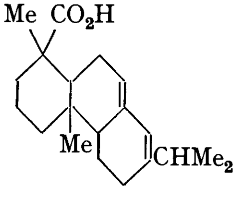
276. *A Synthesis of* 1 : 12-*Dimethyl*-7-iso*propyloctahydrophenanthrene*-1-*carboxylic Acid.*

By Robert D. Haworth and Reuben L. Barker.

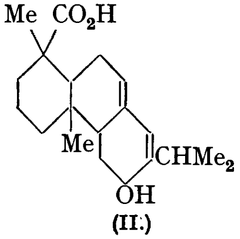
1-*Methyloctahydrophenanthrene*-1-*carboxylic acid* has been prepared by an application of the Bogert–Cook reactions to β-phenylethyl bromide and ethyl 2-methyl*cyclo*hexanone-2-carboxylate, and 1 : 12-*dimethyloctahydrophenanthrene*-1-*carboxylic acid* has been prepared similarly from *ethyl* 2 : 6-*dimethyl*cyclo*hexanone*-2-*carboxylate.* The constitutions of the two acids were established by dehydrogenation to 1-methylphenanthrene.

β-(3-iso*Propylphenyl*)*ethyl bromide* has been prepared and converted by a similar series of reactions into 1 : 12-*dimethyl*-7-iso*propyloctahydrophenanthrene*-1-*carboxylic acid.* The absorption spectrum of this acid, which gives retene on dehydrogenation, resembled closely that of *d*-dehydroabietic acid, and it is concluded that the synthetical acid represents an optically inactive form of either dehydroabietic acid or a diastereoisomeric modification.

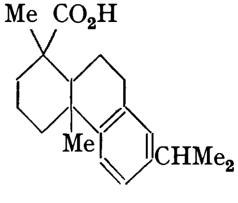
By the action of selenium dioxide in alcoholic solution, Fieser and Campbell (*J. Amer. Chem. Soc.*, 1938, **60**, 159) converted abietic acid (I) into hydroxyabietic acid (II), which was readily dehydrated in boiling acetic acid solution to dehydroabietic acid (III), m. p. 171°, $[\alpha]_D^{25^\circ}$ 61°, and it was subsequently shown (Fieser and Campbell, *ibid.*, p. 2631; Ruzicka, Bacon, Sternbach, and Waldmann, *Helv. Chim. Acta*, 1938, **21**, 591; Fleck and Palkin, *J. Amer. Chem. Soc.*, 1937, **59**, 1593; 1938, **60**, 921, 2621) that pyroabietic acid, obtained by the action of heat on abietic acid, contains considerable quantities of dehydroabietic acid (III).



(I.)



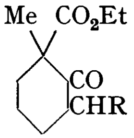
(II.)



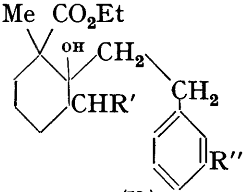
(III.)

A synthesis of an optically inactive form of 1 : 12-*dimethyl*-7-iso*propyloctahydrophenanthrene*-1-*carboxylic acid* (III) is now communicated. Resolution of the acid has not been effected, but the publication of the results in their present stage is desirable in view of the intention of Sterling and Bogert (*J. Org. Chem.*, 1939, **4**, 24) to enter the same field. Our experiments, which have been in progress since April 1938, are based upon an application of the Bogert–Cook synthesis of polycyclic hydrocarbons. Preliminary experiments were made with ethyl 2-methyl*cyclo*hexanone-2-carboxylate (IV; R = H) which with β-phenylethylmagnesium bromide gave an oily carbinol (V; R′ = R″ = H), yielding (VI; R′ = R″ = H) on dehydration with potassium hydrogen sulphate. This cyclo*hexene* derivative was cyclised with acetic–sulphuric acid to 1-*methyloctahydrophenanthrene*-1-

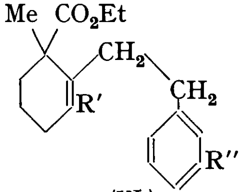
carboxylic acid (VII; R′ = R″ = H), m. p. 187—188°, which yielded 1-methylphenanthrene on dehydrogenation with selenium.



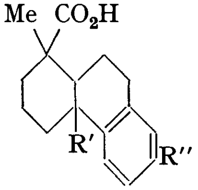
(IV.)



(V.)

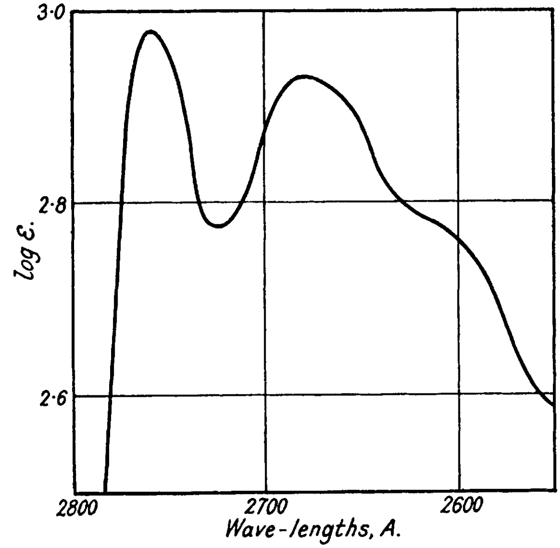


(VI.)



(VII.)

Ethyl 2 : 6-*dimethyl*cyclo*hexanone*-2-*carboxylate* (IV; R = Me), prepared from 2-methyl*cyclo*hexanone by standard methods, was converted similarly *via* the carbinol (V; R′ = Me; R″ = H) and the cyclo*hexene* (VI; R′ = Me; R″ = H), m. p. 122°, into 1 : 12-*dimethyloctahydrophenanthrene*-1-*carboxylic acid* (VII; R′ = Me; R″ = H), m. p. 233°. This acid sublimed during attempted dehydrogenation, but the *methyl* ester, m. p. 129°, was readily converted into 1-methylphenanthrene by the action of selenium at 300°.



After the investigation of a number of alternative routes, the method outlined below was adopted for the preparation of β-(3-iso*propylphenyl*)*ethyl bromide* which was required for the synthesis of dehydroabietic acid (III) :

Cumene ⟶ 4-nitrocumene ⟶ 4-aminocumene
↓
3-*bromo*-4-*aminocumene* ⟵ 3-*bromo*-4-*acetamidocumene* ⟵ 4-acetamidocumene
↓
3-*bromocumene* ⟶ β-(3-iso*propylphenyl*)*ethyl alcohol* ⟶ β-(3-iso*propylphenyl*)*ethyl bromide*

The Grignard compound of β-(3-*iso*propylphenyl)ethyl bromide reacted with ethyl 2 : 6-dimethyl*cyclo*hexanone-2-carboxylate (IV; R = Me), yielding the oily carbinol (V; R′ = Me; R″ = $CHMe_2$) which was dehydrated to the cyclo*hexene* (VI; R′ = Me; R″ = $CHMe_2$). Cyclisation with acetic–sulphuric acid gave 1 : 12-*dimethyl*-7-iso*propyl-octahydrophenanthrene*-1-*carboxylic acid* (III), which yielded retene on dehydrogenation with selenium. This conversion into retene excludes the alternative structure with an 8-*iso*propyl group, and the fact that the absorption spectrum (Figure) of the synthetic acid measured in 0·002 M-alcoholic solution closely resembles that of dehydroabietic acid (Fieser and Campbell, *loc. cit.*) confirms the structure assigned to the acid.

These experiments represent the first synthesis of the entire framework of abietic acid. The synthetic acid can exist in four diastereoisomeric forms, and until the completion of the resolution and reduction experiments which are now in progress it is impossible to state whether the synthetic acid represents *dl*-dehydroabietic acid or a diastereoisomer.

EXPERIMENTAL.

Ethyl 1-β-*Phenylethyl*-2-*methyl*-Δ^6-cyclo*hexene*-2-*carboxylate* (VI; R′ = R″ = H).—The Grignard reagent prepared from β-phenylethyl bromide (20 g.) and magnesium (2·7 g.) in ether (120 c.c.) was added during ½ hour to an ice-cold solution of ethyl 2-methyl*cyclo*hexanone-2-carboxylate (IV; R = H) (10 g.) (Dieckmann, *Ber.*, 1900, **33**, 2683). After standing at 0° for ¼ hour and at 15° for 3 hours, the mixture was decomposed with ice and ammonium chloride. The ether layer was separated, dried, and the solvent removed; ethylbenzene (10 g.) was recovered by heating the residue at 100° under 15 mm. pressure for ½ hour. The residual oil was heated with potassium hydrogen sulphate (30 g.) for 1·5 hours, and the product, isolated with ether, on fractionation gave (VI; R′ = R″ = H) (9 g.), b. p. 160—163°/3 mm. (Found: C, 79·3; H, 8·8. $C_{18}H_{24}O_2$ requires C, 79·4; H, 8·9%). This *ester* (0·5 g.) was refluxed with 20% methyl-alcoholic potassium hydroxide (10 c.c.) for 18 hours, the methyl alcohol removed, water added, and neutral material extracted with ether. Acidification of the alkaline layer yielded 1-β-*phenylethyl*-2-*methyl*-Δ^6-cyclo*hexene*-2-*carboxylic acid* which, isolated with ether, crystallised from light petroleum (b. p. 40—60°) in clusters of colourless prisms, m. p. 97—98° (Found: C, 78·4; H, 8·0. $C_{16}H_{20}O_2$ requires C, 78·7; H, 8·2%), which rapidly decolourised bromine in chloroform solution.

1-*Methyloctahydrophenanthrene*-1-*carboxylic Acid* (VII; R′ = R″ = H).—The ester (VI; R′ = R″ = H) (1 g.) was boiled for 1 hour with a mixture of glacial acetic acid (9 c.c.) and concentrated sulphuric acid (1 c.c.). The mixture was diluted with water, and the product, isolated with ether, crystallised from benzene in colourless prisms (0·15 g.) m. p. 187—188° (Found: C, 78·9; H, 8·0. $C_{16}H_{20}O_2$ requires C, 78·7; H, 8·2%), which did not absorb bromine in chloroform solution. The *methyl* ester, prepared in quantitative yield by the action of diazomethane upon an ethereal solution of the acid (VI; R′ = R″ = H), separated from light petroleum (b. p. 40—60°) in colourless plates, m. p. 75—76° (Found: C, 79·4; H, 8·3. $C_{17}H_{22}O_2$ requires C, 79·1; H, 8·5%). The acid (VII; R′ = R″ = H) or its methyl ester was heated with selenium (2·5 parts) for 24 hours at 280—290° and then for a further 24 hours at 320°; 1-methylphenanthrene, m. p. 118°, was obtained and identified by direct comparison of the hydrocarbon and its picrate, m. p. 135—136°, with authentic specimens.

Ethyl 2 : 6-*Dimethyl*cyclo*hexanone*-2-*carboxylate* (IV; R′ = Me; R″ = H).—Ethyl 6-methyl*cyclo*hexanone-2-carboxylate (Kotz and Michels, *Annalen*, 1906, **348**, 94) (28 g.) was added to a solution of sodium (4·8 g.) in absolute alcohol (84 c.c.) and refluxed during the gradual addition of methyl iodide (30 g.). After 2 hours the alcohol was removed and the product, isolated with ether and washed with dilute sodium hydroxide solution, was obtained as an oil (26 g.), b. p. 111—112°/15 mm. (Found: C, 66·6; H, 9·1. $C_{11}H_{18}O_3$ requires C, 66·7; H, 9·2%), which gave a negative ferric test.

Ethyl 1-β-*Phenylethyl*-2 : 6-*dimethyl*-Δ^6-cyclo*hexene*-2-*carboxylate* (VI; R′ = Me; R″ = H).—The Grignard reagent prepared from β-phenylethyl bromide (12·5 g.) in ether (100 c.c.) was condensed with the ester (IV; R′ = Me; R″ = H) (10 g.) in ether (20 c.c.) exactly as for the lower homologue, and the resulting oil dehydrated by potassium hydrogen sulphate (40 g.) as before. Fractionation of the product yielded (VI; R′ = Me; R″ = H) as a colourless oil (5 g.), b. p. 175—180°/4 mm. (Found: C, 79·8; H, 9·2. $C_{19}H_{26}O_2$ requires C, 79·7; H, 9·2%), which absorbed bromine in chloroform solution. Hydrolysis with boiling 20% methyl-alcoholic potassium hydroxide solution as described in the previous case, yielded the corresponding *acid*, which crystallised from light petroleum (b. p. 40—60°) in rosettes of colourless prisms, m. p. 121—122° (Found: C, 79·2; H, 8·1; equiv., 262. $C_{17}H_{22}O_2$ requires C, 79·1; H, 8·5%; equiv., 258).

1 : 12-*Dimethyloctahydrophenanthrene*-1-*carboxylic acid* (VII; R′ = Me; R″ = H).—Cyclisation of the above ester could not be effected with boiling formic acid or with stannic chloride in carbon disulphide solution. The use of aluminium chloride in carbon disulphide gave a small yield of the acid (VII; R′ = Me; R″ = H) but the best results were obtained with acetic–sulphuric acid mixture precisely as for the monomethyl acid. The dimethyl *acid*, isolated with

ether, separated from benzene (carbon) in colourless prisms (0·2 g.), m. p. 232—233° (Found: C, 79·2, 79·3; H, 8·5, 8·5. $C_{17}H_{22}O_2$ requires C, 79·1; H, 8·5%), which did not react with bromine in chloroform solution. The *methyl* ester crystallised from light petroleum (b. p. 40—60°) in clusters of needles, m. p. 128—129° (Found: C, 79·9; H, 8·8. $C_{18}H_{24}O_2$ requires C, 79·4; H, 8·8%), and dehydrogenation of this with selenium yielded 1-methylphenanthrene, m. p. 118° (picrate, m. p. 135°).

Cumene.—A mixture of *iso*propyl bromide (100 g.) and benzene (190 g.) was added during 3 hours to a suspension of aluminium chloride (12·5 g.) in boiling benzene (440 g.), and the mixture boiled for a further hour; water was added, and the benzene layer dried and fractionated. Cumene, b. p. 149—152°, was thus obtained in much better yield (75 g.) than that recorded by Bert (*Bull. Soc. chim.*, 1925, **37**, 1265).

2- *and* 4-*Nitrocumenes.*—An ice-cold mixture of concentrated nitric acid (50 g.) and concentrated sulphuric acid (100 g.) was added with vigorous stirring during 2 hours to cumene (50 g.). The temperature was kept between 5° and 10°, the stirring was continued for another hour, and the product, isolated with ether, yielded on fractionation 2-nitrocumene (5 g.), b. p. 115—120°/15 mm., and 4-nitrocumene (62 g.), b. p. 128—132°/15 mm. (Vavon and Callier, *ibid.*, 1927, **41**, 357, give 106—107°/9 mm. and 124—125°/11 mm. respectively).

4-*Cumidine.*—Iron filings (50 g.) were added with shaking to a solution of 4-nitrocumene (80 g.) in alcohol (250 c.c.) containing concentrated hydrochloric acid (5 g.). After the vigorous reaction had subsided, the mixture was refluxed for 3 hours, basified, and steam-distilled. 4-Cumidine (38 g.), b. p. 103—105°/20 mm., was isolated with ether from the distillate (Vavon and Callier, *loc. cit.*, p. 671, give b. p. 100—101°/15 mm.). The acetyl derivative, prepared by boiling with an equal volume of acetic anhydride for ½ hour, crystallised from aqueous alcohol in colourless leaflets, m. p. 102° (Constam and Goldschmidt, *Ber.*, 1888, **21**, 1158, give 102°).

3-*Bromo*-4-*acetamidocumene.*—A solution of bromine (20 c.c.) in acetic acid (20 c.c.) was added to a solution of 4-acetamidocumene (44 g.) in acetic acid (60 c.c.) at 45°; the temperature rose and was kept at 55—60° for 2 hours. The solution was diluted with water containing sodium bisulphite, and the solid was collected and crystallised from methyl alcohol; colourless prisms (40 g.), m. p. 129—130° (Found: Br, 31·0. $C_{11}H_{14}ONBr$ requires Br, 31·2%), were obtained.

3-*Bromo*-4-*aminocumene.*—The above *acetamido*-derivative (39 g.) was boiled for 3 hours with alcohol (60 c.c.) and concentrated hydrochloric acid (60 c.c.). The solution was concentrated under diminished pressure, the sparingly soluble hydrochloride was dissolved in water and basified, and the *amine* (30 g.), b. p. 139—141°/20 mm., was isolated with ether (Found: Br, 37·4. $C_9H_{12}NBr$ requires Br, 37·3%).

3-*Bromocumene.*—3-Bromo-4-aminocumene (20 g.) was dissolved in a mixture of alcohol (56 c.c.) and concentrated sulphuric acid (14 c.c.), cooled to $-5°$, and diazotised by the addition of sodium nitrite (10·4 g.) in water (16 c.c.). After ½ hour, washed copper-bronze (2·4 g.) was added, and the mixture heated on the water-bath until a vigorous reaction set in. After this had subsided, the mixture was refluxed for 1 hour, steam-distilled, and the product, isolated with ether, was washed successively with sodium hydroxide solution, water, and concentrated sulphuric acid. 3-*Bromocumene* (11 g.), b. p. 94—96°/20 mm., was obtained (Found: Br, 40·0. $C_9H_{11}Br$ requires Br, 40·2%). Oxidation with alkaline potassium permanganate for 18 hours gave *m*-bromobenzoic acid, m. p. 154—155°, undepressed by admixture with an authentic specimen.

β-3-iso*Propylphenylethyl Alcohol.*—Ethylene oxide (6 g.) was gradually added to an ice-cold solution of the Grignard reagent prepared from 3-bromocumene (20 g.) and magnesium (2·4 g.) in ether (60 c.c.). After 3 hours at 15° the ether was removed, and the residue heated at 100° for 1 hour and decomposed by the addition of ice and dilute hydrochloric acid. The product, isolated with ether, was a colourless oil (8 g.), b. p. 134—138°/20 mm. (Found: C, 80·2; H, 9·6. $C_{11}H_{16}O$ requires C, 80·5; H, 9·8%).

β-3-iso*Propylphenylethyl bromide,* obtained in 60% yields by refluxing the above alcohol with hydrobromic acid (5 parts, *d* 1·45), was a colourless oil, b. p. 130—132°/20 mm. (Found: Br, 35·0. $C_{11}H_{15}Br$ requires Br, 35·2%).

Ethyl 1-β-3-iso*Propylphenylethyl*-2 : 6-*dimethyl*-Δ^6-cyclo*hexene*-2-*carboxylate* (VI; $R' = Me$; $R'' = CHMe_2$).—The Grignard reagent prepared from the foregoing bromide (5 g.), magnesium (0·55 g.), and ether (15 c.c.) was added during ½ hour to an ice-cold solution of ethyl 2 : 6-dimethyl*cyclo*hexanone-2-carboxylate (4 g.) in ether (8 c.c.). After remaining at 17° for 3 hours, the mixture was decomposed with ice and ammonium chloride, the ether and volatile by-products were removed, and the residue was heated with potassium hydrogen sulphate (10 g.) for 1·5 hours at 180°. The *ester* (VI; R = Me; R = $CHMe_2$) (1·5 g.) was isolated as an oil, b. p. 173—180°/20 mm. (Found: C, 80·3; H, 9·7. $C_{22}H_{32}O_2$ requires C, 80·5; H, 9·8%), which decolourised bromine in chloroform solution.

1 : 12-*Dimethyl*-7-iso*propyloctahydrophenanthrene*-1-*carboxylic Acid* (III).—The above ester (0·5 g.) was boiled with glacial acetic acid (4·5 c.c.) and concentrated sulphuric acid (0·5 c.c.) for 1 hour. Water was added, and the product, isolated with ether, was hydrolysed by boiling with 20% methyl-alcoholic potassium hydroxide (5 c.c.) for 18 hours. The methyl alcohol was removed and water added, neutral impurities were removed in ether, and acidification of the alkaline solution liberated the *acid* (III), which was isolated with ether and crystallised from aqueous methyl alcohol (carbon) in colourless prisms (0·06 g.), m. p. 202—203° (Found: C, 79·8; H, 9·5. $C_{20}H_{28}O_2$ requires C, 80·0; H, 9·4%). Dehydrogenation of this acid (III) with selenium yielded retene, m. p. 98—99°, which was identified by comparison of the hydrocarbon and its picrate, m. p. 124—125°, with authentic specimens. The *methyl* ester, prepared by the action of diazomethane in ethereal solution, crystallised from methyl alcohol in jagged prisms, m. p. 91—92° (Found: C, 80·0; H, 9·4. $C_{21}H_{30}O_2$ requires C, 80·3; H, 9·6%).

UNIVERSITY OF DURHAM, KING'S COLLEGE,
NEWCASTLE-UPON-TYNE.

[*Received, June 28th,* 1939.]