Synthetic Œstrogens. Part II. The Synthesis of Tetra-alkyldibenzyls and Substituted Succinonitriles by Free-radical Dimerisation.*

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During the synthesis of the diphenols (I; R = Me, R′ = Et; R = R′ = Et and Pr^n; R = Me, R′ = Pr^n; and R = Et, R′ = CN) for tests as œstrogens, a study was made of the free-radical dimerisation of arylalkanes Ar·CHRR′ and alkylated benzyl cyanides CHRPh·CN, which formed the key reaction in the above synthesis. It was found that with the alkanes dimerisation was successful only if the side chain CHRR′ contained not more than four carbon atoms, whereas the benzyl cyanides with R = methyl to *n*-butyl dimerised normally, though in decreasing yields. This result is explained in terms of the stability of the intermediate free radicals. The limited application of the free-radical method in the former case necessitated the use of a different preparative method for the second, third, and fourth substances mentioned above.

DIMERISATION of free radicals appears particularly well suited to the synthesis of fully substituted dibenzyls of the general structure (I) and has been applied in the present

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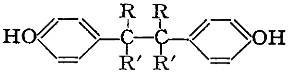
* Part I, *J.*, 1953, 160.

investigation to the synthesis of (i) tetra-alkyldibenzyls (I; R, R′ = alkyl) and (ii) substituted succinonitriles (I; R = alkyl, R′ = CN) in a study of the relation between chemical structure and œstrogenic activity.

Tetra-alkyldibenzyls.—In Part I (*loc. cit.*) the synthesis of 2 : 3-di-*p*-hydroxyphenyl-2 : 3-dimethylbutane (I; R = R′ = Me) by the dimerisation of 2-arylpropanes was described.* The higher homologues (i) *meso*- and racemic (I; R = Me, R′ = Et), (ii) (I; R = R′ = Et), (iii) (I; R = Me, R′ = Pr^n), and (iv) (I; R = R′ = Pr^n) have now been prepared. Of these the first appears to be of particular biological interest in view of (*a*) the structural relation it bears to hexœstrol and to 3 : 4-di-*p*-hydroxyphenyl-3-methylhexane recently reported by Dodds, Huang, Lawson, and Robinson (*Proc. Roy. Soc.*, 1953, *B*, **140**, 470), and (*b*) the possibility of its existing in a *meso*- and a racemic modification, which would facilitate a study of the stereochemical relation with biological activity. A study of the synthesis of these higher homologues incidently revealed the limitations of the free-radical method, which was found applicable only to the synthesis of the first diphenol (I; R = Me, R′ = Et). For the preparation of the other homologues it was necessary to employ a totally different method, involving bimolecular reduction of the appropriate alkylarylcarbinols.



(I)

In attempts to prepare (I; R = Me, R′ = Et; and R = R′ = Et) by the dimerisation method previously described, 2-*p*-methoxyphenylbutane and 3-*p*-methoxyphenylpentane, respectively, were each treated with di-*tert.*-butyl peroxide at 140°. Contrary to expectation, however, apart from polymeric material, none of the desired dimers could be isolated from the product by chromatography, distillation, or recrystallisation. Similarly, 3-*p*-benzoyloxyphenylpentane failed entirely to dimerise in the desired manner (Morsingh, Thesis, Malaya, 1952). This failure of the intermediate free radicals to dimerise was attributed to their instability at the reaction temperature, as a result of which disproportionation became the main reaction and the corresponding styrene so produced underwent additive polymerisation in the presence of *tert.*-butoxy-radicals. Since, according to accepted theory (Ingold, *Trans. Faraday Soc.*, 1934, **30**, 52; cf. Huang, *J.*, in the press) electropositive substituents, such as the *p*-methoxy-group, destabilise free radicals of the type under consideration, the unsubstituted radicals PhEtMeC· and $PhEt_2C\cdot$ should be relatively stable and therefore less prone to disproportionation. This was found to be so in the former case, and dimerisation of 2-phenylbutane in the usual manner did afford in fair yields approximately equal quantities of the *meso*- and racemic 3 : 4-dimethyl-3 : 4-diphenylhexanes, the less soluble and higher-melting isomer being assigned the *meso*-configuration. Nitration of these by an improved method, followed by reduction and a diazo-reaction (as in Part I), furnished the required *meso*- and racemic diphenols (I; R = Me, R = Et). However, with the latter radical, $PhEt_2C\cdot$, derived from 3-phenylpentane, disproportionation was again found to be predominant. Two attempts were accordingly made to stabilise this free radical, *viz.*, (*a*) by the introduction of an electronegative substituent, and (*b*) by operating at a lower temperature. Both proved ineffective. Thus, 3-*p*-nitrophenylpentane on reacting with di-*tert.*-butyl peroxide at 140° similarly gave an intractable product, while the use of acetyl peroxide as the dimerising agent, for which a reaction temperature of 80° suffices (Kharasch, McBay, and Urry, *J. Org. Chem.*, 1945, **10**, 401), also failed. It becomes clear, therefore, that increase in the length of the carbon chain causes a sharp decline in the thermal stability of the free radicals of this type, and hence this method of synthesis of tetra-alkyldibenzyls is limited to the lower homologues, involving the formation of free radicals with a carbon chain of not more than four carbon atoms.

Ziegler and Deparade (*Annalen*, 1950, **567**, 123) recently studied the thermal stability

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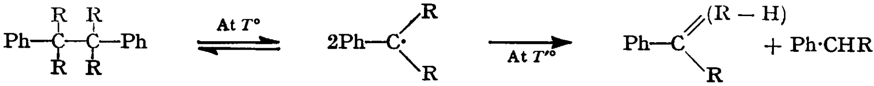
* In this paper, the conversion of X·H into X_2 is referred to, inaccurately but conveniently, as dimerisation; and the substances X·H and X_2 similarly as monomer and dimer, respectively.

of various symmetrical tetra-alkyldibenzyls (II; prepared by another method) and found that these dissociate into free radicals as follows:

(II)



the temperatures of appreciable decomposition T being: R = Me, 240°; R = Et, 142°; R = Pr^n, 110°. The failure of 3-phenylpentane to dimerise at 140° is therefore not surprising. However, it is to be noted that T is not necessarily the same as the temperature T' at which disproportionation of the resulting radicals becomes appreciable, and that the latter can be equal to, or might well be lower than T. This is clearly seen in the case of (II; R = Et) for which T is 142°, but T' is not more than 80° from the experiment using acetyl peroxide described above. Furthermore, since it is generally known that reactive free radicals normally undergo rapid reactions such as hydrogen abstraction, substitution, and disproportionation, whereas dimerisation is a comparatively much slower process characteristic of relatively stable radicals (cf. Kharasch and Buchi, *J. Amer. Chem. Soc.*, 1951, **73**, 632; Kharasch, Kane, and Brown, *ibid.*, 1942, **64**, 1621), the yield of the desired type of dimer compared with that of polymers might be taken as a rough indication of the relative stability of the free radicals. Thus in the cases so far encountered, the products range from a high yield in the case of cumene of almost pure dimer, which readily crystallised from the reaction mixture, to a much lower yield in the case of 2-*p*-methoxyphenylpropane of a product contaminated with by-products removed only after chromatography (Part I, *loc. cit.*). Assessed in this way, some of the free radicals can be arranged in decreasing relative stability as follows: $PhMe_2C\cdot > PhMeEtC\cdot > p\text{-}MeO\cdot C_6H_4\cdot CMe_2\cdot > PhEt_2C\cdot$.

The higher homologues (I; R = R′ = Et; R = Me, R′ = Pr^n; and R = R′ = Pr^n) were prepared by a modification of the method by which Klages synthesised 2 : 3-dimethyl-2 : 3-diphenylbutane (*Ber.*, 1902, **35**, 2638; cf. Ziegler and Deparade, *loc. cit.*), namely, by the reduction of 2-phenylpropan-2-ol with zinc and hydrogen iodide in acetic acid. Although the yield was low, the synthesis was a short one. Thus the crude alcohols 3-*p*-methoxyphenylpentan-3-ol, 2-*p*-methoxyphenylpentan-2-ol, and 4-*p*-methoxyphenylheptan-4-ol, obtained from the appropriate Grignard reactions, were each reduced according to Klages's method, and the resulting products demethylated directly with hydriodic acid in acetic acid at 80°, yielding the required diphenols. Only one of the two possible isomers (I; R = Me, R′ = Pr^n) was obtained, presumably the *meso*-isomer. The failure of such dimerisation by classical methods to give both isomers, when such are capable of existence, has often been encountered, and reflects on the advantage of free-radical methods whenever applicable.

Of the tetra-alkyldibenzyls synthesised above which were subjected to a Zeisel methoxy-determination, all exhibited the same anomalous behaviour as described for the tetramethyl derivatives reported in Part I.

Substituted Succinonitriles.—The free radicals derived from alkylated benzyl cyanides (III) appeared worthy of study for a comparison with the free radicals already investigated, since the former type are further stabilised by a cyano-group. From the point of view of œstrogens, our approach was mainly stereochemical, namely, the preparation of the *meso*- and racemic series of the homologous succinonitriles (I; R = alkyl, R′ = CN), by the free-radical method, which has been shown to be distinctly successful in the preparation of such isomers. Further biological interest in these succinonitriles lies in their possible conversion into the corresponding succinic acids, one member of which (I; R = H, R′ = CO_2H) has recently been reported to be highly potent (Hoch, *Compt. rend.*, 1950, **231**, 625).

The free-radical dimerisation of substituted benzyl cyanides (III) does not appear to have been studied previously and was therefore investigated in some detail. Dimerisation by the usual method of (III; R = Me, Et, Pr^n, or Bu^n), best prepared by alkylation of benzyl cyanide with sodamide, gave varying yields of mixtures of the *meso*- and racemic

(III) $Ph\cdot CHR(CN)$ $PhR(CN)C\cdot C(CN)RPh$ (IV) dimers (IV), the less soluble and higher-melting isomer in each case being assigned the *meso*-configuration. As expected, the lower homologues (III; R = Me, Et) gave good yields of the respective *meso*- and racemic dimers, uncontaminated by any impurities or polymeric materials. With increase in the length of the carbon chain (R = Pr^n, Bu^n) polymeric substances increased with a resulting diminution in yield of the dimer, although this diminution was much less pronounced than in the alkylbenzene series. This result is to be attributed to the stabilising influence of the cyano-group.

As an œstrogen the diphenol (I; R = Et, R′ = CN) has already been reported by Niederl and Ziering (*J. Amer. Chem. Soc.*, 1942, **64**, 2486) whose synthesis involves the dimerisation of the sodio-derivative of *p*-nitrophenylbutyronitrile with iodine. No experimental details or yields were given, and only one of the two isomers, presumably the *meso*-, was obtained. In an attempt to synthesise both isomeric diphenols, the *meso*- and the racemic dimer (IV; R = Et) obtained as described above were separately subjected to nitration and reduction, and each of the resulting diamines was diazotised in pyridine in the manner already described. Only one diphenol, m. p. 225—226°, was obtained, however, and it seems likely that one of the isomers (probably the racemic) had suffered isomerisation under the conditions of the decomposition of the diazo-compound. This diphenol differed from that reported by Niederl and Ziering, m. p. 218° (although their intermediate dinitro- and diamino-compounds agreed in m. p. with our higher-melting series), but it is evident that theirs is an impure sample since it gave an incorrect elemental analysis. In the course of this work it was also found that the usual methods of nitration, reduction, and diazotisation (*e.g.*, nitric acid at 60°; iron filings or zinc or tin and hydrochloric acid in ethanol; and diazotisation in aqueous sulphuric acid, respectively) gave poor results. For all these operations methods which give reasonable yields have been worked out.

Hydrolysis of the cyano-groups in (IV; R = Et) was attempted by (*a*) refluxing with 70% sulphuric acid in ethanol, (*b*) prolonged contact with concentrated sulphuric acid at room temperature (28°), and (*c*) refluxing with 40% aqueous potassium hydroxide. All proved unsuccessful, the starting material in each case being totally recovered, although the last reagent was effective in the hydrolysis of tetramethylsuccinonitrile (Bickel and Waters, *Rec. Trav. chim.*, 1950, **69**, 312).

EXPERIMENTAL

The 3 : 4-*Dimethyl*-3 : 4-*diphenylhexanes*.—(*a*) *sec.*-Butylbenzene (47 g.) and di-*tert.*-butyl peroxide (36 g., Milas and Surgenor, *J. Amer. Chem. Soc.*, 1946, **68**, 205) were heated under reflux at 140—150° for 48 hr. Distillation removed the volatile fractions (19 g.) and the unchanged hydrocarbon, b. p. 34—36°/2 mm. (30 g.). The residue on distillation gave fractions: (i) b. p. 122°/0·5 mm. (8·1 g.), (ii) b. p. 135°/0·5 mm. (5·0 g.), (iii) b. p. 180—187°/0·5 mm. (2·2 g.), and (iv) b. p. 220—230°/0·5 mm. (2·1 g.). Fractions (i) and (ii) partially crystallised, yielding a solid, m. p. 54—59°, very soluble in benzene, but less so in *cyclo*hexane and light petroleum. It was crystallised from methanol, giving meso-3 : 4-*dimethyl*-3 : 4-*diphenylhexane*, prisms, m. p. 93° (5·5 g.) (Found : C, 90·2; H, 10·1; OMe, 2·6. $C_{20}H_{26}$ requires C, 90·2; H, 9·8; OMe, 0%). The mother-liquors were combined, concentrated, and distilled, yielding a nearly colourless viscous oil, b. p. 135—138°/0·5 mm. (6·0 g.). This crystallised on chilling, giving *racemic* 3 : 4-*dimethyl*-3 : 4-*diphenylhexane*, m. p. 40—41° (Found : C, 89·8; H, 9·6; OMe, 2·2%). Attempts to induce crystallisation in fractions (iii) and (iv) failed.

(*b*) *sec.*-Butylbenzene (16·5 g.) and di-*tert.*-butyl peroxide (13·5 g.) were heated in a sealed tube at 150° for 24 hr. Distillation of the product afforded a colourless viscous liquid, b. p. 126—147°/1 mm. (6·4 g.), separable by fractional crystallisation into the *meso*- (2·4 g.) and the racemic (2·6 g.) isomer as described above.

meso-3 : 4-*Dimethyl*-3 : 4-*di*-p-*nitrophenylhexane*.—Finely powdered *meso*-3 : 4-dimethyl-3 : 4-diphenylhexane (m. p. 91°; 2·73 g.) was added during 3 hr. to fuming nitric acid (30 c.c.; *d* 1·515) at 0° with vigorous stirring. After 2 hours' more stirring the mixture was poured on chipped ice, and the yellowish solid which separated was filtered off and washed thoroughly with water. It was then dissolved in benzene and dried by azeotropic distillation of the solvent, yielding a light yellow solid, m. p. 195—198° (3·1 g.). Further recrystallisation furnished the pure *dinitro*-compound, m. p. 201—202° (Found : C, 67·2; H, 6·55; N, 7·7; OMe, 3·3. $C_{20}H_{24}O_4N_2$ requires C, 67·4; H, 6·7; N, 7·9; OMe, 0%). It was soluble in benzene, chloroform, and dioxan but sparingly so in ethanol. This method of nitration was superior to that of Reinbach and Aaronson (*J. Amer. Chem. Soc.*, 1930, **52**, 5050) used in Part I, which gave a much lower yield (23%).

meso-3 : 4-*Di*-p-*aminophenyl*-3 : 4-*dimethylhexane*.—The above dinitro-compound (3·1 g.) on reduction with iron filings and hydrochloric acid in ethanol, as previously described, gave the *diamine*, which separated from benzene in prisms, m. p. 176° (1·2 g.) (Found : C, 80·9; H, 9·6; N, 9·3. $C_{20}H_{28}N_2$ requires C, 81·1; H, 9·5; N, 9·5%). It was soluble in *cyclo*hexane, and in dilute hydrochloric acid. Reduction by zinc and hydrochloric acid in dioxan was more convenient but gave a much reduced yield.

meso-3 : 4-*Di*-p-*hydroxyphenyl*-3 : 4-*dimethylhexane*.—The above diamine (1·0 g.) in pyridine (15 c.c.) was diazotised, and the resulting diazo-compound decomposed as described previously. The diphenol was thus obtained first as an oil (0·53 g.) and after five recrystallisations from benzene as woolly needles, m. p. 175° (0·13 g.) (Found: C, 80·5; H, 8·7; OMe, 1·8. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·7; OMe, 0%). It was soluble in aqueous potassium hydroxide but only slightly so in sodium hydroxide.

Racemic 3 : 4-*Dimethyl*-3 : 4-*di*-p-*nitrophenylhexane*.—Nitration of the racemic hydrocarbon (4·0 g.) by the method described above gave the *dinitro*-derivative, soluble in benzene and chloroform, m. p. 152° (2·4 g.) (Found : C, 67·1; H, 6·9%).

Racemic 3 : 4-*Di*-p-*aminophenyl*-3 : 4-*dimethylhexane*.—Reduction of the above dinitro-compound (1·75 g.) with iron filings and hydrochloric acid in ethanol yielded the diamine (1·1 g.), soluble in benzene and in *cyclo*hexane, and from a mixture of these solvents it crystallised in prisms, m. p. 149°; mixed m. p. with the dinitro-compound (of m. p. 152°), 137—142°. It was used directly for the next operation.

Racemic 3 : 4-*Di*-p-*hydroxyphenyl*-3 : 4-*dimethylhexane*.—The above diamine (0·80 g.) on diazotisation in the usual manner afforded the required *diphenol*, which crystallised from benzene–*cyclo*hexane in woolly needles, m. p. 156° (0·13 g.) (Found: C, 80·4; H, 8·9; OMe, 2·3%). It was soluble in aqueous potassium hydroxide but sparingly so in sodium hydroxide.

Attempted Dimerisation of 3-*Phenylpentane*.—Crude 3-phenylpentan-3-ol (108 g.), from ethyl benzoate and ethylmagnesium iodide, was heated with anhydrous oxalic acid (72 g.) and quinol (*ca.* 0·5 g.) at 120—130° for 3 hr., and the resulting olefin distilled (b. p. 54—55°/2 mm., n_D^{23} 1·5233; 63 g.). This was then catalytically hydrogenated (palladised strontium carbonate), giving the required hydrocarbon, b. p. 118°/80 mm., n_D^{23} 1·4973 (44 g.). Klages (*Ber.*, 1903, **36**, 693) reports n_{16} 1·4988. The pentane (43·5 g.) and di-*tert.*-butyl peroxide (28·2 g.) were heated together at 140—145° for 48 hr. After distillation of the unchanged material (31 g.), etc., a pale yellow residue (11·6 g.) remained which was very soluble in light petroleum, benzene, or ethyl acetate, but sparingly so in methanol. A portion of this (2·0 g.), dissolved in light petroleum, was chromatographed on alumina. Elution with benzene–light petroleum (1 : 5) gave eight fractions of viscous oils, none of which could be induced to crystallise. The main portion from the above was distilled, giving (*a*) b. p. 140—192°/1 mm. (3·7 g.), and (*b*) b. p. 200—220°/1 mm. (2·3 g.). These were further distilled evaporatively, giving samples the analyses of which showed them to contain approx. 5% of oxygen [Found, for (*b*) : *M* (cryoscopic), 530. Calc. for dimer : *M*, 284]. In another experiment acetyl peroxide (3·7 g.; personal communication by Professor M. S. Kharasch), dissolved in 3-phenylpentane (16 g.), was added during 6 hr. to the same hydrocarbon (*ca.* 4 g.) held at 80—85°. The volatile fractions and unchanged hydrocarbon were then distilled *in vacuo* (temperature not exceeding 85°), and the residue (5·7 g.) was chromatographed as before, yielding none of the required dimer nor any crystalline material (Ziegler *et al.*, *loc. cit.*, report m. p. 42° for 3 : 4-diethyl-3 : 4-diphenylhexane).

Similar attempts to dimerise the following compounds with di-*tert.*-butyl peroxide failed: 3-*p*-nitrophenylpentane, 3-*p*-methoxyphenylpentane, 3-*p*-benzoyloxyphenylpentane, and 2-*p*-methoxyphenylbutane.

3 : 4-*Diethyl*-3 : 4-*di*-p-*methoxyphenylhexane* (cf. Klages, *loc. cit.*).—Crude 3-*p*-methoxyphenylpentan-3-ol (42 g., prepared from methyl *p*-anisate and ethylmagnesium bromide) was added in one portion with vigorous stirring to an externally cooled (ice) saturated solution of hydrogen iodide in glacial acetic acid (230 c.c.), followed by zinc dust (35 g.) in small portions, during 30 min. The solution changed in colour from red to pale yellow, with no appreciable evolution of heat. The mixture was poured on chipped ice, and after removal of the water and acetic acid under reduced pressure (temp. not exceeding 80°), the residue was diluted with water and extracted with ether. The ethereal extract was washed with dilute aqueous solutions of sodium hydrogen sulphite, sodium hydrogen carbonate, and sodium hydroxide, and finally with water, and dried. (The alkaline washings gave no phenolic matter on acidification.) Removal

of ether gave a light yellow oil (20 g.) which failed to crystallise and was used directly for the next operation. In another experiment the reaction mixture after addition of zinc was kept at room temperature (28°) for 72 hr. No appreciable demethylation took place.

3 : 4-*Diethyl*-3 : 4-*di*-p-*hydroxyphenylhexane*.—The crude hexane obtained as above (10 g.) was dissolved in a solution of hydriodic acid (50 c.c., *d* 1·74) in acetic acid (75 c.c.), and the mixture warmed at 80—85° for 72 hr. Water was added, the product taken into ether, washed with sodium hydrogen sulphite, sodium carbonate, and water, and the phenolic matter extracted into aqueous potassium hydroxide. Acidification followed by ether extraction and evaporation yielded a solid, m. p. 62—65° (7·1 g.), probably a mixture of the required diphenol and the monomer 3-*p*-hydroxyphenylpentane (m. p. 79—80°; Dianin, *Ber.*, 1892, **25**, 336). Fractional recrystallisations from benzene–*cyclo*hexane afforded 3 : 4-*diethyl*-3 : 4-*di*-p-*hydroxyphenylhexane* in woolly needles, m. p. 97—100° (3·1 g.), raised to 103—104° after further recrystallisations (Found : C, 80·8; H, 9·3; OMe, 2·0. $C_{22}H_{30}O_2$ requires C, 80·9; H, 9·2; OMe, 0%). It gave no colour with alcoholic ferric chloride, and exhibited the same solubilities in aqueous alkalis as the lower homologues. The *dibenzoate* (from dioxan) had m. p. 207° (Found : C, 80·4; H, 7·1. $C_{36}H_{38}O_4$ requires C, 80·9; H, 7·2%).

4 : 5-*Di*-p-*hydroxyphenyl*-4 : 5-*di*-n-*propyloctane*.—Crude 4-*p*-methoxyphenylheptan-3-ol (40 g.) (prepared from ethyl *p*-anisate and *n*-propylmagnesium iodide) was reduced with zinc (35 g.) and hydrogen iodide in acetic acid (250 c.c.) as previously described. A portion (9·0 g.) of the crude 4 : 5-di-*p*-methoxyphenyl-4 : 5-di-*n*-propyloctane (29·4 g.) was demethylated with hydriodic acid (45 c.c., *d* 1·74) in acetic acid (70 c.c.) in the usual manner, giving a viscous oil (7·4 g.) which was benzoylated directly, yielding 4 : 5-*di*-p-*benzoyloxyphenyl*-4 : 5-*di*-n-*propyloctane* as prisms, m. p. 178—181° (3·3 g.) raised after recrystallisation from benzene–ethyl acetate to 182° (Found : C, 81·2; H, 8·1; OMe, 2·4. $C_{40}H_{46}O_4$ requires C, 81·4; H, 7·8; OMe, 0%). (The monomer, 4-*p*-benzoyloxyphenylheptane has m. p. 29—30°; Dianin, *loc. cit.*) Hydrolysis of the dibenzoate with alcoholic potassium hydroxide yielded a diphenol, probably 4 : 5-di-*p*-hydroxyphenyl-4 : 5-di-*n*-propyloctane, obtained as needles (from benzene–*cyclo*hexane), m. p. 103—104°, which became pink and could not be obtained analytically pure.

4 : 5-*Di*-p-*hydroxyphenyl*-4 : 5-*dimethyloctane*.—Crude 2-*p*-methoxyphenylpentan-2-ol (7·5 g.) prepared from *p*-methoxyacetophenone (cf. Burton and Praill, *J.*, 1951, 726) and *n*-propylmagnesium iodide, on reduction followed by demethylation with the usual reagent yielded an oil (2·6 g.) which on treatment with benzene–light petroleum deposited the monomer 2-*p*-hydroxyphenylpentane, m. p. 72—73° (0·2 g.) (Found: *M*, 158. Calc. for $C_{11}H_{16}O$: *M*, 164). Benzoylation of the mother-liquor afforded a semi-solid which was exhaustively extracted with ethyl acetate. A solid remained, m. p. 247—250° (0·6 g.), which was insoluble in all the usual organic solvents, and attempts at recrystallisation failed. The ethyl acetate-soluble fraction on concentration yielded needles, m. p. 211—213° (0·4 g.). Recrystallisation from ethyl acetate–ethanol gave 4 : 5-*di*-p-*benzoyloxyphenyl*-4 : 5-*dimethyloctane*, m. p. 215—216° (Found : C, 80·8, 81·1; H, 7·2, 7·3. $C_{36}H_{38}O_4$ requires C, 80·9; H, 7·2%). It is sparingly soluble in ethanol and benzene but moderately so in dioxan.

Alkylation of Benzyl Cyanide.—Alkylation of benzyl cyanide with sodium ethoxide in ethanol or with sodium *iso*propoxide in *iso*propanol with the appropriate alkyl iodide both gave unsatisfactory results. Potassium *tert.*-butoxide in *tert.*-butanol gave fair but variable yields, satisfactory results being obtained only with pure reagents (Method A). The best reagent was found to be sodamide in benzene solution (Method B; cf. Bodroux and Taboury, *Bull. Soc. chim.*, 1910, **7**, 670). By the last two methods the following substituted benzyl cyanides were prepared (yields in parentheses) : α-phenylpropionitrile (Method A : 52%; Method B : 87%); α-phenylbutyronitrile (A : 64%; B : 80—85%); α-phenylvaleronitrile (A : 45%); α-phenylhexanonitrile (A : 39%; B : 70%). Baldinger and Nieuwland (*J. Amer. Chem. Soc.*, 1933, **55**, 2851) prepared the above benzyl cyanides by alkylation with sodamide in liquid ammonia.

Dimerisation of Substituted Benzyl Cyanides.—The usual methods were used, *viz.*, heating a mixture of the cyanide (1 mole) and di-*tert.*-butyl peroxide (0·6 mole) at 140—150° either under reflux for 48 hr. (method A) or in a sealed tube for 24 hr. (method B). At the end of the reaction the volatile material and the unchanged cyanide were removed by distillation under reduced pressure, and the less soluble dimer (the *meso*-modification) was induced to crystallise by addition of methanol. The more soluble isomer was obtained by fractional recrystallisation from the same solvent, or in some cases by distillation of the mother-liquors. α-Phenylpropionitrile (33·6 g.) when dimerised by method A gave (i) meso-2 : 3-*dicyano*-2 : 3-*diphenylbutane*, prisms (from methanol), m. p. 218—225° (4·7 g.) raised after recrystallisation from benzene to 224—225° (Found : C, 83·1; H, 6·1; N, 11·1. $C_{18}H_{16}N_2$ requires C, 83·1; H, 6·2; N, 10·8%);

and (ii) the racemic *isomer*, m. p. 133—135° (6·0 g.) raised to 143—144° after recrystallisation from methanol, from which it separated in prisms (Found : C, 83·2; H, 6·0; N, 10·8%).

α-Phenylbutyronitrile (24 g.) gave, by method A : (i) *meso*-3 : 4-dicyano-3 : 4-diphenylhexane, prisms (from methanol), m. p. 174—175° (5·3 g.) (Niederl and Ziering, *loc. cit.*, report m. p. 175°) (Found : C, 83·4; H, 7·0; N, 9·6; OMe, 0. Calc. for $C_{20}H_{20}N_2$: C, 83·3; H, 6·9; N, 9·7: OMe, 0%); (ii) the racemic *compound*, needles (from ethanol), m. p. 114—117° (3·8 g.) raised to 117—118° after further recrystallisations (Found : C, 83·4; H, 7·0; N, 9·6; OMe, 0%). By Method B, α-phenylbutyronitrile (20 g.) similarly gave the *meso*- (3·4 g.) and the racemic (4·3 g.) dimer.

α-Phenylvaleronitrile (10 g.) yielded by method B meso-4 : 5-*dicyano*-4 : 5-*diphenyloctane* (1·5 g.), prisms (from methanol), m. p. 171° (Found : C, 83·5; H, 7·6; N, 8·8. $C_{22}H_{24}N_2$ requires C, 83·6; H, 7·6; N, 8·9%). The mother-liquors were distilled, giving a liquid, b. p. 166—168°/1 mm. (2·4 g.), which yielded on crystallisation from methanol more of the *meso*-isomer (0·34 g.) and the racemic *isomer*, prisms (from methanol), m. p. 122—123° (1·24 g.) (Found : C, 83·4; H, 7·5; N, 8·8%). There was an undistillable residue (2·6 g.) from which no crystalline material could be obtained.

α-Phenylhexanonitrile (17·3 g.), when dimerised by method B, afforded meso-5 : 6-*dicyano*-5 : 6-*diphenyldecane*, prisms (from methanol), m. p. 133—135° (1·7 g.), raised to 137—138° on further recrystallisations (Found : C, 83·9; H, 8·4; N, 7·9. $C_{24}H_{28}N_2$ requires C, 83·7; H, 8·2; N, 8·2%). Distillation of the mother-liquors gave (i) a yellowish oil, b. p. 172—188°/2 mm. (4·4 g.), which probably contained mainly the racemic decane, and (ii) a residue (4·5 g.) which failed to crystallise. Redistillation of (i) gave a liquid, b. p. 160—165° (bath-temp./1 mm., n_D^{23} 1·5179 (Found : C, 83·7; H, 8·1; N, 8·5%), which did not crystallise.

meso-3 : 4-*Dicyano*-3 : 4-*di*-p-*nitrophenylhexane*.—Nitration of *meso*-3 : 4-dicyano-3 : 4-diphenylhexane (6·0 g.) with fuming nitric acid as described above gave the dinitro-compound, m. p. 217—218° (6·8 g.) raised to 223—225° by recrystallisation from chloroform–benzene (Niederl and Ziering, *loc. cit.*, report m. p. 225°). It was soluble in dioxan and chloroform, but sparingly so in ether, benzene, acetone, or ethanol.

meso-3 : 4-*Di*-p-*aminophenyl*-3 : 4-*dicyanohexane*.—Reduction of the dinitro-compound with iron filings and concentrated hydrochloric acid (Part I, *loc. cit.*) or with zinc or tin and hydrochloric acid in ethanol, gave poor results for both the *meso*- and the racemic dinitro-compound. The best procedure was found to be the following : concentrated hydrochloric acid (70 c.c.) was added during 2·5 hr. with vigorous stirring, at 20—25°, to a mixture of granulated tin (10 g.) and 3 : 4-dicyano-3 : 4-dinitrophenylhexane (3·7 g.) in dioxan (100 c.c.). The temperature was then raised to 50—60°, and stirring continued for 4 hr. The mixture was filtered, and on removal of the dioxan under reduced pressure the tin double salt of the diamine separated as a white solid. This was decomposed by addition of excess of 10% aqueous sodium hydroxide in the cold, the liberated diamine being then taken into ether. It was further purified by extraction into 2N-hydrochloric acid, precipitated therefrom with aqueous sodium hydroxide (20%), and again extracted into ether. Removal of the solvent gave *meso*-3 : 4-di-*p*-aminophenyl-3 : 4-dicyanohexane, which crystallised from benzene in prisms, m. p. 207—208° (2·1 g.) (Found : C, 75·3; H, 6·8. Calc. for $C_{20}H_{22}N_4$: C, 75·5; H, 6·9%). Niederl and Ziering (*loc. cit.*) report m. p. 208°.

meso-3 : 4-*Dicyano*-3 : 4-*di*-p-*hydroxyphenylhexane*.—Diazotisation of the above diamine (2·0 g.) in pyridine as already described yielded the diphenol, m. p. 214—218° (0·80 g.), obtained as prisms, m. p. 225—226°, on recrystallisation from benzene (Found : N, 8·7. Calc. for $C_{20}H_{20}O_2N_2$: N, 8·8%). Niederl and Ziering (*loc. cit.*) report m. p. 218°, and give N, 7·8%.

Racemic 3 : 4-*Dicyano*-3 : 4-*di*-p-*nitrophenylhexane*.—Nitration of the hydrocarbon (7·6 g.) with fuming nitric acid at 0—10° as previously described gave the required *dinitro*-compound, obtained as pale yellow prisms, m. p. 208° (softening slightly at 185°; 6·4 g.), after recrystallisations from chloroform and from benzene–ethanol (Found : C, 63·6; H, 5·0; N, 14·9. $C_{20}H_{18}O_4N_4$ requires C, 63·5; H, 4·8; N, 14·8%). A solution of this dinitro-compound in dioxan gave a faint pink colour with sodium hydroxide.

Racemic 3 : 4-*Di*-p-*aminophenyl*-3 : 4-*dicyanohexane*.—Reduction of the above dinitro-compound (6·0 g.) as described for the *meso*-isomer afforded the *diamine*, m. p. 182—184° (4·4 g.) raised to 188—189° by recrystallisation from benzene, from which it separated in almost colourless prisms (Found : C, 75·3; H, 7·0. $C_{20}H_{22}N_4$ requires C, 75·5; H, 6·9%). It was soluble in dioxan and benzene, and less so in ethanol and ether.

The diamine (2·5 g.) was diazotised as for the *meso*-isomer, yielding an oil (1·7 g.) which crystallised in contact with benzene, then having m. p. *ca.* 212—214° raised on further recrystallisation to 225—226°, alone or mixed with the *meso*-diphenol obtained above.

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