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SYNTHETIC STUDIES ON RESIN ACIDS—VII[1a]

SYNTHESIS OF TWO ISOMERS OF 4,10-DIMETHYLDECALIN-4-CARBOXYLIC ACIDS

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Abstract—Syntheses of two stereoisomers of 4,10-dimethyldecalin-4-carboxylic acid have been described. The stereochemistry of these acids has been established.

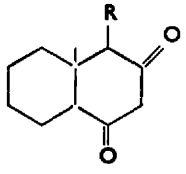
THE synthesis of an isomer of 4,10-dimethyldecalin-4-carboxylic acid, m.p. 120°, shown[2] to exist in another polymorphic form, m.p. 132°, was reported from this laboratory in connection with model studies[3a] on syntheses[3] of the tricarbocyclic resin acids. It was tacitly assumed at that time that the acid would possess the stereochemistry as depicted in I. The *trans* relationship of the angular methyl and carboxyl group was assigned on the basis of the course of reactions involved in its synthesis and an analogy to the formation of II from the corresponding tricyclic ketone (IIa). The ring-junction was presumed to be *trans* from the presence of the α-decalone system in the original ketone (III). In the light of the observations subsequently made by Sondheimer,[4] the decalone (III) has now been found to be a mixture of *cis* and *trans* forms with the *trans* one predominating. Hence it became necessary to review further the concepts regarding the stereochemistry of the bicyclic acid, m.p. 132°. With this objective, several methods have been investigated to achieve the syntheses of other stereoisomers of this acid.

[1] [a] Part VI, C. T. Mathew, G. C. Banerjee and P. C. Dutta, *J. Org. Chem.* **30**, (1965); [b] Communications regarding this paper may be made to this author.

[2] C. T. Mathew and P. C. Dutta, *Proc. Chem. Soc.* 135 (1963).

[3] [a] U. R. Ghatak, N. N. Saha and P. C. Dutta, *J. Amer. Chem. Soc.* **79**, 4487 (1957); [b] N. N. Saha, B. K. Ganguly and P. C. Dutta, *Ibid.* **81**, 3670 (1959); [c] U. R. Ghatak, D. K. Datta and S. C. Ray, *Ibid.* **82**, 1728 (1960); [d] M. Sharma, U. R. Ghatak and P. C. Dutta, *Tetrahedron* **19**, 985 (1963).

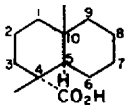
[4] F. Sondheimer and D. Rosenthal, *J. Amer. Chem. Soc.* **80**, 3995 (1958). With reference to the observation (cf. footnote 16*a*, p. 3997) by these authors regarding yield of the ketone (II), the first synthesis of which was reported[3a] by us, it is relevant to record here a few points. In our synthesis the stereo-isomeric mixture of the diketone (i), obtained as a glassy solid through alkaline



i, R = H
ii, R = CO_2Et

hydrolysis of the crude diketo-ester (ii), was directly used after purification by distillation. The overall yield of the ketone (II) from 2-methylacetylcyclohexene is 13–15%.

CHART I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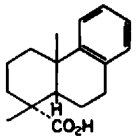
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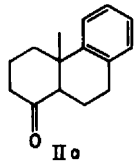
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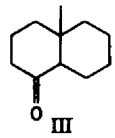
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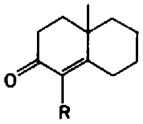
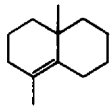

IV, R=Me
XXI, R=H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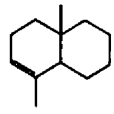
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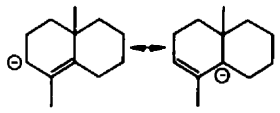
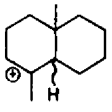

VI VIa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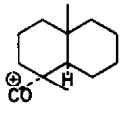
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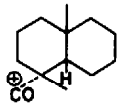
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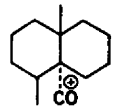
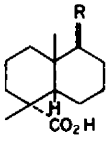
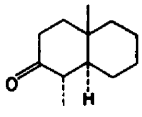

VIIc


VIII, R=O
IX, R=H$_2$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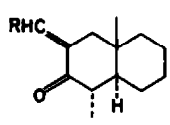
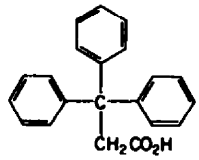
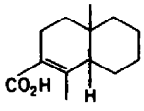
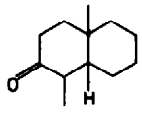

XI, R=OH
XII, R=SC$_6$H$_{13}$(n)


XIII


XIV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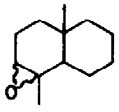
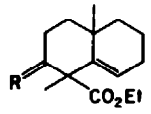
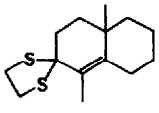
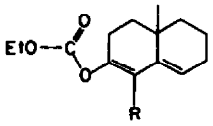
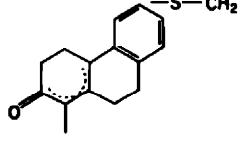

XVI


XVII, R=O
XVIII, R=


XIX


XX, R=Me
XXII, R=H


XXIII

Carbonylation of a suitable cyclic olefin such as V was first attempted. Dimethyloctalone[5] (IV) was reduced according to Huang-Minlon to give V together[6] with Va in the ratio of 75:25, evidently arising through irreversible addition[7] of the proton to the resonating anions VI and VIa. To ensure that the starting material consists mostly of V, the carbonyl group in IV was removed by the procedure of Brown and White.[8] Vapour phase chromatography (VPC) of the product indicated the purity to be 90%. Carbonylation[9] of this octalin in sulphuric acid afforded in poor yield the acid I, m.p. 132°, identified by mixed m.p. with an authentic sample of the acid melting at 132°, mentioned earlier. Regarding the stereochemistry of this acid, it would be reasonable to assume that the attack of carbon monoxide to the protonated hydrocarbon (VII) would be from the side opposite to the angular methyl group. The proton may attach itself to the angular carbon rendering it asymmetric thereby leading to two possibilities VIIa and VIIb. The participation of VIIc is less likely from steric considerations. While Bartlett[10] and House[9] had the view that the carbonylation reaction is kinetically controlled producing one of the isomers with subsequent equilibration, Stork[11] is of the opinion that the nature of the product is determined by thermodynamic considerations and hence subject to steric control. Whatever may be the factors controlling the process, it is significant to note that carbonylation of V gives exclusively a single product, albeit in poor yield. Incidentally, this acid was again identified with the one obtained by Huang-Minlon reduction of the keto-acid (VIII)[2,12] known to possess *cis* ring-junction, through its conversion to desisopropyl-*cis*-dehydroabietic acid (II). So the stereoformula of the 132° melting acid is IX. The p*Ka*[13] (7·96) of this acid (IX) is consistent with the above formulation.

Further efforts to synthesize the other isomer with *trans* ring-junction were next made. Dimethyloctalone (IV) was reduced with sodium and liquid ammonia in the presence of t-butanol, with a view to ensuring[14] *trans* ring-junction. The crude reaction product was oxidized with Jones' reagent.[15] The pure *trans*-ketone[16] (X) obtained through purification[16] of the semicarbazone, was converted into the hydroxymethylene compound (XI) which was condensed with n-hexylmercaptan.[17] The crude thiomethylene derivative (XII) failed to condense with ethyl bromoacetate in the presence of potassium t-butoxide. In an alternative attempt using triphenylmethylsodium, the only product isolated in poor yield was triphenylmethylacetic acid (XIII).[18]

[5] F. D. Gunstone and R. M. Heggie, *J. Chem. Soc.* 1437 (1952); J. K. Chakrabarti, P. Dutt and P. C. Dutta, *Ibid.* 4978 (1956).
[6] G. Lardelli and O. Jeger, *Helv. Chim. Acta* **32**, 1817 (1949).
[7] R. B. Bates, G. Büchi, T. Matsuura and P. R. Shaffer, *J. Amer. Chem. Soc.* **82**, 2327 (1960).
[8] B. R. Brown and A. M. S. White, *J. Chem. Soc.* 3755 (1957).
[9] H. O. House and W. F. Gilmore, *J. Amer. Chem. Soc.* **83**, 3980, 3984 (1961).
[10] R. E. Pincock, E. Grigat and P. D. Bartlett, *J. Amer. Chem. Soc.* **81**, 6332 (1959).
[11] G. Stork and M. Bersohn, *J. Amer. Chem. Soc.* **82**, 1261 (1960).
[12] C. T. Mathew, G. Sengupta and P. C. Dutta, *Proc. Chem. Soc.* 336 (1964).
[13] P. F. Sommer, C. Pascual, V. P. Arya and W. Simon, *Helv. Chim. Acta* **46**, 1734 (1963).
[14] [a] G. Stork and S. D. Darling, *J. Amer. Chem. Soc.* **86**, 1761 (1964); [b] D. H. R. Barton and C. H. Robinson, *J. Chem. Soc.* 3045 (1954).
[15] A. Bowers, T. G. Halsall, E. R. H. Jones and A. J. Lemin, *J. Chem. Soc.* 2548 (1953).
[16] M. Yanagita and R. Futaki, *J. Org. Chem.* **21**, 949 (1956).
[17] R. E. Ireland and J. A. Marshall, *J. Org. Chem.* **27**, 1615 (1962).
[18] G. G. Henderson, *J. Chem. Soc.* 226 (1887).

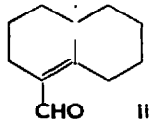
Bowers[19] has elegantly utilized the cleavage of epoxides with potassium cyanide to afford α,β-unsaturated acids. The hydrocarbon mixture (V, Va), obtained by Huang-Minlon reduction was oxidized with perbenzoic acid. The cleavage of the epoxide mixture with potassium cyanide surprisingly gave a reaction mixture which was shown by spectral evidence to contain a carbonyl compound[20] besides other materials. The former was separated as the semicarbazone and the non-carbonyl fraction was dehydrated to afford the α,β-unsaturated nitriles, which on drastic alkaline hydrolysis afforded a crystalline acid, m.p. 121°. The structure XIV, assigned to this acid, is established by the following fact. On treatment with hydrazoic acid it furnished the *cis*-ketone[16] (XV), the 2,4-dinitrophenylhydrazone of which was identified by m.p., mixed m.p. with an authentic specimen kindly provided by Yanagita. This acid has evidently arisen from XVI, which in its turn has been obtained from the olefin (Va).

In our next attempt at the synthesis of the acid (I), ethyl chloroformate was condensed with dimethyloctalone (IV) in presence of potassium t-amylate with a view to isolating the keto-ester (XVII). The reaction product had the analytical data and the boiling point corresponding to XVII. Attempt to reduce the double bond under mild condition led to the regeneration of the ketone (IV) along with other low boiling products. Efforts to prepare solid derivatives, e.g., 2,4-*dinitrophenylhydrazone*, resulted in the formation of those of the ketone (IV). Experiments carried out with a view to isolating XVIII, led to the formation of XIX. The unusual behaviour of the condensation product can be best explained on the basis of the structure XX, and this is further confirmed by its strong UV absorption at 237 mμ. In the IR the compound showed bands at 5·68 (s) and 6·0 (w) μ characteristic of the enol carbonate carbonyl[21] and the double bond respectively. Moreover, the NMR spectrum showed a methyl resonance at 8·35 τ (=C(CH$_3$)—) and vinyl proton as unresolved triplet centred at 4·51 τ, attributable to the structure XX. Similarly, condensation of the ketone (XXI) with ethyl chloroformate yielded the O-acylated product (XXII) characterized by its expected spectral properties and its instability towards acids. Almost exclusive O-acylation with ethyl chloroformate is not surprising in view of the recent observations by House and Kramer.[22a] Wenkert *et al.*[22b] have also found that the tricyclic ketone (XXIII) undergoes only O-acylation with ethyl chloroformate.

Successful methylation of cyclohexenecarboxylic acid to XXIV[3c] with potassium

[19] A. Bowers, E. Denot, M. B. Sanchez, L. M. Sanchez-Hidalgo and H. J. Ringold, *J. Amer. Chem. Soc.* **81**, 5233 (1959).

[20] G. Sengupta, D.Phil. Thesis, Calcutta University, July (1964). The carbonyl compound has

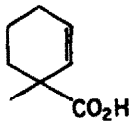


iii

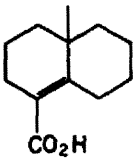
been provisionally assigned the structure (iii), from its oxidation to the acid XXV with silver oxide and from UV studies.

[21] J. P. Ferris, C. E. Sullivan and B. G. Wright, *J. Org. Chem.* **29**, 87 (1964).

[22] [a] H. O. House and V. Kramer, *J. Org. Chem.* **28**, 3362 (1963); [b] E. Wenkert, A. Afonoso, J. B. Son Bredenberg, C. Kareko and A. Tahara, *J. Amer. Chem. Soc.* **86**, 2038 (1964).



XXIV



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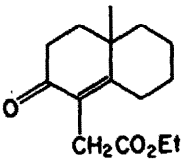

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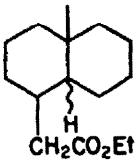
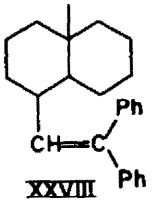
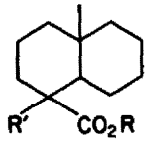


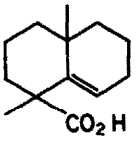
XXVII



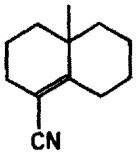
XXVIII



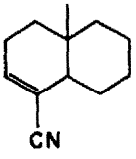
XXIX, R = R′ = H
XXX, R′ = Br; R = Et



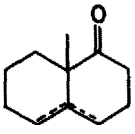
XXXI



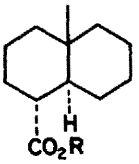
XXXII



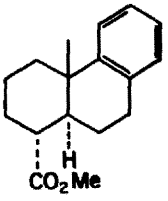
XXXII a



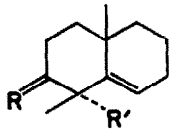
XXXIII



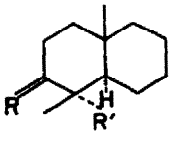
XXXIV, R = Me
XXXV, R = H



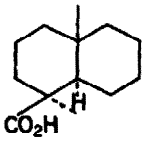
XXXVI



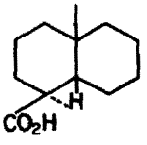
XXXVII, R = O; R′ = CH_2CO_2Et
XXXVIII, R = O; R′ = CH_2CO_2Me
XXXIX, R = S—CH_2 / S—CH_2; R′ = CH_2CO_2Me
XL, R = H_2; R′ = CH_2CO_2Me



XLI, R = H_2; R′ = CH_2CO_2Me
XLII, R = O; R′ = CH_2CO_2Me
XLIIa, R = O; R′ = CH_2CO_2H



XLIII



XLIV

amide in liquid ammonia according to Birch[23] has already been reported from this laboratory. Similar methylation of the bicyclic acid (XXV) appeared quite attractive to achieve the present goal. The synthesis of the unsaturated acid XXV has been realised by several methods.

Clemmensen reduction of the keto ester (XXVI),[24] esterification and catalytic hydrogenation gave the saturated ester (XXVII).[25] This was allowed to react with excess of phenylmagnesium bromide and the carbinol dehydrated with iodine in

[23] A. J. Birch, *J. Chem. Soc.* 1551 (1950).
[24] T. G. Halsall and M. Moyle, *J. Chem. Soc.* 4931 (1960).
[25] U. R. Ghatak, D.Phil. Thesis, Calcutta University, January (1957).

glacial acetic acid to afford the olefin (XXVIII). On oxidation with chromic acid it furnished the acid (XXIX) as a waxy solid, which could not be characterized by any definite m.p. The acid (XXIX) was brominated and the bromo-ester (XXX) obtained in a satisfactory yield. Attempts at dehydrobromination with molten potassium hydroxide in refluxing toluene[26] led to incomplete reaction as was evident from elemental analyses. Treatment of this crude acidic product with large excess of potassium amide in liquid ammonia, followed by addition of methyl iodide, was carried out with the expectation of completing dehydrohalogenation and α-methylation in one step. The product isolated was an oil, the elemental analyses of which corresponded to the unsaturated acid (XXV). Evidently methylation had not taken place. With a view to obtaining the acid (XXV) in a pure state, the cyanohydrin of the ketone (III) was dehydrated to afford a mixture of XXXII and XXXIIa. The latter was removed through Michael condensation with diethyl malonate. Alkaline hydrolysis of the purified nitrile (XXXII) furnished the crystalline acid (XXV) m.p. 127°. This acid has again been prepared in a comparable yield from the ketone (XXXIII)[27] the position of the double bond is uncertain, but it does not affect the subsequent stages of synthesis. It was reduced according to W. K. and the unsaturated hydrocarbon was oxidized with perbenzoic acid. The resulting epoxide was decomposed with potassium cyanide in ethylene glycol and the hydroxy-nitrile so obtained was dehydrated and subsequently subjected to drastic alkaline hydrolysis, leading to the acid (XXV). Attempted methylation of this acid was again unsuccessful. Its methyl ester was hydrogenated in glacial acetic acid over Pd–C. The saturated methyl ester (XXXIV) probably consisting of two isomers with the *trans* one predominating,[28] was treated with triphenylmethylsodium followed by methyl iodide. This attempt at methylation again proved to be futile as the product on hydrolysis gave a saturated acid, m.p. 150°, evidently XXXV, as indicated by elemental analysis and measurement of the dissociation constant (p*Ka* 7·76). Wenkert's reported[28] failure to methylate XXXVI is significant in this connection. As no satisfactory explanation for this abnormal behaviour can be put forward, Büchi's[29] postulate of inaccessibility to the C-4 hydrogen atom in XXXIV seems plausible.

Experiments were next designed along the lines successfully exploited for the synthesis of dehydroabietic acid by Stork and Schulenberg,[30] and desisopropyldehydroabietic acid from this laboratory.[3c] Dimethyloctalone (IV) was condensed with ethyl bromoacetate to afford XXXVII probably contaminated with some O-alkylated product. The methyl ester (XXXVIII) obtained on hydrolysis and subsequent esterification, afforded the crystalline ethylenedithioketal (XXXIX) in excellent yield. On treatment with Raney nickel it afforded XL, which was hydrogenated over Pd–C to give the ester (XLI) characterized by its anilide, m.p. 135°. To check the effect of carbonyl group on the steric course of hydrogenation, the process was reversed. Catalytic reduction of the keto-ester (XXXVIII), regenerated from the thioketal (XXXIX) by treatment with cadmium carbonate–mercuric chloride,[31] gave the keto-

[26] A. Campbell and H. N. Rydon, *J. Chem. Soc.* 3002 (1953).
[27] W. E. Bachmann and N. L. Wendler, *J. Amer. Chem. Soc.* **68**, 2580 (1946).
[28] E. Wenkert and B. G. Jackson, *J. Amer. Chem. Soc.* 5601 (1959).
[29] G. Büchi, M. Schach, V. Wittenan and D. M. White, *J. Amer. Chem. Soc.* **81**, 1968 (1959).
[30] G. Stork and J. W. Schulenberg, *J. Amer. Chem. Soc.* **84**, 284 (1962).
[31] D. J. Cram and M. Cordon, *J. Amer. Chem. Soc.* **77**, 1810 (1955).

ester (XLII). On removal of the carbonyl group under identical conditions, it afforded the ester (XLI), characterized again by the identical anilide. VPC indicated that the ester (XLI) consisted of ca. 95% of the isomer. On alkaline hydrolysis, XLII, afforded a crystalline acid, m.p. 132°. The ester (XLI) on Barbier-Wieland degradation gave an acid, m.p. 105° in poor yield.

In a recent publication, McQuillin *et al.*[32] described the synthesis of an acid, m.p. 103°, for which they suggested the stereochemistry as depicted in I. McQuillin's acid was found to be identical with the acid, m.p. 105°, by mixed m.p. The acid had the expected dissociation constant (p*Ka* 8·00).

Recently an acid, m.p. 105–107° has been synthesized by Spencer[33] from the keto acid (VIII) having *trans* ring-junction and a *trans* relationship of the angular methyl and the carboxyl group and this has been identified with our acid, m.p. 105° as well as with McQuillin's acid, m.p. 103°. Of the other two isomers, the acid (XLIII) having a *trans* ring-junction and a *cis*-relationship of the angular methyl group and carboxyl function (e.g., podocarpic acid system), is ruled out from the rate of hydrolysis of its ester[3c,33b] and from the expected[13] p*Ka* value 8·4 of the corresponding acid. Attempts to synthesize the isomer XLIV from XV[16] having *cis* ring-junction, have so far failed.

EXPERIMENTAL[34]

*4β,10β-Dimethyl-*cis*-decalin-4-carboxylic acid* (IX)

LAH (4·2 g) was added to a suspension of anhydrous $AlCl_3$ (30 g) in ether (50 ml). After the vigorous reaction had subsided, IV (10 g) in ether (5 ml) was added during 5–10 min, followed by heating under reflux for 30 min. The reaction mixture was decomposed with ethyl acetate at 0°, poured into cold dil. H_2SO_4 and extracted with ether. The product (6 g) distilled at 85–90° (10 mm). To cold conc. H_2SO_4 (12 ml, 96%) was added dropwise and with stirring the above hydrocarbon (6 g) and formic acid (12 ml, 85%), the two reactants being added simultaneously from two dropping funnels. The mixture was stirred further for 15 min, poured into ice and extracted with ether. The ethereal solution was washed with 5% Na_2CO_3 aq. The alkaline washings on acidification with 6 N HCl afforded an oily residue which solidified on treatment with pet. ether (40–60°) in the cold. Crystallization from the same solvent gave 500 mg of acid, m.p. 132°. (Found: C, 74·1; H, 10·5. $C_{15}H_{22}O_2$ requires: C, 74·2; H, 10·5%.)

β,β,β-Triphenylpropionic acid (XIII)

Sodium ethoxide prepared from Na (1·1 g) and dried *in vacuo* at 140°/10 mm, was suspended in benzene (40 ml) under N_2 at 0° and to this a solution of X (3 g) in ethyl formate (5 ml) was slowly added with shaking and left overnight. The semisolid reaction product was treated with crushed ice and the benzene layer separated. The aqueous layer was acidified with cold dil. HCl aq (1:1), saturated with NaCl and extracted with ether. On removal of the solvent, the formyl derivative (3·5 g) was obtained as a light-brown viscous material. This was refluxed under a Dean-Stark water separator with n-hexyl mercaptan (7 g), dry benzene (100 ml) and toluene-*p*-sulphonic acid (0·1 g) for 6 hr. The benzene solution was washed with 5% $NaHCO_3$ aq, water, dried and evaporated to give a brown viscous residue (5 g). After drying at 180° (0·8 mm), this was dissolved in benzene (50 ml) and treated at 0°, with a 10% excess of triphenylmethylsodium (0·42 N in ether) under dry and O_2-free N_2. After standing at 0° for 5 min, ethyl bromoacetate (10 ml) in benzene (20 ml) was added and the yellow mixture heated under reflux for 2 hr. The solvent was evaporated and the

[32] C. L. Graham and F. J. McQuillin, *J. Chem. Soc.* 4634 (1963).

[33] [a] T. A. Spencer, Private communication; [b] T. A. Spencer, T. D. Weaver, M. A. Schwartz, W. J. Greco, Jr. and J. L. Smith, *Chem. & Ind.* 577 (1964).

[34] All m.ps and b.ps are uncorrected. All compounds described herein are racemic compounds. UV spectra were determined in 95% EtOH. Microanalyses were carried out by Mrs. C. Dutta of this laboratory.

residue was hydrolysed by refluxing for 16 hr with KOH aq (75 ml, 45%) and MeOH (150 ml). The bulk of MeOH was distilled off, the residue diluted with water and the neutral material extracted with ether. Acidification and extraction of the alkaline solution afforded an oil, which was evaporatively distilled at 170–175° (0·4 mm) to yield a solid, m.p. 170–172°. It recrystallized from ethyl acetate, m.p. 178°. (Lit.[18] m.p. 177°). (Found: C, 83·2; H, 5·7. $C_{21}H_{18}O_2$ requires: C, 83·4; H, 5·9%.)

4,10-*Dimethyl*-cis-Δ^3-*octalin*-3-*carboxylic acid* (XIV)

Dimethyloctalone (IV, 37 g) in redistilled diethylene glycol (190 ml) was heated under reflux with hydrazine hydrate (35 ml, 99%) and KOH (28·5 g) for 1½ hr under N_2. The excess of water was then removed by distillation, until the temp reached 185–190° and refluxing was continued for 1 hr more. Working up afforded a sweet-smelling colourless liquid (27 g), b.p. 92–95° (35 mm). This was added slowly with stirring and ice-cooling (below 10°) to a solution of perbenzoic acid (285 ml; 60 mg of the peracid per ml). The reaction mixture was left for 6 hr at ca. 8°. It was washed with NaOH aq, water, dried over K_2CO_3 and the solvent evaporated. The epoxide distilled at 120° (20 mm). It showed no hydroxyl or carbonyl band in the IR. (Found: C, 79·0; H, 10·7. $C_{12}H_{20}O$ requires: C, 79·9; H, 11·1%.)

The mixture of above epoxides (6 g), KCN (12 g) and distilled ethylene glycol (190 ml) was refluxed under N_2 for 1 hr. The product was diluted with water and extracted with ether. On distillation, it afforded the following fractions:

(i) 1 g, b.p. 90–100° (9 mm);

(ii) 2·5 g, b.p. 125–130° (9 mm);

(iii) 2 g, b.p. 135–145° (9 mm).

The combined fractions (ii) and (iii), semicarbazide hydrochloride (8 g), alcohol (90 ml) and pyridine (5 ml) were heated on a steam-bath for 2 hr. It was then poured into cold water (ca. 500 ml) and the crude semicarbazone filtered off. The filtrate was thoroughly extracted with ether. Removal of the solvent afforded the non-ketonic component (3 g). To an ice-cold solution of the above material and fraction (i) in pyridine (10 ml) was added dropwise $POCl_3$ (4 ml). The reaction mixture was allowed to stand at room temp for 12 hr and then heated on the steam-bath for 2 hr. After cooling, it was poured on ice, acidified with conc. HCl and extracted with ether. The ethereal solution was washed with dil. HCl, dil. NaOH aq, water, dried, and evaporated. The residue was distilled to afford the following fractions:

Fraction (i) 0·4 g, b.p. 70–90° (8 mm);

Fraction (ii) 2·2 g, b.p. 125–135° (8 mm).

The fraction (ii) was again dehydrated by heating under reflux with oxalic acid (1 g) in toluene (30 ml) for 8 hr. The toluene layer was washed with 5% Na_2CO_3 aq and water. After removal of the solvent, distillation of the residue at 120–125° (8 mm) afforded the nitrile (1·5 g). A mixture of the crude nitrile (2 g), NaOH (1 g), diethylene glycol (12 ml) and water (0·5 ml) was heated under reflux for 24 hr under N_2. It was diluted with water and extracted with ether to remove any neutral matter. The alkaline solution was acidified and extracted with ether. Evaporation of the solvent gave a viscous residue (1 g), which on keeping in contact with pet. ether (40–60°) in the cold, afforded colourless crystals, m.p. 121°. (Found: C, 74·7; H, 9·8. $C_{12}H_{20}O_2$ requires: C, 74·9; H, 9·6%.)

4,10-*Dimethyl*-cis-*decalin*-3-*one* (XV)

Sodium azide (1 g) was added in small portions to a mixture of XIV (2·5 g) in conc. H_2SO_4 (5 ml) and dry $CHCl_3$ (17 ml) at such a rate that the temp of the reaction mixture remained between 40–50°. Stirring was continued until the frothing, that occurred during the reaction, completely subsided. The reaction mixture was then refluxed for 2 hr, diluted with water and again heated for 2 hr on a steam-bath. The $CHCl_3$ layer was separated, washed with 5% NaOH aq and water. Evaporation of the solvent furnished a residue (1·2 g) which readily gave a yellow 2,4-*dinitrophenylhydrazone*. On crystallization from ethyl acetate–MeOH it afforded fine yellow needles, m.p. 161°, alone or mixed with an authentic sample.

Ethyl (4,10-*dimethyl*-1,2,7,8,9,10-*hexahydronaphthyl*-3-) *carbonate* (XX)

To a cold solution of potassium t-amylate (from K, 5·8 g) in benzene (180 ml), IV (8·9 g) in benzene (20 ml) was added with shaking. The reaction mixture was kept as such for 15 min and at 60–75° (bath-temp) for 1 hr. The dark-reddish brown solution was then cooled in an ice-bath and treated dropwise with ethyl chloroformate (23 g) whereupon the colour faded. After standing as such for 15 min the reaction mixture was refluxed for 2 hr, left overnight at room-temp and finally decomposed with ice-cold water containing acetic acid (5 ml). The benzene layer was separated, washed with 5% Na_2CO_3 aq, water and dried. Distillation of the product afforded a sweet-smelling liquid (10 g), b.p. 152–154° (0·8 mm); λ_{max} 237 mμ (log ε 4·25); $\lambda_{max}^{CHCl_3}$ 5·68 (s), 6·0 (w) μ. (Found: C, 72·0; H, 8·9. $C_{15}H_{22}O_2$ requires: C, 72·0; H, 8·8%.)

Ethyl (10-*methyl*-1,2,7,8,9,10-*hexahydronaphthyl*-3-) *carbonate* (XXII)

10-Methyloctalone (XXI, 8·3 g) in benzene (130 ml) was condensed with ethyl chloroformate (7·8 g) in presence of potassium t-amylate (from K, 2·35 g) in benzene as above to afford XXII (8·1 g), b.p. 140–145° (0·7 mm); λ_{max} 235 mμ (log ε 4·30). (Found: C, 70·9; H, 8·7. $C_{14}H_{20}O_2$ requires: C, 71·2; H, 8·5%.)

Ethyl 10-*methyldecalin*-4-*acetate* (XXVII)

The keto-ester (XXVI, 23 g) was refluxed for 25 hr with amalgamated Zn-wool (120 g), toluene (50 ml), conc. HCl aq (150 ml) and water (75 ml). During this period conc. HCl aq (50 ml) was added every 5 hr. The toluene layer was separated and the aqueous layer extracted with ether. The crude residue obtained after evaporation of the solvent was dried *in vacuo* and was refluxed for 8½ hr with EtOH (140 ml) and conc. H_2SO_4 (13 ml). After working up, the reaction product yielded a colourless oil (10·4 g), b.p. 160–165° (15 mm).

The above oil (10·4 g) was hydrogenated at room temp and press. over PtO_2 (100 mg) in glacial acetic acid (25 ml). Two equivalents of H_2 were absorbed during 15 hr. After working up, a colourless mobile liquid (9·2 g), b.p. 118–120° (4 mm) was obtained. (Found: C, 75·3; H, 10·7. $C_{15}H_{26}O_2$ requires: C, 75·6; H, 10·9%.)

10-*Methyl*-4-(α',α'-*diphenyl*)-*vinyl-decalin* (XXVIII)

To the well-cooled Grignard reagent from Mg (3·7 g), bromobenzene (24 g) and ether (80 ml), the solution of the XXVII (9 g) in ether (20 ml) was added dropwise with stirring. After refluxing for 3 hr, the bulk of the solvent was distilled off, replaced by benzene (130 ml) and refluxing was continued for 6 hr. The product, isolated after decomposition with ice-cold H_2SO_4 was separated from diphenyl through steam-distillation. Extraction with ether afforded a product (15 g) which was dehydrated by refluxing with acetic acid (60 ml) and I_2 (20 mg) to give XXVIII as a viscous liquid (11 g), b.p. 195–205° (0·3 mm); λ_{max} 252 mμ (log ε 4·21). (Found: C, 90·4; H, 9·1. $C_{26}H_{30}$ requires: C, 90·9; H, 9·1%.)

10-*Methyldecalin*-4-*carboxylic acid* (XXIX)

To a stirred solution of XXVIII (105 g) in purified glacial acetic acid (60 ml) was added dropwise a solution of CrO_3 (9·5 g) in water (7 ml) and acetic acid (60 ml) during 2 hr at 85–90°. Heating and stirring were continued for further 3 hr. After decomposing the excess CrO_3 with EtOH, acetic acid was removed by passing through steam. The reaction product was extracted with ether (NaCl). The acidic material was separated through extraction with 10% NaOH aq and finally with ether on acidification. After removal of the solvent, the residue on distillation afforded a colourless viscous liquid (2 g), b.p. 136–138° (0·1 mm). (Found: C, 73·0; H, 9·9. $C_{15}H_{26}O_2$ requires: C, 73·4; H, 10·2%.)

Ethyl-10-*methyl*-4-*bromo-decalin*-4-*carboxylate* (XXX)

A mixture of XXIX (4·7 g), purified $SOCl_2$ (4·7 ml) and dry benzene (12 ml) was refluxed for 4 hr. To the crude residue, left after removal of the low-boiling products was added dry Br_2 (2·5 ml) and a trace of red P when a vigorous reaction ensued. After refluxing for 4 hr the reaction mixture was cooled, treated cautiously with EtOH (30 ml) and then refluxed for 2 hr. Isolation with ether in

the usual way afforded the bromo-ester (6 g), b.p. 137° (5 mm). (Found: C, 55·7; H, 7·7. $C_{14}H_{23}O_2Br$ requires: C, 55·4; H, 7·5%.)

10-*Methyl*-Δ^4-*octalin*-4-*carboxylic acid* (XXV)

Molten KOH (7 g) was stirred vigorously under refluxing toluene (90 ml) for a few min. Toluene (20 ml) was distilled off and XXX (6 g) in toluene (25 ml) was added dropwise to the reaction mixture. After addition, heating was resumed for 40 min. The mixture was then cooled and treated with water. The aqueous layer was washed with pet. ether (40–60°) and acidified with 6 N HCl. The product, isolated by extraction with ether, distilled at 140° (0·4 mm) as a colourless viscous oil (1·6 g). (Found: C, 71·1; H, 9·0. $C_{13}H_{18}O_2$ (unsaturated acid) requires: C, 74·2; H, 9·3%.) The acid showed positive Beilstein test for halogen.

To a stirred solution of KNH_2 (K 3·8 g) in liquid ammonia (ca. 250 ml), the solution of the above acid (1·5 g) in dry ether (20 ml) was added. After 1 hr, MeI (13 ml) was added dropwise. Ammonia was allowed to evaporate off and the acid recovered in the usual way. The above process was repeated twice to afford a colourless viscous liquid (1 g), b.p. 130–140° (0·4 mm); λ_{max} 221 mμ (log ε 3·6). (Found: C, 73·9; H, 9·5. $C_{14}H_{20}O_2$ (methylated acid, XXXI) requires: C, 74·9; H, 9·7%.)

4-*Cyano*-10-*methyl*-Δ^4-*octalin* (XXXII)

Hydrocyanic acid generated from KCN (200 g) and 18 N H_2SO_4 (200 ml) was passed into III (10 g) containing a few drops of KOH aq at −10°. After keeping at 0° overnight, the yellow reaction product was treated with conc. HCl aq and the excess HCN removed *in vacuo*. The dried crude cyanohydrin (13 g) was dissolved in pyridine (26 ml), treated dropwise with $POCl_3$ at 0° and left overnight at room temp. It was finally heated on the steam-bath for 2 hr and the unsaturated nitrile distilled, yield 7 g, b.p. 134° (8 mm). The above nitrile (7 g) and diethyl malonate (12 g) were added to a cold solution of EtONa from Na (1·3 g) in anhydrous EtOH (22 ml) and left overnight. The reaction mixture was refluxed for 3 hr, acidified with dil. HCl aq and extracted with ether. The fraction (9 g) b.p. 85–140° (8 mm) was treated with ethanolic KOH (100 ml, 5%) and left at room temp for 40 hr. After usual work-up the neutral matter afforded the unsaturated nitrile (2 g), b.p. 132–134° (8 mm), λ_{max} 224 mμ (log ε 3·84). (Found: C, 82·0; H, 9·7. $C_{13}H_{17}N$ requires: C, 82·2; H, 9·7%.)

10-*Methyl*-Δ^4-*octalin*-4-*carboxylic acid* (XXV)

(a) To a solution of NaOH (1 g) in diethylene glycol (10 ml) and water (0·4 ml) was added the above nitrile (2 g) under N_2 and the mixture heated at 200–210° for 10 hr. The reaction mixture was diluted with water and the neutral matter removed with ether. The aqueous solution was acidified with 6 N HCl and extracted with ether. The acid (500 mg) distilled at 135–140° (0·4 mm). On crystallization from ethyl acetate–pet. ether (40–60°) it afforded the crystalline acid, m.p. 127°. (Found: C, 74·2; H, 9·5. $C_{13}H_{18}O_2$ requires: C, 74·2; H, 9·3%.)

(b) The octalone XXXIII[27] (10 g) in redistilled diethylene glycol (60 ml) with hydrazine hydrate (11·1 ml, 99%) and KOH (9 g) was reduced according to the procedure described for the reduction of IV. The octalin (7 g), b.p. 92–95°/35 mm, thus obtained was slowly added to a cold (below 10°) stirred solution of perbenzoic acid in $CHCl_3$ (173 ml, containing 7·2 g of perbenzoic acid) and kept as such for 6 hr. On working up the epoxide (7 g), b.p. 110–112° (15 mm) was obtained. It showed no hydroxyl or carbonyl band in the IR (Found: C, 79·3; H, 10·8. $C_{11}H_{18}O$ requires: C, 79·5; H, 10·8%.)

A mixture of the above epoxide (7 g), dried and powdered KCN (14 g) in redistilled ethylene glycol (210 ml) was refluxed under N_2 for 1 hr. The light brown solution on working up yielded a liquid (5·3 g), b.p. 120–160° (7 mm). To an ice-cold solution of the above product (5·3 g) in dry pyridine (11 ml) was added dropwise $POCl_3$ (5·3 ml). The resulting reaction mixture was kept at room temp for 24 hr and finally heated on water bath (85–90°) for 3 hr. After working up, XXXII (3.3 g), b.p. 138–148° (14 mm), was obtained as colourless mobile liquid. λ_{max}^{alc} 220 mμ, log ε 4·1. (Found: C, 81·5; H, 9·6. $C_{13}H_{17}N$ requires: C, 82·2; H, 9·8%.)

The above nitrile (2·9 g) on hydrolysis with NaOH (1·6 g) in diethylene glycol (16 ml) and water (0·6 ml) by heating at 200–210° under N_2 for 15 hr yielded the acid (1·5 g), m.p. 110°. On recrystallization from ethyl acetate–pet. ether (40–60°), the acid melted at 127°, alone or mixed with the sample described above. (Found: C, 74·2; H, 9·6. $C_{13}H_{18}O_2$ requires: C, 74·2; H, 9·3%.)

10-Methyldecalin-4-carboxylic acid (XXXV)

The methyl ester (1·6 g) of XXV, b.p. 130° (7 mm), prepared through esterification with diazomethane, was hydrogenated in glacial acetic acid over Pd–C (0·1 g, 10%). The reduced ester (1·5 g) distilled at 112° (6 mm). The above ester was dissolved in dry benzene (30 ml) and methylation was attempted with MeI (5 ml) in presence of triphenylmethylsodium (0·19 N; 60 ml). After working up, a product (1 g), b.p. 140–145° (5 mm) was obtained which on hydrolysis with ethylene glycolic KOH yielded an oily acid, which after purification through evaporative distillation and crystallization from pet. ether yielded a solid, m.p. 142–144°. On repeated crystallization from the same solvent the acid melted at 150°. (Found: C, 73·2; H, 10·1. $C_{13}H_{22}O_2$ (methylated) requires: C, 74·2; H, 10·5; $C_{12}H_{20}O_2$ (un-methylated) requires: C, 73·4; H, 10·2%.)

Methyl 4β,10β-dimethyl-3-keto-Δ⁵-octalin-4-acetate (XXXVIII)

To a solution of potassium t-amylate (K 21 g) in benzene (1000 ml) under N_2, IV (40 g) in benzene (100 ml) was added with shaking, whereupon the solution assumed a red colour. It was heated at 60–70° for 1 hr, cooled in ice and ethyl bromoacetate (65 ml) was added dropwise with shaking; the mixture was allowed to stand overnight and then refluxed for 12 hr (N_2). Usual working-up afforded the ethyl ester (38·5 g), b.p. 135–145° (0·4 mm). (Found: C, 72·4; H, 9·1. $C_{15}H_{24}O_3$ requires: C, 72·6; H, 9·1%.)

The condensation product (20 g) was refluxed with ethanolic KOH (150 ml, 10%) for 8 hr. The acidic fraction isolated in the usual way was esterified with MeOH (30 ml) and H_2SO_4 (3 ml) to give the methyl ester (16 g), b.p. 130° (0·4 mm). No γ-lactonic band was found in the IR. (Found: C, 71·8; H, 9·0. $C_{15}H_{22}O_3$ requires: C, 71·9; H, 8·8%.)

Methyl 4β,10β-dimethyl-3-ethylenedithio-Δ⁵-octalin-4-acetate (XXXIX)

To freshly fused $ZnCl_2$ (2·4 g) and freshly ignited Na_2SO_4 (2·4 g) was added with shaking and cooling the keto-ester (5 g) followed by ethane dithiol (4·6 ml). After allowing it to stand at room temp for 40 hr, the reaction product was treated with cold water and extracted with ether. The ethereal extract was washed thoroughly with 10% NaOH aq, followed by water. Removal of the solvent and crystallization from MeOH afforded the white crystalline thioketal (7 g), m.p. 100°. (Found: C, 62·6; H, 7·9. $C_{17}H_{28}O_2S_2$ requires: C, 62·5; H, 8·0%.)

Methyl 4β,10β-dimethyl-Δ⁵-octalin-4-acetate (XL)

A mixture of W-5 Raney Ni (from 227 g of the alloy), the above thioketal (7 g), EtOH (200 ml) and ethyl acetate (50 ml) was refluxed for 18 hr. The filtrate was evaporated and the residue distilled to yield a colourless sweet-smelling liquid (4·4 g), b.p. 145° (10 mm). (Found: C, 76·4; H, 10·4. $C_{15}H_{24}O_2$ requires: C, 76·2; H, 10·2%.)

Methyl 4β,10β-dimethyl-trans-decalin-4-acetate (XLI)

A solution of XL (4·4 g) in glacial acetic acid (26 ml) was hydrogenated over Pd–C (0·25 g, 10%) for 2 hr to give the desired product (4·3 g), b.p. 136° (6 mm). (Found: C, 75·4; H, 10·9. $C_{15}H_{26}O_2$ requires: C, 75·6; H, 11·0%.)

The anilide was prepared by interaction of the above ester (0·25 g) with the reaction product of aniline (5 ml) and Grignard reagent obtained from Mg (0·25 g) and MeI (1 ml). On crystallization from ethyl acetate–pet. ether (40–60°), it melted at 135°. (Found: C, 80·0; H, 9·9. $C_{20}H_{29}ON$ requires: C, 80·2; H, 9·7%.)

4β,10β-Dimethyl-2-keto-trans-decalin-4-acetic acid (XLII)

The crystalline XXXIX (6 g) was treated with $HgCl_2$ (16 g), acetone (120 ml), $CdCO_3$ (16 g) and water (20 ml) and stirred for 22 hr. Additional quantities of $CdCO_3$ were added occasionally. The acetone solution was then filtered and the solvent was evaporated under red. press. The residual oil was extracted with ether. The colourless ester (3 g) distilled at 130° (0·4 mm). (Found: C, 72·1; H, 8·7. $C_{15}H_{22}O_3$ requires: C, 71·9; H, 8·8%.)

The above ester (5 g) in glacial acetic acid (30 ml) was hydrogenated over Pd–C (0·5 g, 10%). The uptake of H_2 was completed in 2 hr. The reduced ester (5 g) distilled at 138° (6 mm). The saturated ester (5 g) was hydrolysed for 8 hr with ethanolic KOH (100 ml, 10%). On working up the

crystalline keto-acid (2 g), m.p. 130° was obtained. On crystallization from ethyl acetate–pet. ether (40–60°), it yielded shining crystals, m.p. 132°. (Found: C, 70·4; H, 9·2. $C_{14}H_{22}O_3$ requires: C, 70·5; H, 9·2%.)

The keto group of the saturated ester after reduction with Raney Ni through thioketal under the identical experimental conditions yielded XLI, characterized through its anilide, m.p. 135°, alone or mixed with the sample previously described.

4β,10β-Dimethyl-trans-decalin-4-carboxylic acid (I)

To a well-cooled Grignard reagent from Mg (3 g) and bromobenzene (20 ml) a solution of XLI (3 g) in ether (10 ml) was added dropwise with stirring. After refluxing for 3 hr, most of ether was replaced by benzene (75 ml). The reaction mixture was refluxed for 6 hr and decomposed. The viscous liquid product (5·2 g) isolated in the usual way and separated from diphenyl and bromobenzene through steam distillation, was refluxed with methanolic KOH (100 ml, 5%) for 1 hr in order to remove any unreacted ester. The neutral material available after usual working up, was dehydrated by refluxing with acetic acid (30 ml) and I_2 (20 mg) for 2 hr. The desired product (3·3 g) distilled at 185–187° (0·2 mm). A stirred solution of this compound (5 g) in purified acetic acid (28 ml) was oxidized with a solution of CrO_3 (4·4 g) in water (3 ml) and acetic acid (28 ml) during 1 hr. at room temp. It was stirred and heated at 85–90° for 4 hr. The acidic material was isolated following the procedure used to isolate XXIX. The crude acid was evaporatively distilled in a cold finger. The fraction (510 mg) collected at bath temp 140–145° (6 mm) on treatment with ethyl acetate–pet. ether (40–60°) at 0° solidified and on crystallization from the same solvent it afforded the desired acid (200 mg), m.p. 105°. (Found: C, 73·9; H, 10·2. $C_{13}H_{22}O_2$ requires: C, 74·2; H, 10·5%.)