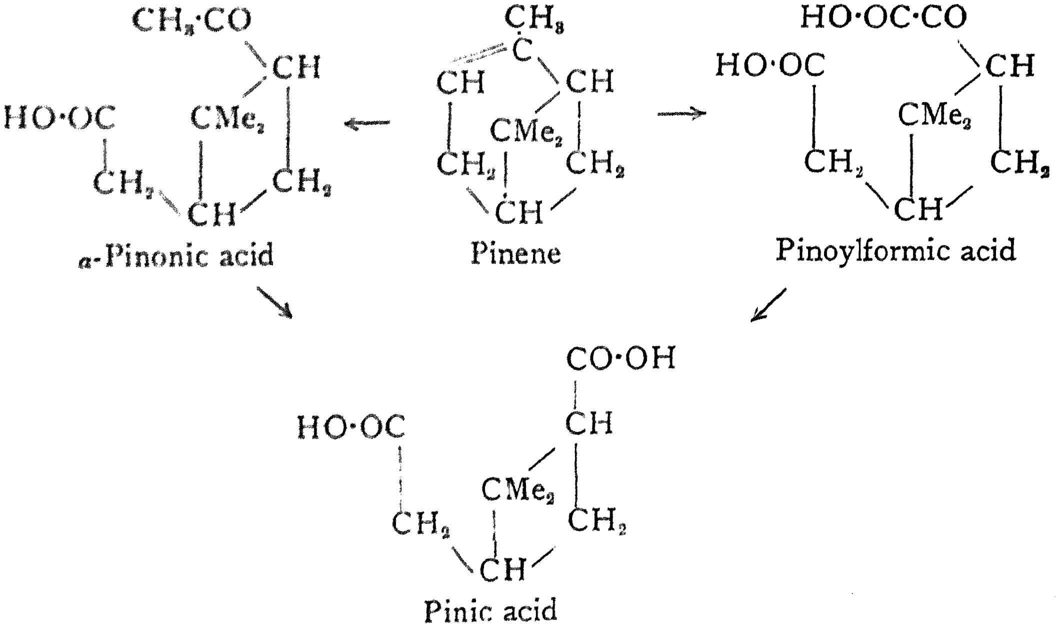
AN ATTEMPTED SYNTHESIS OF NORPINIC ACID.

By Kanai Lal Ganguly.

α-Pinene, a common constituent of many essential oils, on treatment with potassium permanganate solution, gives a series of oxidation products.[1] Among the first products formed are the two acids: α-pinonic acid, $C_{10}H_{16}O_3$ and pinoylformic acid, $C_{10}H_{14}O_5$.

α-Pinonic acid contains the group, $CH_3 \cdot CO \cdot$, as on treatment with bromine and potash it is converted into an acid, $C_8H_{13}O_2.CO_2H$, pinic acid, containing one less carbon atom in the molecule. Pinoylformic acid can be converted into pinic acid by further oxidation, and the different changes are indicated in the following formulæ :—



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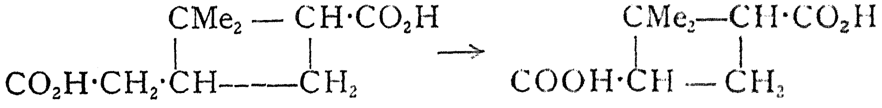
[1] Baeyer. *Ber.*, 1896, **29**, 1907.

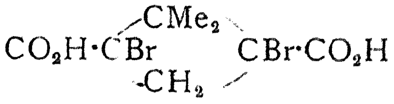
Pinic acid is very stable, but, by first bromination and subsequent hydrolysis, it may be further oxidised to its lower homologue norpinic acid



Pinic acid Norpinic acid

The structure of norpinic acid is of importance, as on it is based to a large extent the elucidation of the structure of pinene and of the products derived from pinene, and it is clear that the undisputed establishment of the structure of norpinic acid and thus of pinene has a great effect in discussions dealing with the structures of many members of the terpene series. Hence the importance of the synthesis of norpinic acid.

The synthesis of this acid offers further interest from the fact that it is a polymethylene derivative, and, as compared with many acids derived from polymethylene hydrocarbons, is an extremely stable compound. It resists all attempts at fission of the ring by such reactions as :—*a*) treatment with concentrated sulphuric acid for several hours on the water bath ; *b*) heating with hydrobromic acid at 120°; and *c*) boiling with 10 per cent. sulphuric acid for several hours. It is attacked with great difficulty by bromine at 100°, and at 120° a bromo-derivative,



is obtained.[1]

It exists in two stereoisomeric forms—*cis* melting at 173° and *trans* melting at 144°—and is a homologue of another polymethylene derivative, caronic acid, which also exists in *cis* and *trans* forms, and which was first synthesised by Perkin and Thorpe[2] by the action of alcoholic potash on ethyl α-bromo-ββ-dimethylglutarate.

Perkin and Simonsen[3] have drawn the conclusion that the cyclobutane ring is rendered stable by the presence of carboxylic groups in the 1 : 3 positions and that *gem*-dimethyl groups also exert a stabilising influence.

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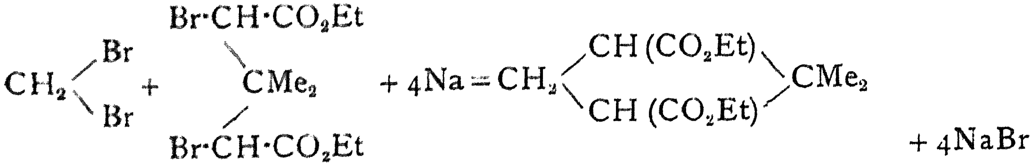
[1] Perkin and Simonsen, *J. Chem. Soc.*, 1909, **95**, 1170.
[2] *Ibid.*, 1899, **75**, 56.
[3] *Ibid.*, 1909, **95**, 1171.

Ingold[1] draws attention to the strain involved in the closure of the ring in the case of different polymethylene compounds, and in the series, cyclopropane, cyclobutane, cyclopentane and cyclohexane, claims to prove that the strain is greatest in the case of cyclobutane derivatives and least with cyclohexane compounds. These conclusions appear to be in harmony with the values obtained by Stohmann and Kleber[2] for the heats of formation of the different compounds and also with the difficulty experienced by many experimenters in closing the four carbon chain to a ring. Ingold's experiments on the action of concentrated alkali on α-halogenated glutaric acids and α-halogenated adipic acids illustrate, in a marked manner, the low yields obtained for a cyclobutane acid when working under conditions quite similar to those which produce good yields in the cyclopropane series. These facts indicate that although it is comparatively easy to synthesise the cyclopropane analogue of norpinic acid, viz. caronic acid, it does not necessarily follow that good yields of norpinic acid can be obtained by following similar methods.

Ingold has also drawn attention to the stabilising effect of *gem*-dimethyl groups and has pointed out that many of the cyclopropane and cyclobutane compounds which occur naturally possess such *gem*-groups.

EXPERIMENTAL

Attempted Synthesis of Ethyl Norpinate from Ethyl αα′-Dibromo-ββ-dimethylglutarate, Methylene Iodide (or Bromide) and Sodium



$$CH_2\begin{cases}Br\\Br\end{cases} + \begin{matrix}Br\cdot CH\cdot CO_2Et\\ \diagdown \\ CMe_2 \\ \diagup \\ Br\cdot CH\cdot CO_2Et\end{matrix} + 4Na = CH_2\begin{cases}CH(CO_2Et)\\CH(CO_2Et)\end{cases}CMe_2 + 4NaBr$$

The glutaric ester was first synthesised by Perkin and Thorpe[3] by the action of bromine and phosphorus pentabromide on ββ-dimethylglutaric anhydride, which was prepared from ethyl α-cyano-ββ-dimethylglutarate. For the preparation of the dibromodimethylglutaric ester the following procedure has been adopted. By the

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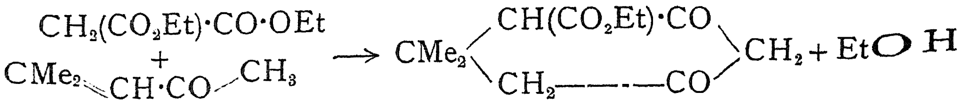
[1] *J. Chem. Soc.*, 1921, **119**, 305, 951.

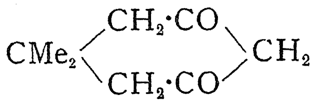
[2] *J. Pr. Chem.*, 1892 [ii] **45**, 475.

[3] *J. Chem. Soc.*, 1901, **79** 754.

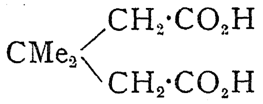
condensation of mesityl oxide with ethyl sodiomalonate ethyl dimethyldihydroresorcylate was obtained.[1]



and on hydrolysis with concentrated barium hydroxide solution gave dimethyldihydroresorcinol,



which was oxidised with sodium hypobromite at 0° to ββ-dimethylglutaric acid [2]



The method of conversion of this acid into its αα-dibromo-derivative was that used by Perkin, viz. conversion into the anhydride [3] bromination of the anhydride and formation of the ester.[4]

In these reactions the following points are worthy of note :—

(a) *Preparation of Mesityl Oxide.*—100 grams of pure dry acetone (redistilled over calcium chloride) were cooled in a Dewar flask by means of a freezing mixture of ice and salt and saturated with dry hydrogen chloride, a reaction which required about four hours. The mixture was kept at the same temperature in the Dewar flask for a week and was then poured onto powdered ice, neutralised with strong sodium hydroxide solution, extracted with ether and the ether removed by distillation. The hydrochloride of mesityl oxide was then heated for some time with powdered sodium hydroxide, filtered and the filtrate fractionated. A yield of 25 grams boiling at 130° was obtained, corresponding with a 30 per cent. yield of the theoretical.

(b) *Preparation of Phosphorus Pentabromide.*—The tribromide was prepared in the usual manner from 10 grams of red phosphorus

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[1] Vorlander, *Annalen*, 1897, **294**, 300 and 314 ; Komppa, *Ber.*, 1899, **32**, 1422.

[2] Compare also Walker and Wood, *J. Chem. Soc.*, 1906, **89**, 599.

[3] *Ibid.*, 1896, **69**, 1475.

[4] *Ibid.*, 1901, **79**, 754.

and 20 c.c. of dry bromine, 56 grams of tribromide boiling at 170° under 680 mm. pressure were obtained. This tribromide was cooled in a freezing mixture and 12 c.c. of dry bromine added carefully with constant stirring. 86 grams of a *green* form of phosphorus pentabromide were obtained.

SYNTHETICAL EXPERIMENTS

1. 0·8 gram of sodium wire was added to a mixture of 50 c.c. of pure dry benzene, 3 grams of methylene bromide and 4 grams of *αα*-dibrom-*ββ*-dimethylglutaric ester, and the whole heated on the water bath in a reflux apparatus during 21 hours. The mass was then filtered, the benzene removed by distillation and the residual oil, which was too small in quantity to be fractionated, was hydrolised with alcoholic potash. A small amount of an acid was isolated, but this could not be norpinic acid as it contained halogen and its melting point, 150°, was quite different from that of norpinic acid.

2. 24 grams of the *αα*-dibrom ester were mixed with 17·4 grams of methylene bromide and 50 c.c. of pure dry benzene, and 12 grams (4 atomic proportions) of sodium added and the whole left over night. Next morning the mixture was heated during 48 hours on the water bath in a reflux apparatus provided with a calcium chloride tube. No appreciable reaction was noticed and the benzene layer was removed, the benzene and methylene bromide distilled off and the residual oil fractionated under reduced pressure, when the following fractions were obtained:—

No. 1 boiling at 140-150° under 15 mm. pressure.
„ 2 „ 170-180° „ 15 „ „

The boiling point of the first fraction, which was very small in amount, corresponds with that of ethyl norpinate. This oil was mixed with 50 per cent. hydrochloric acid and heated on the water bath for 12 hours in a reflux apparatus. After removal of the water and hydrochloric acid on the water bath a viscous mass was obtained which was drained on porous tile and dried. The solid so obtained crystallised from hot water as a white solid, acid in character and melting at 172°. This melting point corresponds with that of *cis*-norpinic acid, but as the quantity was very small an estimation of carbon and hydrogen was not possible.

3. 15 grams of dibromo ester and 17 grams of methylene iodide were dissolved in 50 c.c. of pure dry benzene and 8 grams (4 atoms) of sodium wire were added and the mixture heated on the water bath

during 12 hours in a reflux apparatus. Very little action was observed, but the oily layer was fractionated and the following fractions collected :—

No. 1 .... 60—80° under 15 mm. pressure.
,, 2 .... 140—150° ,, ,,
,, 3 .... 170—180° ,, ,,

Fraction 1 is unaltered methylene iodide and fraction 3 unaltered dibrom ester. Fraction 2 was very small and when hydrolised gave the same crystalline acid, melting at 171–172°, which was obtained in experiment No. 2.

From these experiments it is clear that norpinic acid cannot be readily synthesised by the action of sodium on a mixture of ethyl αα-dibromo-ββ-dimethylglutarate and methylene bromide or iodide. If the acid is formed at all, the amount is extremely small.

Department of General and Organic Chemistry,
Indian Institute of Science,
Bangalore.