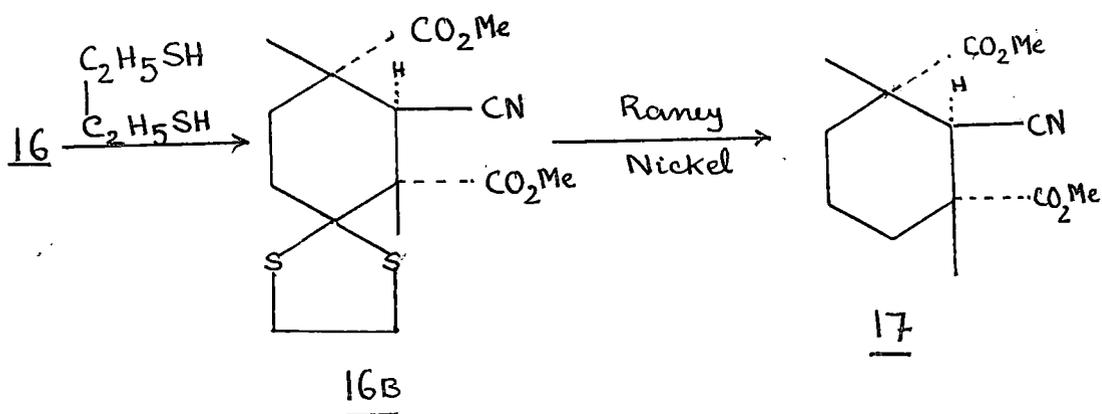
The next part is to introduce a cyano group at the β -position of the carbonyl group of 14. It is well known that $\alpha\beta$ unsaturated carbonyl compounds can be easily hydrocyanated with the use of potassium cyanide in presence of ammonium chloride using dimethyl formamide as solvent^{14b} (1:4 addition) giving rise of stereoisomers 15 and 15a



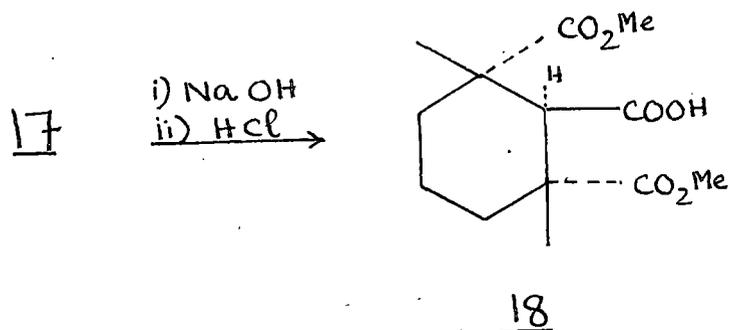
After separating the desired isomer 15 we like to introduce the angular methyl group at C-2 i.e. α to the carbonyl group by the conventional method i.e. treatment of with methyl iodide in presence of base.



Now the carbonyl group from β keto ester is to be removed. This could be easily done from 16 by the well established method i.e. ketalisation with ethane dithiol followed by desulfurisation with Raney nickel.



This compound 17 on alkaline hydrolysis followed by acidification is expected to give 18.



The hindred ester group in 18 could be hydrolysed with dimethyl sulfoxide in presence of potassium tertiary butoxide by the method of Chang and Wood¹⁵ to C₁₁ - acid i.e. 1, 3 -dimethyl cyclohexane 1,2,3-tricarboxylic acid 19. This is expected to be identical in all respects with C₁₁- acid derived from abietic acid by degradation.

