*Synthesis of 2 : 2″-Dimethoxy-*o*-terphenyl and Some Related Substances.*

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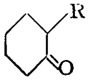
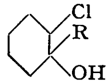
2 : 2″-Dimethoxy-*o*-terphenyl has been prepared. If restricted rotation were operative, this should exist in two forms, but only one was obtained.

Since the benzene rings in *o*-terphenyl are non-planar (Pickett, Walter, and France, *J. Amer. Chem. Soc.*, 1936, **58**, 2296; Merkel and Wiegand, *Z. Naturforsch.*, 1948, **3b**, 93), a derivative of it containing an *ortho*- or a *meta*-substituent in each of the peripheral rings might, by restricted rotation, exist in two geometrical isomers in which the substituents are " *cis* " or " *trans* " to each other with respect to the central ring. We have synthesised such a compound, in which the two substituents are *o*-methoxy : although Fisher–Taylor–Hirschfelder models indicate that rotation is restricted, only one form has been isolated.

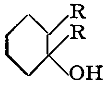
Reaction of 2-chloro*cyclo*hexanone with *p*-methoxyphenylmagnesium bromide gave a fair yield of the ketone (I; R = *p*-MeO·C_6H_4) (Bachmann, Fujimoto, and Wick, *J. Amer. Chem. Soc.*, 1950, **72**, 1995), but use of *o*-methoxyphenylmagnesium bromide furnished only the chlorohydrin (II) and traces of the alcohol (III) (Huang, *J. Org. Chem.*, 1954, **19**, 1363). Prolonged heating, in *p*-xylene, of the magnesium complex formed from the Grignard reagent and the chloro-ketone gave a modest yield of a mixture of the diaryl*cyclo*hexenes (IV and V) (cf. Mueller and Pickens, *J. Amer. Chem. Soc.*, 1950, **72**, 3626), but this mixture could not be dehydrogenated by sulphur or palladium–charcoal. Heating the alcohol (III) with palladised charcoal caused only dehydration.



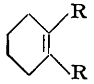
(I)



(II)



(III)



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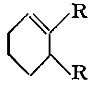
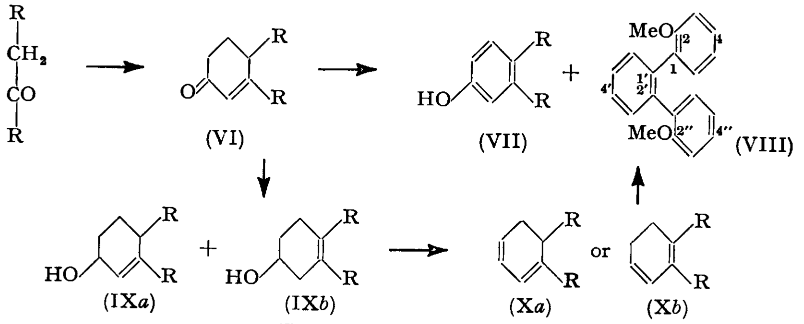


(V)

(R = *o*-OMe·C_6H_4 unless otherwise specified)

2 : 2′-Dimethoxydeoxybenzoin, prepared in three steps from salicylaldehyde, condensed with 4-diethylaminobutan-2-one in presence of sodium ethoxide (cf. Dodds, Huang, Lawson, and Robinson, *Proc. Roy. Soc.*, 1953, *B*, **140**, 470) to give the diaryl*cyclo*hexenone (VI) in 52—56% yield. On dehydrogenation at 180—300° this gave approximately 4 parts of the phenol (VII) and 1 part of 2 : 2″-dimethoxy-*o*-terphenyl (VIII), the latter being always a homogeneous single compound. Since the postulated isomers would differ in thermal stability, milder methods for this transformation were tried, including catalytic dehydrogenation in lower-boiling solvents, *e.g.*, *p*-xylene and cumene, but these proved ineffective.



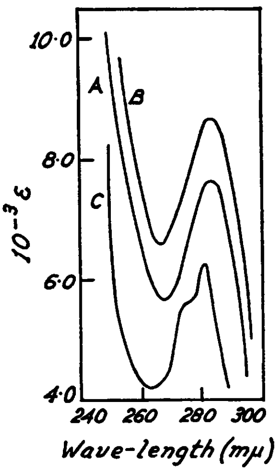
(VI) (VII) (VIII) (IX*a*) (IX*b*) (X*a*) (X*b*)

(R = *o*-OMe·C_6H_4)

Lithium aluminium hydride reduced the *cyclo*hexenone (VI) at 28° (reaction was incomplete at 0°) to a mixture containing small amounts of diaryl*cyclo*hexenol and the diaryl*cyclo*hexene (IV). The former product was a mixture, perhaps of structural isomers (IX*a* and *b*) as well as of stereoisomers, and no homogeneous individual was isolated.

Reduction by aluminium *iso*propoxide in *iso*propyl alcohol gave a much better yield (58%) of a similar inseparable mixture of diaryl*cyclo*hexenols; prolonged heating of the reaction mixture did not cause double-bond migration leading to a single product (cf. Heilbron, Kennedy, Spring, and Swain, *J.*, 1938, 869).

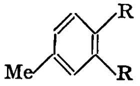
When the mixture of *cyclo*hexenols was dehydrated by potassium hydrogen sulphate in boiling *p*-xylene and the crude product dehydrogenated with palladised charcoal in the same solvent, there were obtained, after chromatography and crystallisation, only the same terphenyl as previously and a small amount of the *cyclo*hexadiene (X*a* or *b*). When the temperature of dehydrogenation was reduced, by use of benzene instead of xylene, approximately equal quantities of the same two substances were isolated. The diene was converted into the same terphenyl by further dehydrogenation: the relatively small tendency to aromatisation is probably due to the lack of coplanarity, and so of resonance, of the benzene rings of the terphenyl.

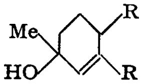


A, 2 : 2''-*Dimethoxy*-o-*terphenyl. B*, 2 : 2''-*Dimethoxy-4'-methyl*-o-*terphenyl. C*, 1 : 2-*Di*-o-*methoxyphenyl*cyclo*hexadiene.*

The postulated isomerism might be shown, not merely by the terphenyl (VIII), but also by the phenol (VII) and by the methyl derivative (XI). The phenol (VII), derived from the *cyclo*hexenone (VI) by dehydrogenation (see above), was obtained in only one form. Attempts were therefore made to secure the postulated isomer by varying the conditions of the aromatisation of (VI), the phenyl homologue (VI, R = Ph) being also prepared (Dodds *et al.*, *loc. cit.*) for use as a model. However, bromination of these *cyclo*hexenones with bromine in acetic acid or with *N*-bromosuccinimide, followed by dehydrobromination with pyridine, led to intractable oils.

In the synthesis of the methyl derivative (XI), the *cyclo*hexenone (VI) reacted stereospecifically with methylmagnesium iodide to give only one form of the alcohol (XII) which was readily dehydrated but could be obtained pure by using a slight excess of magnesium and excluding acidic or other dehydrating agents during its isolation. Conversion of this alcohol into the terphenyl (XI) by dehydration and dehydrogenation was effected in one operation, by heating it with palladised charcoal at 275°, in boiling *p*-xylene, or in boiling *p*-cymene. Again only one form of the terphenyl was obtained.

(XI)




(XII)

(R = o-OMe·C_6H_4)

Very similar absorption spectra were observed for 2 : 2''-dimethoxy-*o*-terphenyl (VIII) ($\lambda_{max.}$ 283 mμ; ε 7680) and 2 : 2''-dimethoxy-4'-methyl-*o*-terphenyl (XI) ($\lambda_{max.}$ 283; ε 8700), but that of 1 : 2-di-*o*-methoxyphenyl*cyclo*hexadiene (X*a* or *b*) ($\lambda_{max.}$ 281; ε 6240) was different in type (see Figure).

EXPERIMENTAL

Some of the analyses are by Dr. W. Zimmermann, University of Melbourne.

1 : 2-*Di*-o-*methoxyphenyl*cyclo*hexene.*—2-Chloro*cyclo*hexanone (21 g.) in ether (50 c.c.) was added during 20 min. to a stirred solution of *o*-methoxyphenylmagnesium bromide, prepared from *o*-bromoanisole (34 g.) and magnesium (4·4 g.) in ether (100 c.c.). Heat was evolved causing gentle reflux during the addition. Xylene (100 c.c.) was then introduced, the ether removed, and the resulting mixture heated under reflux and with stirring for 20 hr. It was then poured into a saturated solution of ammonium chloride and the organic matter isolated by extraction with ether, washed with ammonium chloride solution and water, dried, and concentrated. Fractionation of the product gave the diaryl*cyclo*hexene (probably a mixture of isomers) as a pale yellow viscous oil, b. p. 168—180°/1 mm. (6 g.), n_D^{29} 1·5801 [Found: C, 81·5; H, 7·4; *M* (cryoscopic), 261. Calc. for $C_{20}H_{22}O_2$: C, 81·6; H, 7·5; *M*, 294], soluble in light petroleum and ethanol.

Attempted dehydrogenation. The above *cyclo*hexene (1·3 g.; freshly redistilled) and 5% palladised charcoal (0·4 g.) were heated in nitrogen to 280° for 40 min. and finally to 300° for 20 min. The product was adsorbed on a column of alumina and eluted with light petroleum–benzene and finally with benzene, giving twenty fractions, none of them crystalline. Dehydrogenation with sulphur at 230° for 30 min. was also unsuccessful.

Dehydrogenation of 1 : 2-*Di*-o-*methoxyphenyl*cyclo*hexanol.*—The *cyclo*hexanol (0·3 g.) (Huang, *loc. cit.*) was heated with palladised charcoal at 300—320° for 30 min. in carbon dioxide. The product gave a yellow oil, b. p. 145° (bath)/0·2 mm. (Found: C, 80·9; H, 7·4%), which was apparently a mixture of the *cyclo*hexenes.

2 : 2′-*Dimethoxydeoxybenzoin.*—2 : 2′-Dimethoxybenzoin was reduced with a tin–copper couple (Allen and Buck, *J. Amer. Chem. Soc.*, 1930, **52**, 312). The product was best isolated by extraction with benzene, and crystallised from light petroleum (b. p. 60—80°) (yield, 50%).

3 : 4-*Di*-o-*methoxyphenyl*cyclo*hex*-2-*en*-1-*one.*—2 : 2′-Dimethoxydeoxybenzoin (36 g.), dissolved in a mixture of dry benzene (125 c.c.) and absolute ethanol (25 c.c.), was added to the methiodide prepared from methyl iodide (21 g.) and 4-diethylaminobutan-2-one (21 g.) (Wilds and Shunk, *ibid.*, 1943, **65**, 469) cooled in ice and under an atmosphere of nitrogen. A solution from sodium (6·8 g.) in ethanol (150 c.c.) was added during 1 hr. with ice-cooling, the mixture being then kept at *ca.* 10° for one more hour during which the methiodide gradually disappeared. The mixture was then warmed to the b. p. (*ca.* ½ hr.) and allowed to boil gently for 15 min., after which it was poured on cracked ice containing a slight excess of sulphuric acid. The organic matter was taken up in ether, washed with water, dried, and concentrated. The product passed in benzene through alumina, giving the required cyclo*hexenone* as pale yellow prisms, m. p. 111—115° (24 g.) raised to 115—117° by recrystallisation from benzene–*cyclo*hexane (Found: C, 78·1; H, 6·7. $C_{20}H_{20}O_3$ requires C, 77·9; H, 6·5%). It was very soluble in benzene and ethanol, but only slightly so in *cyclo*hexane. The 2 : 4-*dinitrophenylhydrazone*, formed readily with Brady's reagent, crystallised from glacial acetic acid in deep red leaflets, m. p. 211—213° (Found: C, 63·7; H, 4·75. $C_{26}H_{24}O_6N_4$ requires C, 63·9; H, 4·95%).

Dehydrogenation experiments. The above *cyclo*hexenone was treated with Raney nickel in boiling ethanol before the following dehydrogenation experiments.

(i) Refluxing with 5% palladised charcoal in ethylbenzene for 36 hr. or with Adams catalyst in *p*-xylene for 72 hr. gave no phenol. Refluxing with palladised charcoal in cumene for 60 hr. gave a small quantity of phenol. In each case most of the starting material was recovered.

(ii) The *cyclo*hexenone was heated with palladised charcoal under carbon dioxide at (*a*) 210—240°, (*b*) 270—280°, and (*c*) 290—300° for 1—1½ hr. For (*b*), a typical experiment, the *cyclo*hexenone (1·0 g.) gave a solid, m. p. *ca.* 138—142° (0·78 g.), which did not react with 2 : 4-dinitrophenylhydrazine and yielded after repeated crystallisations from benzene 2 : 2″-*dimethoxy*-4′-*hydroxy*-o-*terphenyl* as prisms, m. p. 169—170° (*ca.* 0·3 g.) (Found: C, 78·6; H, 6·15. $C_{20}H_{18}O_3$ requires C, 78·4; H, 5·9%). This was very soluble in ethanol, but much less so in benzene or *cyclo*hexane, and did not dissolve in aqueous potassium hydroxide even on heating. Crops obtained from the mother-liquors were repeatedly crystallised from ethanol, giving 2 : 2″-*dimethoxy*-o-*terphenyl* in rhombic plates, m. p. 109—110·5° (*ca.* 80 mg.) (Found: C, 82·3; H, 6·4. $C_{20}H_{18}O_2$ requires C, 82·7; H, 6·3%), very soluble in benzene, but much less so in ethanol and decolorising bromine readily in chloroform.

Reduction with Lithium Aluminium Hydride.—(*a*) Reduction at 0° for 0·5 hr. leaves most of the preceding *cyclo*hexenone unchanged (2 : 4-dinitrophenylhydrazone). (*b*) Lithium aluminium hydride (2 g.) was added to the *cyclo*hexenone (5·0 g.) in ether (150 c.c.) at 15°, and the mixture stirred for 2 hr. at room temperature (28°). Moist ether was then added, followed by water and dilute sulphuric acid. The product was taken up in ether, washed with water, and dried, and the ether removed, giving an oil which was very soluble in benzene and ethanol but sparingly so in *cyclo*hexane and petroleum; on slow fractional crystallisation from benzene–*cyclo*hexane this yielded 3 : 4-di-*o*-methoxyphenyl*cyclo*hex-2-en-l-ol (probably with other isomers), m. p. 87—89°, with preliminary softening. Repeated crystallisations from the same solvents gave solids of varying m. p.s (87—92°) which depended on the rate of heating (Found: C, 76·9; H, 6·9. Calc. for $C_{20}H_{22}O_3$: C, 77·4; H, 7·1%). The mother-liquors deposited another solid, probably 1 : 2-*di*-o-*methoxyphenyl*cyclo*hexene*, m. p. 173—177° (0·3 g.) raised to 184—185° after further recrystallisation from benzene–ethanol from which it separated in prisms (Found: C, 81·9; H, 7·4. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5%).

Meerwein–Pondorff Reduction.—The *cyclo*hexenone (3·8 g.) was heated with aluminium *iso*propoxide (12 g.) and dry *iso*propyl alcohol (60 c.c.) for 24 hr. under a fractionating column at such a rate that the acetone produced was slowly removed. The mixture was poured into ice and dilute hydrochloric acid, and the organic material extracted into benzene, washed with dilute hydrochloric acid, water, and aqueous sodium carbonate, and dried. Evaporation of most of the benzene gave an oil which did not react with 2 : 4-dinitrophenylhydrazine and, on addition of *cyclo*hexane, gradually deposited the *cyclo*hexenol as a colourless solid, m. p. 85—88° (2·2 g.). A recrystallised sample (m. p. 87—89°) did not depress the m. p. of the product from the previous reduction (Found : C, 77·6; H, 7·2%).

Dehydration of the Isomeric cyclo*Hexenols.*—(*a*) On addition of phosphoric anhydride (3 g.) to a solution of the *cyclo*hexenols (1·4 g.) in hot benzene (25 c.c.) a green colour developed which soon darkened. The solution was heated under reflux for 6 hr. Chromatography (twelve fractions) gave small quantities of yellow amorphous substances of indefinite m. p.s.

(*b*) The mixture of *cyclo*hexenols (1·5 g.) was heated under reflux with freshly fused potassium hydrogen sulphate (1·5 g.) in benzene (10 c.c.) for 24 hr., more sulphate (1 g.) being added after the first 10 hr. Water was then introduced and the benzene layer separated. The aqueous layer was extracted with fresh benzene, and the combined organic fractions were washed with a solution of sodium hydrogen carbonate and with water, dried, and concentrated to about 15 c.c. After addition of 5%-palladised charcoal (*ca.* 0·5 g.) the mixture was refluxed for another 24 hr. during which time a second lot of the catalyst (*ca.* 0·5 g.) was added. The product was adsorbed on alumina, and eluted with light petroleum (b. p. 60—80°)–benzene (1 : 1). Fractions 1—4 (15 c.c. each) on evaporation yielded crystalline solids which were separately recrystallised from ethanol, giving two substances A and B. Very small quantities of amorphous substances of indefinite m. p. were found in some of the later fractions (4—15), which were not investigated.

Substance A (0·38 g.) was the less soluble in ethanol and was found to be identical with the 2 : 2''-dimethoxy-*o*-terphenyl obtained previously (m. p. and mixed m. p. 109—110°) (Found : C, 83·0; H, 6·3%). It was unaffected by irradiation with ultra-violet light in benzene solution for 7 hr. Demethylation by refluxing hydriodic acid (*d* 1·7)–acetic acid (1 : 2) for 4 hr. gave 2 : 2''-*dihydroxy*-o-*terphenyl*, soluble in cold aqueous potassium hydroxide and crystallising from benzene in needles, m. p. 148—150° (Found : C, 82·6; H, 5·3. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·4%).

Substance B which was present in comparatively larger quantities in the first two fractions, was obtained from the mother-liquors of the ethanol recrystallisations. It had m. p. 84—87° (0·34 g.), raised to 85·5—87° after four recrystallisations from ethanol, and was found to be 1 : 2-*di*-o-*methoxyphenyl*cyclo*hexa*-1 : 3-*diene*, or an isomer thereof (Found : C, 82·3, 81·8; H, 6·9, 7·1; O, 10·4. $C_{20}H_{20}O_2$ requires C, 82·15; H, 6·9; O, 10·95%). It was very soluble in benzene and *cyclo*hexane, and decolorised bromine instantaneously. With palladised charcoal in boiling *p*-xylene (bath 160°) (14 hr.) it was converted quantitatively into substance A (m. p. and mixed m. p.).

3 : 4-*Di*-o-*methoxyphenyl*-1-*methyl*cyclo*hex*-2-*en*-1-*ol.*—3 : 4-Di-*o*-methoxyphenyl*cyclo*hex-2-en-l-one (3·0 g.) in ether (120 c.c.) was added to the Grignard reagent prepared from methyl iodide (14 g.) and magnesium (2·7 g.) in ether (75 c.c.) during ½ hr., and the mixture was stirred under gentle reflux for a further 2 hr. Next day it was poured into ice and water containing a trace of sodium hydrogen sulphite, and further treated with a saturated solution of ammonium chloride. The organic matter was extracted in ether in the usual manner, giving an oil which in contact with light petroleum deposited the cyclo*hexenol*, m. p. *ca.* 110—112° (1·9 g.), raised to 122—124° after four recrystallisations (leaflets) from *cyclo*hexane (Found : C, 77·5; H, 7·5. $C_{21}H_{24}O_3$ requires C, 77·75; H, 7·5%).

Dehydration and dehydrogenation. The *cyclo*hexenol was heated with 5% palladised charcoal (*a*) at 275° for 45 min., without a solvent, (*b*) in refluxing *p*-cymene for 7 hr., under nitrogen, and (*c*) in *p*-xylene for 44 hr. In each case *ca.* 60% of 2 : 2''-*dimethoxy*-4'-*methyl*-o-*terphenyl* was obtained, which crystallised from ethanol in prisms, m. p. 85—86°, and reacted with bromine rapidly (Found : C, 82·85, 82·7; H, 6·6, 6·7. $C_{21}H_{20}O_2$ requires C, 82·9; H, 6·6%). In (*a*) it was necessary to chromatograph the product before the pure hydrocarbon could be obtained. When heated in benzene with anhydrous copper sulphate for 7 hr. and then with palladised charcoal for 24 hr., or with potassium hydrogen sulphate in *p*-xylene for 12 hr. and then with palladised charcoal for 12 hr., the *cyclo*hexenol gave no crystalline product.

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