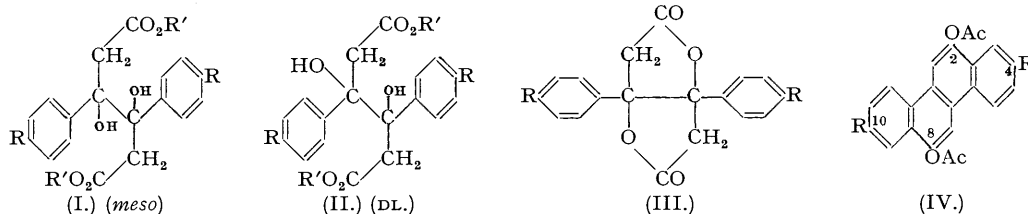


194. A Modified Synthesis of Chrysene.

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Chrysene, and some chrysene derivatives, have been prepared by modifications of the syntheses by Beschke (*Annalen*, 1911, **384**, 143) and of von Braun and Irmisch (*Ber.*, 1931, **64**, 2461).

IN the original chrysene synthesis by Beschke (*loc. cit.*), a mixture of the isomeric esters (I and II; R = H, R' = Et) was prepared from benzil by the Reformatsky reaction. The *meso*-ester (I) was converted into a half lactone, hydrolysed, and then reduced with sodium amalgam to $\beta\beta'$ -diphenyl- $\alpha\alpha'$ -dihydromuconic acid, the *trans*-modification of which (V; R = H) was



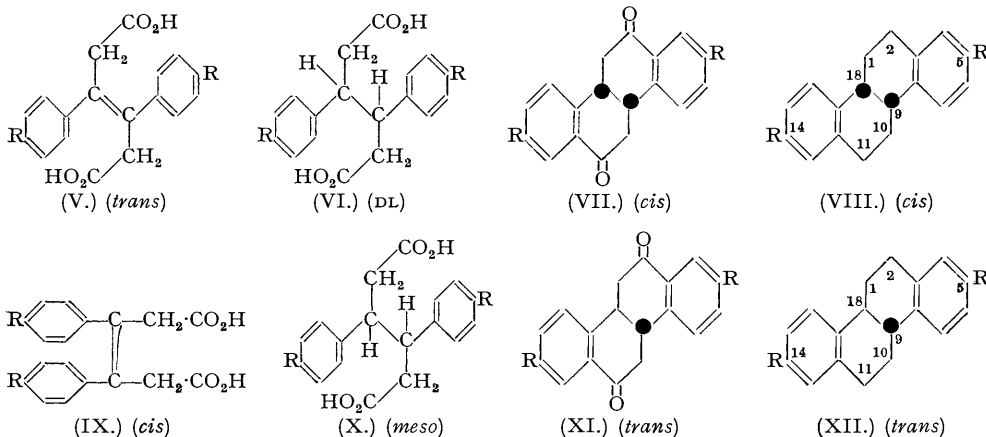
converted into 2 : 8-diacetoxychrysene (IV; R = H). The synthesis by von Braun and Irmisch (*loc. cit.*), the details of which were greatly improved by Ramage and Robinson (*J.*, 1933, 607; see also Lewis, Ramage, and Robinson, *J.*, 1935, 1412), involved the preparation of two stereoisomeric $\beta\beta'$ -diphenyladipic acids (VI and X) by bimolecular reduction of methyl cinnamate, followed by cyclisation and reduction to *cis*- and *trans*-hexahydrochrysene (VIII and XII; R = H). The present method involves the preparation of the $\beta\beta'$ -diphenyladipic acids by reduction of the isomeric diphenyldihydromuconic acids (V and IX), which in turn are prepared by an improved method from the esters (I and II) obtained from benzil by the Reformatsky reaction.

meso- $\beta\beta'$ -Dihydroxy- $\beta\beta'$ -diphenyladipic acid (I; R = H, R' = H) was reduced with zinc dust and boiling alkali to a mixture of *trans*- $\beta\beta'$ -diphenyl- $\alpha\alpha'$ -dihydromuconic acid (V; R = H), and an isomeric acid, presumably *cis*- $\beta\beta'$ -diphenyl- $\alpha\alpha'$ -dihydromuconic acid (IX; R = H). The dilactone (III; R = H) resulting from the hydrolysis of DL- $\beta\beta'$ -dihydroxy- $\beta\beta'$ -diphenyladipic ester (II; R = H, R' = Et) was converted into a similar mixture of *cis*- and *trans*-diphenyldihydromuconic acids by the same treatment. Attempted reduction of the *meso*-acid (I, R = R' = H) with nickel-aluminium alloy and 10% sodium hydroxide (Papa, Schwenk, and Whitman, *J. Org. Chem.*, 1942, **7**, 587) gave only water-soluble derivatives, but similar treatment of the dilactone (III; R = H) gave *meso*-diphenyladipic acid (X; R = H) although not in good yield.

Reduction of *trans*-diphenyldihydromuconic acid (V; R = H) with nickel-aluminium alloy and sodium hydroxide gave DL-diphenyladipic acid (VI; R = H) in good yield. This result is interesting in view of the observation of Schwenk, Papa, Whitman, and Ginsberg (*J. Org. Chem.*, 1944, **9**, 175) that stilboestrol is reduced to a mixture of hexoestrol and *isohexoestrol* by this method. On the other hand, Docken and Spielman (*J. Amer. Chem. Soc.*, 1940, **62**, 2163) reduced stilboestrol to *isohexoestrol* (DL-dihydrostilboestrol) quantitatively with hydrogen and Raney nickel in alcohol. Reduction of *cis*-diphenyldihydromuconic acid (IX; R = H) with nickel-aluminium alloy and sodium hydroxide gave *meso*-diphenyladipic acid (X; R = H) almost quantitatively.

trans-Diphenyldihydromuconic acid has also been converted into 2 : 8-diacetoxychrysene (IV; R = H) and hydrolysed to the dihydroxy-derivative by the method of Beschke (*loc. cit.*). Reduction by the zinc dust-zinc chloride melt method of Clar (*Ber.*, 1939, **72**, 1645) gave chrysene. Diacetoxychrysene was also converted into 2 : 8-diethoxychrysene with sulphuric

acid and absolute alcohol. Under similar conditions with "alcohol" and sulphuric acid, Beschke obtained 2 : 8-dihydroxychrysene.



The stereoisomeric diphenyladipic acids (VI and X; R = H) were cyclised to *cis*- and *trans*-diketohexahydrochrysene (VII and XI; R = H) by the method of Ramage and Robinson (*loc. cit.*), and then were reduced to the corresponding hexahydrochrysenes by the Huang–Minlon modification of the Kishner–Wolff method (*J. Amer. Chem. Soc.*, 1946, **68**, 2487).

The Reformatsky reaction with anisil was found to proceed smoothly; but in agreement with Cook and Lawson (*J.*, 1933, 827) only one isomer could be isolated, a considerable quantity of a viscous gum also being formed. The configuration of the ester (I; R = OMe, R' = Et) is evidently *meso*, for hydrolysis gave $\beta\beta'$ -*dihydroxy*- $\beta\beta'$ -*di-p-methoxyphenyladipic acid* (I; R = OMe, R' = H), and not the dilactone (III; R = OMe) which would be expected from the racemic ester (*cf.* Beschke, *loc. cit.*). Hydrolysis of the viscous gum, which probably contained some racemic ester in addition to mono-acetic acid derivatives (Cook and Lawson, *loc. cit.*), followed by attempted reduction, also gave intractable gums. Reduction of the *meso*-acid (I; R = OMe, R' = H) with zinc dust and alkali gave *trans*- $\beta\beta'$ -*di-p-methoxyphenyl- $\alpha\alpha'$ -dihydromuconic acid* (V; R = OMe) and an oily acid. The latter, on treatment with nickel–aluminium alloy and sodium hydroxide gave *meso*-*di-p-methoxyphenyladipic acid* (X; R = OMe), but the former could not be reduced by this method, and was recovered unchanged. *trans*-*Di-p-methoxyphenyldihydromuconic acid* was, however, converted into 2 : 8-*diacetoxy-4 : 10-dimethoxychrysene* (IV; R = OMe). *meso*-*Di-p-methoxyphenyladipic acid* was cyclised by the Friedel–Crafts method, and the product was reduced to *trans*-5 : 14-*dimethoxy-1 : 2 : 9 : 10 : 11 : 18-hexahydrochrysene* (XII; R = OMe) by the Huang–Minlon–Kishner–Wolff method.

EXPERIMENTAL.

$\beta\beta'$ -Diphenyl- $\alpha\alpha'$ -dihydromuconic Acid.—(a) *meso*-Diethyl $\beta\beta'$ -*dihydroxy- $\beta\beta'$ -diphenyladipate* was prepared from benzil and ethyl bromoacetate, and separated from the accompanying racemic modification by fractional crystallisation from benzene (Beschke, *loc. cit.*). After hydrolysis with alcoholic potash, the acid (I; R = R' = H) (10 g.) was dissolved in 2*N*-sodium hydroxide (200 c.c.) and refluxed with zinc dust (30 g.) for 72 hours. After filtration and acidification, the product was crystallised from alcohol. The first crop (2.5 g.) consisted of *trans- $\beta\beta'$ -diphenyl- $\alpha\alpha'$ -dihydromuconic acid*, m. p. 295–297°. After further recrystallisation, it formed colourless elongated prisms, m. p. 297–299° (decomp.) (Found: C, 73.2; H, 5.2. Calc. for C₁₈H₁₄O₄: C, 73.0; H, 5.4%).

The alcoholic liquors, on evaporation, gave a crude acid (1.5 g.) which, after recrystallisation from water, had m. p. ca. 170–180°. The diethyl ester prepared from this acid (which was, presumably, *cis- $\beta\beta'$ -diphenyl- $\alpha\alpha'$ -dihydromuconic acid*) with absolute alcohol and sulphuric acid formed colourless needles, m. p. 54–55.5° (Beschke gives m. p. 56°) (Found: C, 75.1; H, 6.7. Calc. for C₂₂H₂₄O₄: C, 75.0; H, 6.8%). The pure acid, obtained on hydrolysis of the ester, had m. p. 195° in agreement with Beschke.

(b) *DL*-Diethyl $\beta\beta'$ -*dihydroxy- $\beta\beta'$ -diphenyladipate* on hydrolysis with alcoholic potash, followed by acidification with acetic acid, gave the dilactone (III; R = H), m. p. 186°. This lactone (5 g.) was refluxed with 2*N*-sodium hydroxide (150 c.c.) and zinc dust (15 g.) for 72 hours. After treatment as above, it gave the *trans*-acid (1.6 g.) and crude *cis*-acid (2.1 g.). The constitution of the latter was proved in the same manner as above.

DL- $\beta\beta'$ -Diphenyladipic Acid (VI).—A solution of the *trans*-acid (V) (3.8 g.) in 10% sodium hydroxide (150 c.c.) was warmed on the steam-bath and treated with nickel–aluminium alloy (15 g.) in small portions. After a further hour on the steam-bath, the filtered solution was added carefully to excess of

concentrated hydrochloric acid, with vigorous stirring. The acid, after recrystallisation from water, formed colourless needles, m. p. 184—186° (3.2 g.). (Found : C, 72.7; H, 6.0. Calc. for $C_{18}H_{18}O_4$: C, 72.5; H, 6.0%.)

meso- $\beta\beta'$ -Diphenyladipic Acid (X).—(a) The crude *cis*-acid (IX) was reduced in 80% yield in the same manner as for the *trans*-acid. *meso*- $\beta\beta'$ -Diphenyladipic acid formed colourless needles from alcohol, m. p. 274.5—276.5° (lit., 270—271°) (Found : C, 72.45; H, 6.0. Calc. for $C_{18}H_{18}O_4$: C, 72.5; H, 6.0%). The same acid was obtained almost quantitatively by similar treatment of the pure *cis*-acid, regenerated from the ester.

(b) A solution of the dilactone (III; R = H) (1 g.) in 10% sodium hydroxide (60 c.c.), on the steam-bath, was treated with nickel-aluminium alloy (10 g.) in small portions. The acidic product was boiled with water (100 c.c.) and rapidly filtered. The water-insoluble product, after recrystallisation from alcohol, had m. p. 271—274° (0.45 g.) not depressed by a specimen of *meso*- $\beta\beta'$ -diphenyladipic acid. The aqueous solution deposited, on cooling, colourless micro-crystals (0.35 g.), m. p. 180—183°, of the original dilactone.

cis-Hexahydrochrysene.—DL-Diphenyladipic acid was cyclised with 85% sulphuric acid by the method of Ramage and Robinson (*loc. cit.*). A mixture of the resulting diketone (VII; 0.8 g.), sodium hydroxide (1 g.), hydrazine hydrate (85%, 1 c.c.), and ethylene glycol (15 c.c.) was boiled under reflux for 1 hour. The condenser was then removed and the boiling continued until the temperature reached 195°. After a further period of refluxing for 3 hours, the mixture was cooled, diluted with hydrochloric acid, and extracted with benzene. *cis*-Hexahydrochrysene (0.6 g.) distilled at 118°/0.01 mm., and formed colourless elongated prisms, m. p. 74—75°, from alcohol (Found : C, 92.3; H, 7.7. Calc. for $C_{18}H_{18}$: C, 92.3; H, 7.7%).

trans-Hexahydrochrysene.—*meso*-Diphenyladipic acid was cyclised as above. The *trans*-diketone (XI; 1 g.) was reduced as for the *cis*-isomeride, and gave 0.72 g. of *trans*-hexahydrochrysene, b. p. 150°/0.15 mm., m. p. 114—115° (Found : C, 92.2; H, 7.7. Calc. for $C_{18}H_{18}$: C, 92.3; H, 7.7%).

2 : 8-Diethoxychrysene.—A suspension of 2 : 8-diacetoxychrysene (1.5 g.) (Beschke, *loc. cit.*) in absolute alcohol (60 c.c.) and sulphuric acid (7.5 c.c.) was refluxed for 2 hours. After cooling, the crystalline 2 : 8-diethoxychrysene was collected (1.1 g.) and recrystallised from acetic acid, forming colourless needles, m. p. 207—208° (Found : C, 83.35; H, 6.2. Calc. for $C_{22}H_{20}O_2$: C, 83.5; H, 6.3%). Beschke gives m. p. 207°.

Chrysene.—A mixture of 2 : 8-dihydroxychrysene (0.85 g.), zinc dust (2 g.), sodium chloride (2 g.), and zinc chloride (10 g.) was heated at about 300° for $\frac{1}{4}$ hour. The melt was extracted with hydrochloric acid, warm dilute sodium hydroxide, and hot water. After sublimation at 200°/0.1 mm., the product (0.28 g.) had m. p. 250—251° alone or mixed with authentic chrysene. The alkaline liquors, on acidification, gave 0.24 g. of crude dihydroxychrysene.

meso- $\beta\beta'$ -Dihydroxy- $\beta\beta'$ -di-*p*-methoxyphenyladipic Acid.—The ester (I; R = OMe, R' = Et) (Cook and Lawson, *loc. cit.*) was hydrolysed with alcoholic potash to the acid, which formed colourless elongated prisms, m. p. 187—188° (decomp.), from alcohol (Found : C, 61.6; H, 5.7. $C_{20}H_{22}O_8$ requires C, 61.5; H, 5.6%).

$\beta\beta'$ -Di-*p*-methoxyphenyl- $\alpha\alpha'$ -dihydromuconic Acid.—A solution of the ester (I; R = OMe, R' = Et) (10 g.) in alcohol (50 c.c.), water (25 c.c.), and potassium hydroxide (12 g.) was refluxed for 2 hours. After removal of the alcohol, water (50 c.c.), 2N-sodium hydroxide (150 c.c.), and zinc dust (30 g.) were added, and the mixture refluxed for 65 hours. The acidic product was dissolved in hot alcohol, from which *trans*- $\beta\beta'$ -di-*p*-methoxyphenyl- $\alpha\alpha'$ -dihydromuconic acid (2.1 g.) was obtained as colourless prisms, m. p. 252—254° (decomp.) (Found : C, 67.6; H, 5.5. $C_{20}H_{20}O_8$ requires C, 67.4; H, 5.6%). The alcoholic liquors, on evaporation, gave an oil which could not be induced to crystallise. After dissolution of this in 10% sodium hydroxide (120 c.c.) and heating on the steam-bath, nickel-aluminium alloy (12 g.) was added in small portions. The filtered solution, added slowly to excess of hydrochloric acid with vigorous stirring, gave *meso*- $\beta\beta'$ -di-*p*-methoxyphenyladipic acid, m. p. 255—257° from butanol (lit., 250°), yield 3.1 g. (Found : C, 67.3; H, 6.3. Calc. for $C_{20}H_{22}O_8$: C, 67.0; H, 6.15%).

trans-5 : 14-Dimethoxy-1 : 2 : 9 : 10 : 11 : 18-hexahydrochrysene.—*trans*-Diketodimethoxyhexahydrochrysene (XI; R = OMe; 1.2 g.), prepared from *meso*- $\beta\beta'$ -di-*p*-methoxyphenyladipic acid by the method of Ramage and Robinson, (*loc. cit.*), was reduced with hydrazine hydrate (85%; 1.5 c.c.), sodium hydroxide (1.2 g.), and ethylene glycol (15 c.c.) as described for hexahydrochrysene. The product was sublimed at 180°/0.1 mm. and recrystallised from acetic acid to form colourless needles, m. p. 184—185° (lit., 185°). Yield, 0.75 g.

2 : 8-Diacetoxy-4 : 10-dimethoxychrysene.—*trans*-Di-*p*-methoxyphenyldihydromuconic acid (0.5 g.) was suspended in acetic anhydride (3 c.c.), and concentrated sulphuric acid (0.15 c.c.) added with cooling. After $\frac{1}{2}$ hour, the solid (0.4 g.) was collected, washed with acetic acid, and recrystallised from acetic acid. 2 : 8-Diacetoxy-4 : 10-dimethoxychrysene formed colourless silky needles, m. p. 275—276° (decomp.) (Found : C, 71.5; H, 5.2. $C_{24}H_{20}O_8$ requires C, 71.3; H, 5.0%).

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