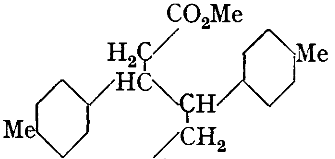
79. *Symmetrical Derivatives of Chrysene. Part I.*

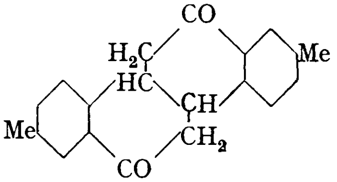
By G. R. Ramage.

The double ring closure of substituted diphenyladipic acids to give symmetrical chrysene derivatives has been extended, and 5 : 14-dimethylchrysene is now described. Of particular interest is the preparation of dimethylhexahydrochrysenes (VI), having two angle methyl groups in *cis*- and *trans*-positions, and the selenium dehydrogenation of these is to be investigated.

In the early stages of attempts to synthesise substances related to the sex-hormones, Ramage and Robinson (J., 1933, 607) employed a method of possible general application for the preparation of symmetrical chrysene derivatives. It was shown that *meso*- and *r*-βγ-diphenyladipic acids could be converted into *trans*- and *cis*-hexahydrochrysenes respectively, and the corresponding series from βγ-dianisyladipic acids was completed later (Lewis, Ramage, and Robinson, J., 1935, 1412). The method appears to be suitable for the preparation of chrysene homologues and 5 : 14-dimethylchrysene has now been synthesised. *p*-Tolualdehyde was condensed with methyl acetate and the resulting crystalline methyl *p*-methylcinnamate was reduced in ethereal solution by amalgamated aluminium. About half formed bimolecular product, which was separated by ether into pure crystalline *methyl* βγ-*di*-p-*tolyladipate*-a (I) and the crude isomer-*b*. These by analogy with the diphenyladipic acid series represent the *meso*- and the racemic form respectively. Ring closure of βγ-*di*-p-*tolyladipic*-a *acid* was effected with sulphuric acid, or by the Friedel–Crafts reaction on the acid chloride. The *b*-form was similarly cyclised by the Friedel–Crafts reaction. The resulting 2 : 11-*diketo*-5 : 14-*dimethylhexahydrochrysene*-a and -b (II) gave on reduction the corresponding two forms of the *hydrocarbon* (III), both of which were smoothly dehydrogenated by selenium to 5 : 14-*dimethylchrysene*, m. p. 218°, characterised by a *trinitrobenzene* derivative, m. p. 195°, a *picrate*, m. p. 171—172°, and a *styphnate*, m. p. 204°. These derivatives are quite stable, whereas only a trinitrobenzene compound from chrysene can be prepared and 2 : 11-dimethylchrysene failed to give a picrate (J., 1935, 1414).



(I.)



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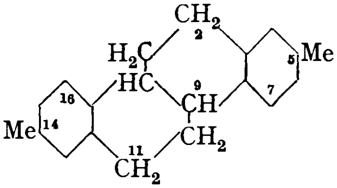
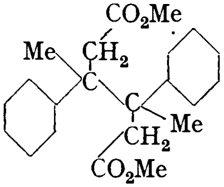


(III.)

An interesting extension of the work followed from the aluminium reduction of methyl β-methylcinnamate, although the substituted adipic esters (IV) were isolated in very poor yield. These on ring closure with sulphuric acid gave 2 : 11-*diketo*-9 : 18-*dimethylhexahydrochrysene*-a and -b (V), but for the first time in this series difficulty was experienced with the reduction of the carbonyl groups. The ordinary Clemmensen reduction or its modification by the addition of solvent gave solid products, higher melting than the original ketones, dissolving only in pyridine, and considered to be the corresponding alcohols.

Clemo and Metcalfe (J., 1937, 1520) have recently drawn attention to, and discussed similar unusual behaviour in the Clemmensen reduction. Attempts were therefore made to find an alternative procedure, and the more readily available methyl *r*-diphenyladipate was submitted to a Bouveault reduction, but the glycol isolated in low yield was not cyclised to *cis*-hexahydrochrysene by phosphoric oxide in xylene. On the other hand, although the Wolff reduction of the semicarbazones of *cis*- and *trans*-diketohexahydrochrysenes gave non-crystallisable gums, from the *hydrazones*, *cis*- and *trans*-hexahydrochrysene were isolated in good yield. By applying the latter method to the two forms of (V), 9 : 18-*dimethylhexahydrochrysene*-a, m. p. 144°, and -b (VI), m. p. 105°, were obtained and it is proposed to examine the selenium dehydrogenation of these substances, which contain angle methyl groups presumably in *trans*- and *cis*-positions respectively. Preliminary experiments on the small amounts of hydrocarbons available show that at 360° dehydrogenation is very slow, but following prolonged heating, chrysene has been isolated together with derivatives of either a methyl- or dimethyl-chrysene. This result is in accord with previously observed migration or elimination of angle methyl groups under such treatment.



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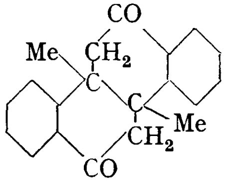
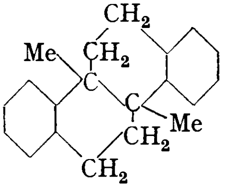


(V.)



(VI.)

EXPERIMENTAL.

Methyl p-*Methylcinnamate*.—*p*-Tolualdehyde (11 g.) and anhydrous methyl acetate (50 c.c.) were added to powdered sodium (2·1 g.) and heated for 1 hour on the water-bath with occasional shaking. The mixture was treated with dilute hydrochloric acid, and the ester layer dried and fractionated, giving a colourless oil (12·5 g.), b. p. 145—165°/22 mm. After addition of an equal volume of methyl alcohol, methyl *p*-methylcinnamate (10·5 g.) crystallised on strong cooling and had m. p. 57—58°, b. p. 157°/22 mm.

βγ-Di-p-*tolyladipic*-a *Acid*.—The above crystalline ester (50 g.), dissolved in ether (1·5 l.), was poured on amalgamated aluminium foil (100 g.) (J., 1930, 2148), and water (40 c.c.) added, with cooling in running water and frequent shaking during 8 hours. The ether was filtered and combined with washings from the aluminium sludge, and, after evaporation of the ether, methyl β-*p*-tolylpropionate (23 g.), b. p. 132°/20 mm., was removed by distillation as a colourless oil which solidified on standing, m. p. 39° (Found : C, 74·2; H, 7·8. Calc. : C, 74·2; H, 7·8%). The undistilled residue with ether gave an insoluble portion, from which, by crystallisation from methyl alcohol, *methyl βγ-di*-p-*tolyladipate*-a (9·0 g.) was obtained in colourless needles, m. p. 150° (Found : C, 75·0; H, 7·2. $C_{22}H_{26}O_4$ requires C, 74·6; H, 7·3%). On hydrolysis with aqueous-alcoholic potassium hydroxide *βγ-di*-p- *olyladipic*-a *acid* was obtained in almost quantitative yield; it crystallised from butyl alcohol in small prisms, m. p. 320° (Found : C, 73·8; H, 6·8. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·7%). A further small quantity (0·7 g.) of this acid was obtained by dissolving the aluminium sludge in hydrochloric acid. From the ethereal mother-liquor, crude methyl βγ-di-*p*-tolyladipate-*b* (18 g.) was recovered.

2 : 11-*Diketo*-5 : 14-*dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-a (II).—Di-*p*-tolyladipic-*a* acid (2·0 g.) and purified thionyl chloride (5 c.c.) were refluxed (1 hour), the excess of solvent removed from the clear solution, and the powdered solid residue, in dry tetrachloroethane (20 c.c.), treated with powdered aluminium chloride (4 g.), slowly warmed to 60° with shaking, and maintained at this temperature for 12 hours. The solvent was steam-distilled, and the alkali-insoluble *diketodimethylhexahydrochrysene*-a extracted with boiling anisole or nitrobenzene, which gave, on cooling, long colourless prisms (1·2 g.), m. p. 312° (decomp.) after a further crystallisation (Found : C, 82·7; H, 6·3. $C_{20}H_{18}O_2$ requires C, 82·8; H, 6·2%). The diketone-*a* (1·8 g.) was also obtained by heating the acid (3·0 g.) with sulphuric acid (40 c.c., 85%) for 3 hours.

5 : 14-*Dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-a (III).—The above diketone (1·0 g.), anisole (20 g.), amalgamated zinc (70 g.), and concentrated hydrochloric acid (10 c.c.) were refluxed for 36 hours with two additions of acid (5 c.c.) at 12-hour intervals. The anisole layer was separated, the solvent removed, and the residue distilled under reduced pressure; *dimethylhexahydrochrysene*-a (0·65 g.) crystallised from ethyl alcohol in long needles, m. p. 140° (Found : C, 91·6; H, 8·4. $C_{20}H_{22}$ requires C, 91·6; H, 8·4%).

2 : 11-*Diketo*-5 : 14-*dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-b (II).—The crude ether-soluble ester (18 g.) obtained in the reduction above was hydrolysed and gave a solid acid mixture, precipitated by ice; this was dried, and the sticky product cyclised through its acid chloride as described for the diketone-*a*. The alkali-insoluble material was extracted with boiling anisole, which, on cooling, gave the diketone-*a* (0·7 g.); after removal of the solvent, *diketodimethylhexahydrochrysene*-b solidified in contact with ethyl alcohol and crystallised from butyl alcohol in almost colourless plates (4·4 g.), m. p. 193—194°, raised to 201—202° by distillation under reduced pressure and a further crystallisation (Found : C, 82·7; H, 6·1. $C_{20}H_{18}O_2$ requires C, 82·8; H, 6·2%).

5 : 14-*Dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-b (III).—The diketone-*b* (1·0 g.), by a Clemmensen reduction without anisole, gave *dimethylhexahydrochrysene*-b, which solidified after distillation under reduced pressure (0·6 g.) and crystallised from ethyl alcohol in colourless plates, m. p. 108° (Found : C, 91·4; H, 8·3. $C_{20}H_{22}$ requires C, 91·6; H, 8·4%).

5 : 14-*Dimethylchrysene*.—Either dimethylhexahydrochrysene-*a* or -*b* (0·5 g.) was dehydrogenated in 6 hours by heating with selenium (1·5 g.) at 280°, raised to 320°, the sublimate being repeatedly melted and returned down the tube. The *dimethylchrysene* (0·4 g.) was sublimed from the selenium under reduced pressure, then from sodium; it crystallised from benzene in large plates, m. p. 218° (Found : C, 93·9; H, 6·0. $C_{20}H_{16}$ requires C, 93·8; H, 6·2%).

The 1 : 3 : 5-*trinitrobenzene* compound, prepared in benzene solution, crystallised from this solvent in yellow needles, m. p. 195° (Found : N, 9·3. $C_{20}H_{16},C_6H_3O_6N_3$ requires N, 9·0%). The *styphnate* crystallised in orange needles, m. p. 204° (Found : N, 8·5. $C_{20}H_{16},C_6H_3O_8N_3$ requires N, 8·4%), and the *picrate* in red needles, m. p. 171—172° (Found : N, 8·8. $C_{20}H_{16},C_6H_3O_7N_3$ requires N, 8·7%), both from benzene.

General Procedure in Wolff Reductions.—The diketone (1·0 g.), hydrazine hydrate (2 c.c. of 50%), and absolute alcohol (100 c.c.) were refluxed over-night, most of the alcohol distilled, and the hydrazone precipitated by cooling and dilution with water if necessary. The hydrazone (1·0 g.) and sodium ethoxide (0·5 g. of sodium in 8 c.c. of absolute alcohol) were heated for 15 hours at 180°, the solution extracted with ether, the extract washed with water and dried, the solvent removed, and the residual oil crystallised from alcohol.

1 : 2 : 9 : 10 : 11 : 18-*Hexahydrochrysene*.—*cis*-Diketohexahydrochrysene (1·0 g.) (J., 1933, 609) gave a *dihydrazone*, which crystallised from aqueous alcohol in fine needles, decomp. about 120° (Found : N, 19·6. $C_{18}H_{18}N_4$ requires N, 19·3%), and from which *cis*-hexahydrochrysene (0·3 g.), m. p. 79°, identical with the product from a Clemmensen reduction, was obtained.

The *dihydrazone* from *trans*-diketohexahydrochrysene (1·0 g.) (J., 1933, 608) crystallised from quinoline in needles, m. p. 360° (Found : N, 19·3. $C_{18}H_{18}N_4$ requires N, 19·3%). It was converted as above into *trans*-hexahydrochrysene (0·4 g.), m. p. 112°.

Aluminium Reduction of Methyl β-*Methylcinnamate*.—From methyl bromoacetate (500 g.), by the method of v. Auwers (*Annalen*, 1917, **413**, 272), methyl β-methylcinnamate (320 g.), b. p. 129—133°/12 mm., was obtained (Found : C, 74·6; H, 6·9. Calc. : C, 75·0; H, 6·8%); this was reduced in five separate experiments, in each of which prepared aluminium foil (100 g.) was used. After removal of the ether, the combined residues were distilled and gave methyl β-phenyl-*n*-butyrate (270 g.), b. p. 120—122°/15 mm. (Found : C, 74·1; H, 7·8. Calc. : C, 74·2; H, 7·8%). The residual gum (30 g.), treated with methyl alcohol, partly crystallised, giving *methyl* βγ-*diphenyl*-βγ-*dimethyladipate*-a (5·5 g.), m. p. 134° (Found : C, 74·9; H, 7·3. $C_{22}H_{26}O_4$ requires C, 74·6; H, 7·3%); the mother-liquor contained the methyl ester-*b*, which was not further purified.

2 : 11-*Diketo*-9 : 18-*dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-a (V).—The above ester-*a* (1·0 g.), concentrated sulphuric acid (12 c.c.), and water (4 c.c.) were heated on the water-bath for 3 hours. On cooling and dilution with water, the *diketodimethylhexahydrochrysene*-a was precipitated; after filtration and digestion with sodium carbonate solution, it crystallised from pyridine in prisms (0·7 g.), m. p. 256° (Found : C, 82·7; H, 6·0. $C_{20}H_{18}O_2$ requires C, 82·8; H, 6·2%).

2 : 11-*Diketo*-9 : 18-*dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-b (V).—The above methyl ester-*b*, recovered from the mother-liquor, was treated in 2-g. portions with sulphuric

acid as above; the *diketodimethylhexahydrochrysene*-b obtained (7·2 g. in all) crystallised from pyridine in large well-formed prisms, m. p. 229° (Found: C, 82·7; H, 6·1%).

9 : 18-*Dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-a (VI).—The *dihydrazone* from the diketone-*a* (1·0 g.) was not quite pure (Found: N, 16·7. $C_{20}H_{22}N_4$ requires 17·6%), but gave *dimethylhexahydrochrysene*-a (0·6 g.) by the Wolff reduction; this was purified by distillation under reduced pressure from potassium, followed by crystallisation from ethyl alcohol, giving colourless prisms, m. p. 144° (Found: C, 91·8; H, 8·3. $C_{20}H_{22}$ requires C, 91·6; H, 8·4%).

9 : 18-*Dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-b (VI).—The diketone-*b* (1·0 g.) gave a *dihydrazone*, which crystallised from xylene in fine needles, m. p. 232—234° (decomp.) (Found: N, 17·4. $C_{20}H_{22}N_4$ requires N, 17·6%). This was converted into *dimethylhexahydrochrysene*-b (0·5 g.), which was distilled from potassium under reduced pressure and crystallised from methyl alcohol, forming fine needles, m. p. 105—106°. Slow crystallisation from a cold solution gave a second form in prisms, m. p. 101°, which after resolidifying cleared at 105° (Found: C, 91·7; H, 8·4%).

Part of the work was completed in the Dyson Perrins Laboratory, Oxford. The author thanks Prof. R. Robinson, F.R.S., and Prof. J. L. Simonsen, F.R.S., for their interest and encouragement, and the Chemical Society for a research grant.

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