## 14. *The Synthesis of Compounds related to the Sterols, Bile Acids, and Oestrus-producing Hormones. Part X. Ruzicka's Hydrocarbon "* $C_{21}H_{16}$ *" from Cholic Acid.*

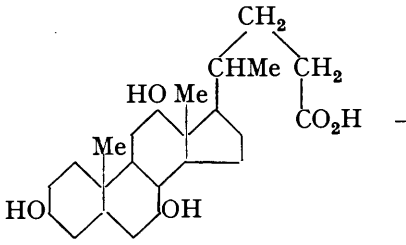
By W. E. Bachmann, J. W. Cook, C. L. Hewett, and John Iball.

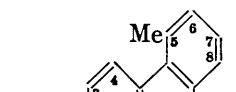
From the complex mixture of hydrocarbons formed by the selenium dehydrogenation of cholic acid at various temperatures Ruzicka and his collaborators (*Helv. Chim. Acta*, 1933, **16**, 216, 812; 1934, **17**, 200) have isolated 3'-methyl-1 : 2-*cyclo*pentenophenanthrene, chrysene, picene, and a hydrocarbon, m. p. 274° (corr.), to which the formula $C_{21}H_{16}$ has been ascribed. From a spectroscopic comparison of the homologous hydrocarbon "$C_{25}H_{24}$" from cholesterol with synthetic specimens of 2' : 1'-naphtha-1 : 2-fluorene and 1' : 2'-naphtha-2 : 3-fluorene, we suggested (J., 1935, 1319) that the hydrocarbon "$C_{21}H_{16}$" from cholic acid is a methyl derivative of 2' : 1'-naphtha-1 : 2-fluorene. This corresponds with the formula $C_{22}H_{16}$, which accords with the *X*-ray crystallographic evidence of Bernal and Crowfoot (J., 1935, 98) that the hydrocarbon contains 22 rather than 21 carbon atoms in the molecule. It is easy to devise possible dehydrogenation-mechanisms which might lead to a methylnaphthafluorene with the methyl group at one of the positions 4, 5, 6, 7, and 8. Accordingly, we have undertaken the synthesis of all five of these methylnaphthafluorenes. Of these, the 5-methyl compound had m. p. 275—276° (corr.) and the 8-methyl compound had m. p. 281—281·5° (corr.). The other three synthetic hydrocarbons had m. p.'s so far removed from that of the cholic acid hydrocarbon that they could be excluded on this ground alone. 8-*Methyl*-2' : 1'-*naphtha*-1 : 2-*fluorene* crystallised in two forms; the unit cell dimensions of the orthorhombic modification were different from the values for Ruzicka's hydrocarbon quoted by Bernal and Crowfoot (*loc. cit.*) (see table on p. 56) and hence there remained for consideration only the 5-methyl compound.

Through the kindness of Professor Ruzicka, who generously placed at our disposal his whole stock of the hydrocarbon from cholic acid, we have been able to compare his compound with our synthetic 5-*methyl*-2' : 1'-*naphtha*-1 : 2-*fluorene*. On account of the very small quantity of pure hydrocarbon available, the comparison has not been so complete as we would have wished, but the results completely support the view that the two compounds are identical. The m. p.'s of the two hydrocarbons (synthetic and from cholic acid) correspond within a few degrees, and the mixed m. p. shows no depression. This is not of great significance, however, as the 2'- and 3'-methylnaphthafluorenes and also the parent hydrocarbons have very similar m. p.'s (about 330°) which are not depressed by mixing. But all of the synthetic naphthafluorene hydrocarbons which we have examined are oxidised to characteristic yellow or orange ketones which give intense permanganate-like colours with concentrated sulphuric acid, and although the m. p.'s of several of these ketones lie close together, mixed m. p.'s show large depressions. By oxidation of an impure specimen of the cholic acid hydrocarbon we obtained a crude ketone, which after purification corresponded completely in its properties with synthetic 5-*methyl*-2' : 1'-*naphtha*-1 : 2-*fluorenone*, and the mixed m. p. showed no depression.

The formation of the hydrocarbon (II) from cholic acid (I) is thus due to simple cyclisation of the side chain during dehydrogenation, with elimination of oxygen from a hypothetical intermediate ketone :

(I.)



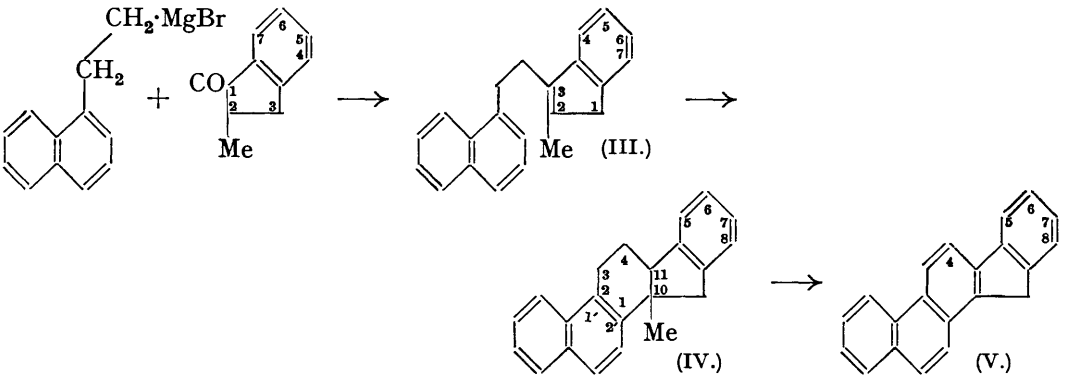




(II.)

Unfortunately, this identification of Ruzicka's hydrocarbon throws no further light

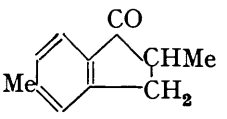
on the structure of the pentacyclic hydrocarbons of analogous structure obtained by dehydrogenation of sterols, for if a similar mechanism prevailed, cholesterol should give 5-methyl-8-*iso*propyl-2′ : 1′-naphtha-1 : 2-fluorene, which has been synthesised and is different from the cholesterol hydrocarbon (Cook, Hewett, Mayneord, and Roe, J., 1934, 1727). We regard it as certain, however, that these hydrocarbons from sterols are derived from 2′ : 1′-naphtha-1 : 2-fluorene.

The method used for the synthesis of the new homologues of 2′ : 1′-naphtha-1 : 2-fluorene is essentially that employed for the parent hydrocarbon (Cook, Hewett, Mayneord, and Roe, *loc. cit.*). It was found that the influence of the methyl group (III) in promoting cyclisation to the desired polycyclic structure was so great that the use of β-5-tetralylethyl alcohol as a starting point in the synthesis was unnecessary. The more easily accessible β-1-naphthylethyl alcohol was employed in all cases, and no difficulties were encountered due to spiran formation by *peri*-cyclisation in the naphthalene system. The following scheme represents the course of the synthesis, 2-methylhydrindone and three dimethyl compounds being obtained through the malonic acids arising from condensation of benzyl chloride and the three xylyl bromides, respectively, with ethyl methylmalonate :

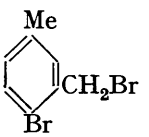



For the synthesis of 4-*methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*, the β-1-naphthylethyl alcohol was replaced by α-1-*naphthyl*iso*propyl alcohol*, obtained from 1-naphthylmagnesium bromide and propylene oxide. The Grignard condensation of the corresponding *naphthyl*-iso*propyl chloride* with 2-methylhydrindone gave unsatisfactory results, the desired product being obtained in poor yield, contaminated with αδ-*di*-1-*naphthyl*-βγ-*dimethylbutane*, but this was removed in a subsequent stage, and a small quantity of the pure 4-methylnaphthafluorene was isolated.

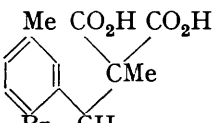
The hydrindone obtained from *m*-xylyl bromide was apparently homogeneous, and evidently had the structure (VI), formed by cyclisation in the *p*-, and not the *o*-position with respect to the methyl group, for the final 7-methylnaphthafluorene was different from 5-methylnaphthafluorene, which would be the product of *o*-ring-closure of the substituted phenylpropionic acid.




(VI.)

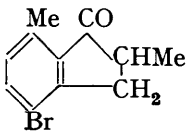


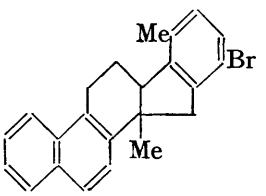

(VII.)




(VIII.)

(IX.)




(X.)

In order to obtain 5-methyl-2′ : 1′-naphtha-1 : 2-fluorene this *o*-ring-closure was brought about by blocking the *p*-position. For this purpose, ethyl methylmalonate was condensed with the mixture of chloromethyl compounds obtained by chloromethylation of *p*-bromotoluene (Fieser and Seligman, *J. Amer. Chem. Soc.*, 1935, **57**, 942). From the resulting mixture of substituted malonic acids, *2-bromo-5-methylbenzylmethylmalonic acid* (VIII) was isolated. The same acid was obtained from the mono-bromination product (evidently mainly VII) of *m*-xylyl bromide, and the fact that the same acid was formed from both *p*-bromotoluene and *m*-xylyl bromide is conclusive proof of its structure, from which it follows that the substituted hydrindone prepared from this acid must have structure (IX). Grignard condensation with this hydrindone, and cyclisation of the indene proceeded normally, the resulting pentacyclic *bromo*-compound (X) being debrominated by catalytic hydrogenation before dehydrogenation. This was not essential, however, as 5-methyl-2′ : 1′-naphtha-1 : 2-fluorene (II) was obtained directly from (X) by selenium dehydrogenation.

*Crystal Structure of* 5- *and* 8-*Methyl-2′ : 1′-naphtha-1 : 2-fluorenes.*—*8-Methyl-2′ : 1′-naphtha-1 : 2-fluorene.* Two kinds of crystals were obtained by crystallisation from amyl acetate: (*a*) white ill-bounded plates of moderate size, which proved to be monoclinic; and (*b*) a few extremely thin transparent plates elongated in one direction (*b* axis); these were orthorhombic. The orthorhombic form has a large unit cell, and the table shows that the dimensions are sufficiently different from those of Ruzicka's hydrocarbon for there to be no doubt that the two compounds are different. The halvings observed on moving-film photographs suggest that the space group is $C_{2v}^{15}$ — *B mam.*

The monoclinic variety has a unit cell one-fourth the size of the orthorhombic cell. The cell chosen has a β-angle of almost 90°, but the cell is genuinely monoclinic, as is shown by the moving-film photographs about the symmetry axis (*b*). The intensity of the (*h*0*l*) planes is widely different from that of the (*h*0$\bar{l}$) planes. The only halvings observed are the (0*k*0) planes when *k* is odd. Two space groups are available, *viz.*, $C_2^2$ — $P2_1$, and $C_{2h}^2$ — $P2_1/m$. As it is impossible from its chemical structure for this compound to possess the plane or centre of symmetry required by the space group $C_{2h}^2$ with only two molecules in the cell, it is probable that the space group is $C_2^2$ — $P2_1$.

*5-Methyl-2′ : 1′-naphtha-1 : 2-fluorene.* The crystals of this compound, though also very thin plates, were better developed than those of either form of the 8-methyl derivative. The crystals show positive birefringence, the optic axial plane being (010) with $b = \beta$ and $\gamma$ slightly inclined to the perpendicular to (001). The halvings observed suggest the space group $C_{2h}^5$ — $P2_1/a$, but, as the unit cell has only two molecules, this would imply that each molecule possesses a centre of symmetry. This is not possible from the chemical formula, so it is probable either that the halvings (*h*0*l*) when *h* is odd are accidental, or that the halvings (0*k*0) when *k* is odd are accidental. In the former case the space group would be $C_2^2$ — $P2_1$ and in the latter $C_s^2$ — *Pa*. It is of interest that in the case of the monoclinic variety of the 8-methyl compound, only a few planes were observed having indices (*h*0*l*) when *h* is odd, and all these gave very weak reflections.

*Table of Unit Cell Dimensions.*

| Compound. | *a*. | *b*. | *c*. | β. | Probable space group. |
|---|---|---|---|---|---|
| 8-Methyl-2′ : 1′-naphtha-1 : 2-fluorene (orthorhombic) | 17·54 Å. | 5·88 Å. | 27·8 Å. | 90° | *B mam* |
| 8-Methyl-2′ : 1′-naphtha-1 : 2-fluorene (monoclinic) ... | 8·17 | 6·68 | 13·67 | 90·5 | $P2_1$ |
| 5-Methyl-2′ : 1′-naphtha-1 : 2-fluorene (monoclinic) ... | 9·53 | 5·78 | 13·37 | 92·5 | *Pa* or $P2_1$ |
| Ruzicka's hydrocarbon * (orthorhombic) ..... | 8·70 | 6·41 | 27·2 | 90 | *Aba* |

* Quoted from Bernal and Crowfoot (*loc. cit.*).

*Comparison between Ruzicka's Hydrocarbon and 5-Methyl-2′ : 1′-naphtha-1 : 2-fluorene.*—The crystals obtained for the 5-methyl compound were monoclinic and therefore it is impossible to compare the unit cell dimensions of these crystals with those given by Bernal and Crowfoot for Ruzicka's hydrocarbon which has an orthorhombic cell. Since there was not sufficient of the purest sample of Ruzicka's compound for recrystallisation, no attempt could be made to obtain a monoclinic variety. Impure samples gave crystals

much too small for any measurements to be made. However, by the melting of a small quantity of the purest sample and of the synthetic 5-methyl-2′ : 1′-naphtha-1 : 2-fluorene in Lindemann glass capillary tubes under identical conditions, specimens which gave almost identical powder photographs were obtained. A comparison between powder photographs of the synthetic compound taken before and after melting showed clearly that this substance did not crystallise from the melt in the monoclinic form previously obtained from solution. When the powder photographs of each specimen produced from the melt were superimposed, the rings appeared exactly to coincide, the relative intensity of the rings being also apparently the same in each case. Careful measurement of the rings showed, however, that there was a slight difference between the diameters of the outer rings. The difference was slightly greater than the maximum error of measurement, but in no case did the difference between the diameters of corresponding rings represent a difference in spacing of more than 1%. It is possible that this difference may be caused by traces of impurities in Ruzicka's hydrocarbon, as this did not melt so sharply as the synthetic compound.

The conclusion from these facts is that the synthetic compound, though normally crystallising in a monoclinic form, can crystallise in some other form, presumably orthorhombic. There is nothing in the crystal structure data inconsistent with the identity of the two samples; in fact, the similarity between the powder photographs is sufficiently close to make it highly probable that they do consist of the same substance.

## Experimental.

*Preparation of Hydrindones.*—A solution of β-tolyl-α-methylpropionyl chloride (1 part) in ligroin (b. p. 80—100°; 1·5 parts) was added drop by drop to a suspension of powdered anhydrous aluminium chloride (1 part) in ligroin (1 part) with continuous shaking (compare Ingold and Piggott, J., 1923, **123**, 1502); the mixture was then heated gradually to the boiling point. The hydrindone obtained on hydrolysis of the mixture was purified by vacuum distillation.

*Dehydration of Carbinols to Indenes.*—The crude carbinols (1 part) obtained from the Grignard reaction between the hydrindones and β-1-naphthylethylmagnesium bromide were heated with potassium hydrogen sulphate (1·5 parts) at 160° for 1 hour. The mixture was treated with water and the indene was purified by crystallisation or distillation.

*Cyclisation of Indenes.*—A mixture of the indene (1 part), carbon disulphide (10 parts), and anhydrous aluminium chloride (1 part) was kept at 0° for 3 hours with occasional shaking. The solution was decanted from the sludge into water and the product was isolated from the solution by vacuum distillation.

*Dehydrogenation.*—The cyclised product (1 part) was heated with selenium (1 part) at 310° for 7 hours; if heated for 20 hours, the compounds were usually completely decomposed. The naphthafluorene hydrocarbons were recrystallised from xylene, and separated from traces of selenium by sublimation at 0·1 mm.; the selenium sublimed at 180—200°, and the hydrocarbon at 230—240°. The compounds were then recrystallised from xylene.

2′ : 1′-*Naphtha*-1 : 2-*fluorene.*—3-(β-1′-*Naphthylethyl*)-2-*methylindene* (III). A solution of 2-methyl-1-hydrindone (10 g.) in anhydrous ether (10 c.c.) was added drop by drop to an ice-cold Grignard reagent prepared from β-1-naphthylethyl bromide (24 g.) in anhydrous ether (60 c.c.). After the solution had been kept in a refrigerator for 12 hours a large amount of crystalline addition compound (A) was present; the crystals were collected and hydrolysed with ice-cold ammonium chloride solution separately from the solution (B). The indene resulting from the dehydration of the liquid carbinol obtained from the crystals (A) was recrystallised twice from benzene–alcohol; 3-(β-1′-*naphthylethyl*)-2-*methylindene* formed colourless diamond-shaped plates (8·2 g.), m. p. 99—99·5° (Found: C, 92·7; H, 7·15. $C_{22}H_{20}$ requires C, 92·9; H, 7·1%). An additional quantity of the indene, bringing the total yield to 63%, was obtained from the carbinol formed by hydrolysis of solution B; this crude indene was distilled in a vacuum and purified through its picrate. The *dipicrate* of the indene crystallised from benzene in orange needles, m. p. 161—161·5° (Found: C, 55·1; H, 3·5. $C_{22}H_{20},2C_6H_3O_7N_3$ requires C, 55·0; H, 3·5%).

10-*Methyl*-3 : 4 : 10 : 11-*tetrahydro*-2′ : 1′-*naphtha*-1 : 2-*fluorene* (IV). Vacuum distillation of the cyclised product from the indene (3·5 g.) gave a glassy mass (2·7 g.), b. p. 190—195°/0·2 mm. A solution of this in benzene–alcohol deposited colourless needles (0·95 g.) of 10-*methyl*-

3 : 4 : 10 : 11-*tetrahydro*-2′ : 1′-*naphtha*-1 : 2-*fluorene*, m. p. 111—112° after recrystallisation from benzene–alcohol (Found: C, 92·85; H, 7·4. $C_{22}H_{20}$ requires C, 92·9; H, 7·1%).

2′ : 1′-*Naphtha*-1 : 2-*fluorene*. This was obtained in 90% yield * by dehydrogenation of the crystalline methyltetrahydro-derivative; it had m. p. 328° and was identical with that obtained by the use of β-5-tetralylethyl chloride (Cook, Hewett, Mayneord, and Roe, J., 1934, 1737). A further quantity of naphthafluorene was obtained by dehydrogenation of the mother-liquors of the cyclised product, the total yield being 34% with respect to the indene.

6-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*.—2 : 6-*Dimethylhydrindone*. *p*-Xylyl bromide (28 g.) was condensed with the sodio-derivative of ethyl methylmalonate (32 g.) in absolute alcohol (70 c.c.) and yielded ethyl *p*-methylbenzylmethylmalonate, which was purified by distillation, b. p. 203—210°/26 mm. This ester (23 g.) was hydrolysed to p-*methylbenzylmethylmalonic acid* (18 g.); a sample of the acid crystallised from benzene in colourless needles, m. p. 178—180° with evolution of carbon dioxide (Found: C, 64·7; H, 6·4. $C_{12}H_{14}O_4$ requires C, 64·7; H, 6·35%). The substituted malonic acid was converted into β-p-*tolyl*-α-*methylpropionic acid* by heating at 180°, and this acid distilled, b. p. 181—182°/23 mm. (yield, 90%). For analysis, a sample was recrystallised from light petroleum, forming colourless needles, m. p. 30—31·5° (Found: C, 73·7; H, 8·0. $C_{11}H_{14}O_2$ requires C, 74·2; H, 7·9%). A mixture of the acid (11 g.) and thionyl chloride (15 c.c.) was refluxed for 2 hours and the resulting acid chloride was purified by distillation (b. p. 139—140°/21 mm.; yield, 98%).

2 : 6-Dimethylhydrindone, b. p. 145—148°/21 mm., was obtained in 97% yield from the foregoing acid chloride. It was analysed in the form of its crystalline *phenylhydrazone*, which formed long cream-coloured needles from benzene–alcohol, m. p. 173—175° (decomp.) (Found: C, 81·5; H, 7·6. $C_{17}H_{18}N_2$ requires C, 81·6; H, 7·3%).

3-(β-1′-*Naphthylethyl*)-2 : 5-*dimethylindene*. 2 : 6-Dimethylhydrindone (8 g.) in anhydrous ether (8 c.c.) was added to the ice-cold Grignard reagent from β-1-naphthylethyl bromide (18 g.); the mixture soon deposited crystals of the addition product. The indene obtained from the carbinol isolated from the crystalline portion crystallised readily; the indene from the mother-liquors was purified through its picrate; total yield, 7·7 g. or 51%. 3-(β-1′-*Naphthylethyl*)-2 : 5-*dimethylindene* crystallised from benzene–alcohol in colourless rectangular plates, m. p. 81—81·5° (Found: C, 92·3; H, 7·4. $C_{23}H_{22}$ requires C, 92·6; H, 7·4%). The *dipicrate* crystallised from benzene in orange needles, m. p. 144—144·5° (Found: N, 11·3. $C_{23}H_{22},2C_6H_3O_7N_3$ requires N, 11·1%).

6 : 10-*Dimethyl*-3 : 4 : 10 : 11-*tetrahydro*-2′ : 1′-*naphtha*-1 : 2-*fluorene*. Vacuum distillation of the cyclised product from the aforesaid indene (5·3 g.) gave a gum (4 g.), b. p. 190—200°/0·1 mm.; an alcohol–acetone solution of this product after 2 days in a refrigerator deposited fine colourless needles of 6 : 10-*dimethyl*-3 : 4 : 10 : 11-*tetrahydro*-2′ : 1′-*naphtha*-1 : 2-*fluorene* (1 g.), m. p. 106·5—107° after recrystallisation from acetone–alcohol (Found: C, 92·7; H, 7·4. $C_{23}H_{22}$ requires C, 92·6; H, 7·4%). The *semipicrate* crystallised from benzene in stout needles, m. p. 133·5—134° (Found: N, 5·6. $2C_{23}H_{22},C_6H_3O_7N_3$ requires N, 5·4%).

6-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*. Dehydrogenation of the crystalline dimethyltetrahydronaphthafluorene gave a 70% yield of the methylnaphthafluorene; the compound can also be obtained conveniently by dehydrogenation of the crude cyclisation product. 6-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene* crystallised from xylene in colourless leaflets, m. p. 330°,† in a bath preheated to 300° (Found: C, 94·2; H, 5·9. $C_{22}H_{16}$ requires C, 94·2; H, 5·8%). The total yield of 6-methylnaphthafluorene based on the indene was 30%. Oxidation of the hydrocarbon (0·1 g.) by 1 hour's heating with potassium dichromate (0·3 g.) in acetic acid (5 c.c.) gave a 60% yield of 6-*methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorenone*; the ketone after sublimation at 230°/0·1 mm. was obtained in fine golden-yellow needles, m. p. 225—226°, by recrystallisation from acetic acid (Found: C, 89·7; H, 4·9. $C_{22}H_{14}O$ requires C, 89·8; H, 4·8%). Like the parent naphthafluorenone, this and all the other methylnaphthafluorenones give with concentrated sulphuric acid an intense purple colour which changes gradually to magenta. This ketone depressed the m. p. of 2′ : 1′-naphtha-1 : 2-fluorenone.

* As Edisburg, Morton, and Lovern (*Biochem. J.*, 1935, **29**, 907) have recently remarked on "the well-known inefficiency of the selenium dehydrogenation process (order of yield 3—10%)," it seems necessary to add that in our hands this process has given consistently good yields (50—90%) with simple polycyclic hydroaromatic compounds. For a discussion of special cases which do not give good results by this method, see J., 1934, 1734; following paper.

† The m. p.'s of the three naphthafluorene hydrocarbons having m. p.'s above 300° were very much influenced by the rate of heating, on account of decomposition.

7-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*.—2 : 5-*Dimethylhydrindone* (VI). The ester (30 g., b. p. 185—188°/21 mm.) resulting from the condensation of *m*-xylyl bromide (37 g.) with the sodio-derivative of ethyl methylmalonate (40 g.) was hydrolysed to m-*methylbenzylmethylmalonic acid* (19 g.); this acid crystallised from benzene in colourless needles, m. p. 152—153°, with liberation of carbon dioxide (Found: C, 64·6; H, 6·4. $C_{12}H_{14}O_4$ requires C, 64·7; H, 6·35%). At 180° the substituted malonic acid (18 g.) was decarboxylated to β-m-*tolyl*-α-*methylpropionic acid*, which was purified by distillation, b. p. 178—179°/20 mm.; yield, 97% (Found: C, 73·4; H, 7·9. $C_{11}H_{14}O_2$ requires C, 74·2; H, 7·9%). This acid was converted into its chloride (97% yield), b. p. 137—138°/21 mm., which was then cyclised to 2 : 5-*dimethylhydrindone* (80% yield), b. p. 142—144°/21 mm. (Found: C, 81·5; H, 7·7. $C_{11}H_{12}O$ requires C, 82·5; H, 7·6%). The 2 : 4-*dinitrophenylhydrazone* of the hydrindone crystallised from chloroform in scarlet needles, m. p. 225—226° (decomp.) (Found: N, 16·6. $C_{17}H_{16}O_4N_4$ requires N, 16·5%).

3-(β-1′-*Naphthylethyl*)-2 : 6-*dimethylindene*. The liquid carbinol which was obtained by interaction of 2 : 5-dimethylhydrindone (7 g.) with the Grignard reagent from β-1-naphthylethyl bromide (16 g.) was dehydrated to the indene; after two conversions into the picrate, followed by vacuum distillation of the regenerated hydrocarbon, 3-(β-1′-*naphthylethyl*)-2 : 6-*dimethylindene* (6 g.) was obtained as an extremely viscous, yellowish liquid, b. p. 184—186°/0·05 mm. (Found: C, 92·2; H, 7·4. $C_{23}H_{22}$ requires C, 92·6; H, 7·4%).

7-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*. The distilled cyclisation product (3·2 g.), b. p. 195—198°/0·15 mm., from the indene (4·5 g.) formed a glassy mass; a solution of the product in acetone–alcohol deposited colourless prisms (0·5 g.), m. p. 101°, which proved to be αδ-di-1-naphthylbutane, undoubtedly present in the indene as an impurity carried through from the Grignard reaction (Found: C, 93·0; H, 7·0. Calc.: C, 92·85; H, 7·15%). The compound was identical with a sample prepared by interaction of β-1-naphthylethyl bromide and magnesium. The melting points of its yellow *dipicrate*, m. p. 174—175° (Found: N, 11·2. $C_{24}H_{22}$,$2C_6H_3O_7N_3$ requires N, 11·0%) and *s*-trinitrobenzene complex, m. p. 186·5°, were in agreement with Harper, Kon, and Ruzicka (J., 1934, 124). After removal of the dinaphthylbutane, the mother-liquor deposited 7 : 10-*dimethyl*-3 : 4 : 10 : 11-*tetrahydro*-2′ : 1′-*naphtha*-1 : 2-*fluorene* (0·2 g.), which crystallised from alcohol–acetone in colourless triangular prisms, m. p. 134·5—135° (Found: C, 92·9; H, 7·1. $C_{23}H_{22}$ requires C, 92·6; H, 7·4%). Dehydrogenation of the crystals gave 7-*methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*; after purification this compound formed colourless leaflets, m. p. 334—336° in a bath preheated to 300° (Found: C, 94·4; H, 5·8. $C_{22}H_{16}$ requires C, 94·2; H, 5·8%). Dehydrogenation of the cyclisation product without isolation of the crystalline intermediate gave 7-methylnaphthafluorene in 25% yield; in this case the methylnaphthafluorene which was formed after 7 hours was removed, and the oil again subjected to the action of selenium for two like periods. 7-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorenone*, obtained from the hydrocarbon by oxidation with potassium dichromate in acetic acid, formed golden-yellow needles, m. p. 175—176·5°, from acetic acid, after vacuum sublimation (Found: C, 89·7; H, 4·9. $C_{22}H_{14}O$ requires C, 89·8; H, 4·8%).

8-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*.—2 : 4-*Dimethylhydrindone*. Hydrolysis of the ester (31·5 g., b. p. 184—190°/21 mm.) which was obtained by the condensation of *o*-xylyl bromide (43 g.) with the sodio-derivative of ethyl methylmalonate (40 g.) gave o-*methylbenzylmethylmalonic acid* (21 g.); this acid crystallised from benzene–light petroleum in clusters of colourless needles, m. p. 122·5—123° (Found: C, 64·5; H, 6·45. $C_{12}H_{14}O_4$ requires C, 64·7; H, 6·35%). Decarboxylation of the substituted malonic acid at 180° gave a 93% yield of β-o-*tolyl*-α-*methylpropionic acid*, b. p. 179—180°/20 mm. (Found: C, 74·1; H, 8·1. $C_{11}H_{14}O_2$ requires C, 74·2; H, 7·9%). The acid chloride, b. p. 137—138°/21 mm., prepared in 93% yield by the action of thionyl chloride, was cyclised to 2 : 4-*dimethylhydrindone* (90% yield), a yellowish liquid, b. p. 147—149°/20 mm., which was not obtained analytically pure (Found: C, 81·4; H, 7·7. $C_{11}H_{12}O$ requires C, 82·5; H, 7·25%). The *semicarbazone* formed colourless needles (from dioxan), m. p. 224—225° (decomp.) (Found: N, 19·5. $C_{12}H_{15}ON_3$ requires N, 19·4%).

8-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*. Dehydration of the carbinol resulting from interaction of 2 : 4-dimethylhydrindone (9 g.) with the Grignard reagent from β-1-naphthylethyl bromide (21 g.) in anhydrous ether (60 c.c.) gave the indene; after two recrystallisations from benzene–alcohol 3-(β-1′-*naphthylethyl*)-2 : 7-*dimethylindene* formed colourless plates, m. p. 96°; the melt quickly solidified and remelted at 113·5—114° (Found: C, 92·1; H, 7·4. $C_{23}H_{22}$ requires C, 92·6; H, 7·4%). Vacuum distillation of the cyclisation product of the indene (8·9 g.) gave a viscous oil (7·2 g.), b. p. 195—200°/0·2 mm.; crystals of 8 : 10-*dimethyl*-3 : 4 : 10 : 11-*tetrahydro*-2′ : 1′-*naphtha*-1 : 2-*fluorene* (1·7 g.) separated from an alcohol–acetone

solution of the product; this crystallised from acetone in colourless rectangular plates, m. p. 121—122° (Found: C, 92·55; H, 7·4. $C_{23}H_{22}$ requires C, 92·6; H, 7·4%). The *semipicrate* crystallised from absolute alcohol in broad crimson needles, m. p. 130·5—131·5° (Found: C, 75·3; H, 5·8. $2C_{23}H_{22},C_6H_3O_7N_3$ requires C, 75·6; H, 5·7%). Two 7-hour treatments with selenium gave a 98% yield of *8-methyl-2′ : 1′-naphtha-1 : 2-fluorene*, which after the usual purification crystallised from xylene in broad colourless needles, or leaflets, m. p. 272·5—273° (281—281·5° corr.) (Found: C, 94·5; H, 5·5. $C_{22}H_{16}$ requires C, 94·2; H, 5·8%); the total yield of the hydrocarbon, including that obtained from the mother-liquors, was 27% based on the indene. Oxidation yielded *8-methyl-2′ : 1′-naphtha-1 : 2-fluorenone* (70% yield), which crystallised from acetic acid in fine golden-yellow needles, m. p. 237—238° (Found: C, 89·8; H, 5·0. $C_{22}H_{14}O$ requires C, 89·8; H, 4·8%).

*5-Methyl-2′ : 1′-naphtha-1 : 2-fluorene.*—*7-Bromo-3-(β-1′-naphthylethyl)-2 : 4-dimethylindene.* A mixture of 2- and 3-chloromethyl-4-bromotoluenes (Fieser and Seligman, *loc. cit.*) was added gradually to the sodio-derivative of ethyl methylmalonate (40 g.) in absolute alcohol (90 c.c.); after 1½ hours' refluxing, the mixture was treated with water, and the resulting ester purified by vacuum distillation (b. p. 135—138°/0·05 mm.; yield, 48 g.). Hydrolysis of the ester was accomplished by ½ hour's heating with a solution of potassium hydroxide (70 g.) in methyl alcohol (70 c.c.) and water (70 c.c.); acidification yielded a mixture of the malonic acids (37 g.). In one experiment this mixture was used in the subsequent steps and gave a satisfactory yield of the desired indene. In another experiment the mixture was subjected to repeated recrystallisations from benzene–methyl alcohol (6 : 1) and 4·5 g. of pure *2-bromo-5-methylbenzylmethylmalonic acid* (VIII), the less soluble isomeride, were obtained as large colourless plates, m. p. 179—180° with liberation of carbon dioxide (Found: C, 48·3; H, 4·6. $C_{12}H_{13}O_4Br$ requires C, 47·8; H, 4·35%). The structure of this compound was proved by its synthesis from *m*-xylyl bromide; the latter compound (15 g.) was treated with bromine (13 g.) at 0° in presence of iron powder; the purified product (mostly VII) (6·5 g., b. p. 148—152°) was condensed with ethyl sodiomethylmalonate and the resulting ester on hydrolysis yielded 2-bromo-5-methylbenzylmethylmalonic acid (2·2 g.), m. p. 179—180°, identical with the malonic acid obtained as described above. Decarboxylation of the substituted malonic acid at 180° gave *α-2-bromo-5-methylbenzylpropionic acid* in 90% yield; this acid formed colourless plates, m. p. 84—85°, from light petroleum (Found: C, 51·8; H, 5·4. $C_{11}H_{13}O_2Br$ requires C, 51·4; H, 5·1%). Cyclisation of the acid chloride, b. p. 173—174°/20 mm., obtained from the acid in 97% yield, gave an 86% yield of 4-bromo-2 : 7-dimethylhydrindone (IX), which formed a yellowish liquid, b. p. 115—117°/0·15 mm.

Dehydration of the carbinol resulting from interaction of the hydrindone with β-1-naphthylethylmagnesium bromide gave a 41% yield of *7-bromo-3-(β-1′-naphthylethyl)-2 : 4-dimethylindene*, which crystallised from benzene–alcohol in colourless needles, m. p. 84—85° (Found: C, 73·3; H, 5·8. $C_{23}H_{21}Br$ requires C, 73·2; H, 5·6%). The *dipicrate* crystallised from benzene in clusters of fine orange needles, m. p. 142·5—143·5° (Found: C, 50·7; H, 3·4. $C_{23}H_{21}Br,2C_6H_3O_7N_3$ requires C, 50·3; H, 3·3%).

*5-Methyl-2′ : 1′-naphtha-1 : 2-fluorene.* The indene (3 g.) was cyclised and the product was taken up in benzene–alcohol; after several hours the solution deposited crystals of *8-bromo-5 : 10-dimethyl-3 : 4 : 10 : 11-tetrahydro-2′ : 1′-naphtha-1 : 2-fluorene* (X) (1·57 g.). This compound, after two recrystallisations from absolute alcohol containing a trace of benzene, formed colourless plates, m. p. 137·5—138·5° (Found: C, 73·5; H, 6·0. $C_{23}H_{21}Br$ requires C, 73·2; H, 5·6%). By passing a stream of hydrogen through a boiling mixture of the aforementioned compound (1 g.) and palladium-black (0·5 g.) in acetic acid (25 c.c.) for 3 hours, the debrominated product (0·3 g.) was obtained in addition to unchanged material. Selenium dehydrogenation gave *5-methyl-2′ : 1′-naphtha-1 : 2-fluorene* (0·15 g.), which crystallised from xylene in leaflets, m. p. 275—276° (corr.) (Found: C, 94·1; H, 6·0. $C_{22}H_{16}$ requires C, 94·2; H, 5·8%); mixed with the 8-methyl isomeride, it melted at 271·5—272·5° (corr.). *5-Methyl-2′ : 1′-naphtha-1 : 2-fluorenone*, obtained in 70% yield by oxidation, crystallised from ethyl acetate in golden-yellow needles, m. p. 209—210° (Found: C, 89·3; H, 4·6. $C_{21}H_{14}O$ requires C, 89·8; H, 4·8%). The mixed m. p. with 8-methylnaphthafluorenone was 187—195°.

*4-Methyl-2′ : 1′-naphtha-1 : 2-fluorene.*—*α-1-Naphthylisopropyl alcohol.* Propylene oxide (40 g.) was added to an ice-cold Grignard solution prepared from 1-bromonaphthalene (67 c.c.), magnesium turnings (12 g.), and anhydrous ether (500 c.c.). After being kept over-night at room temperature, the ether was distilled off, and the residue heated on the water-bath for an hour. The whole was extracted with ether and ammonium chloride solution, and the ethereal extract dried (sodium sulphate) and distilled. The product (43 g.) formed a pale yellow,

viscous oil, b. p. 148—155°/25 mm. A sample for analysis was purified through the 3 : 5-*dinitrobenzoate*, which separated from ethyl acetate as a yellowish microcrystalline powder, m. p. 171—172° (Found : C, 63·25; H, 4·4. $C_{20}H_{16}O_6N_2$ requires C, 63·1; H, 4·2%). Hydrolysis with boiling alcoholic potash gave α-1-*naphthyliso*propyl *alcohol*, which was distilled at 0·1 mm. from an air-bath at 130—140°. It formed a colourless syrup (Found : C, 83·4; H, 7·6. $C_{13}H_{14}O$ requires C, 83·8; H, 7·6%). The corresponding *chloride*, formed by slow addition of the crude distilled naphthyl*iso*propyl alcohol (13·5 g.) to a mixture of phosphorus trichloride (15·5 g.) and carbon tetrachloride (35 c.c.), followed by 1 hour's heating on the water-bath, was a pale yellow liquid (7·5 g.), b. p. 131°/6 mm. (Found : C, 75·2; H, 6·0. $C_{13}H_{13}Cl$ requires C, 76·25; H, 6·4%).

4-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*. In the Grignard condensation between naphthyl-*iso*propylmagnesium chloride and 2-methylhydrindone, better results were obtained in the presence of a molecule of ethylmagnesium bromide. An ice-cold Grignard reagent from naphthyl*iso*propyl chloride (15·3 g.), ethyl bromide (8·2 g.), magnesium turnings (5·4 g.), and anhydrous ether (100 c.c.) was treated with 2-methylhydrindone (10·5 g.), kept at 0° for ½ hour, and then boiled for 1½ hours. The product was decomposed with ice and ammonium chloride, and the ethereal solution washed, dried, and distilled. The fraction, b. p. 195—215°/0·8 mm. (5·5 g.), was cyclised with aluminium chloride (5·5 g.) in carbon disulphide (55 c.c.), the mixture being kept over-night at 2—3°. The cyclised product gave a crystalline picrate, which was decomposed, and the resulting hydrocarbon was recrystallised from benzene–alcohol until it melted constantly at 131—132°. This was not dehydrogenated by selenium and hence was αδ-*di*-1-*naphthyl*-βγ-*dimethylbutane* (Found : C, 92·4; H, 7·7; *M*, Rast method, 344. $C_{26}H_{26}$ requires C, 92·5; H, 7·5%; *M*, 338).

The liquors from which the crystalline picrate had been obtained were freed from picric acid, and the resinous hydrocarbon mixture was heated with selenium (1·4 g.) at 300—320° for 24 hours. The resulting 4-*methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene* crystallised from benzene–alcohol in colourless needles, m. p. 202—203° (Found : C, 94·3; H, 5·6. $C_{22}H_{16}$ requires C, 94·2; H, 5·8%). Oxidation of this hydrocarbon (20 mg.) gave the corresponding ketone, which, after purification, crystallised from acetic acid in light brown, slender needles, m. p. 214—215°. There was insufficient for analysis.

*Comparison of Ruzicka's Hydrocarbon from Cholic Acid with* 5-*Methyl*-2′ : 1′-*naphtha*-1 : 2-*fluorene*.—(a) *Mixed m. p. determination.* The purest specimen of the cholic acid hydrocarbon supplied by Professor Ruzicka had m. p. 274·5—276° (uncorr.). The m. p. of the synthetic hydrocarbon taken at the same time on the same thermometer was 269—270°, and the mixed m. p. was 271—273·5°.

(b) *Comparison of ketones.* Three specimens of the hydrocarbon from cholic acid having m. p.'s 267—275°, 270—275°, and 259—262° (uncorr.) were combined. The combined sample amounted to 70 mg., of which 50 mg. was the specimen, m. p. 259—262°. This was oxidised with potassium dichromate (0·2 g.) in boiling glacial acetic acid (3·5 c.c.). The crude oxidation product was sublimed at 180—210°/0·05 mm., and then recrystallised five times from acetic acid, benzene, and ethyl acetate. The ketone then formed golden-orange needles, m. p. 207—208°, and the mixed m. p. with 5-methyl-2′ : 1′-naphtha-1 : 2-fluorenone (m. p. 209—210°) was 207·5—208·5°. The mixed m. p. with 2′ : 1′-naphtha-1 : 2-fluorenone (m. p. 207—208°) was about 180°. This specimen of the ketone prepared from Ruzicka's hydrocarbon gave the usual naphthafluorenone colour reaction with concentrated sulphuric acid.

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