

825. Structure and Configuration of the Two Solid Dimerides of *isoSafrole*.

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The dimerides of *isosafole*, m. p. 92° and 144°, have been converted by demethylenation followed by methylation into the *trans-trans*-(α -) and the *cis-trans*-(γ -)racemate, respectively, of *diisoeugenol* dimethyl ether, thus establishing their structures and configurations.

THREE dimerides of *isosafole* (3:4-methylenedioxypropenylbenzene) are known. A solid dimeride, m. p. 145°, has been obtained from *isosafole* by treatment with ethanolic hydrogen chloride at 160° (Angeli and Mole, *Gazzetta*, 1894, **24**, 127; Mayer, *Atti R. Accad. Lincei*, 1914, **23**, 358—in our hands this method gave a 13% yield), by exposure to light for a year in presence of iodine (8% yield; Ciamician and Silber, *ibid.*, 1909, **18**, 216; *Ber.*, 1909, **42**, 1389), and by the action of sulphuric acid in acetic acid (yield unstated; G. M. Robinson, *J.*, 1915, 275).^{*} A second solid, m. p. 92°, has also been obtained by the last method (Schimmel, *Chem. Zentr.*, 1905, I, 1569), and by the action of boiling ethanolic hydrogen chloride (Mayer, *loc. cit.*; Puxeddu, *Gazzetta*, 1913, **43**, 128). When *isosafole* was heated with 90% formic acid, the higher-melting *diisosafole* was said to be formed (Glichitch, *Bull. Soc. chim.*, 1924, **35**, 1163), but we have only obtained the lower-melting form under these conditions (see Experimental). A liquid and a solid dimeride were obtained by the action of silicon tetrachloride on *isosafole* (Imoto, *J. Chem. Soc. Japan*, 1937, **58**, 1329, 1386). Takebayashi (*ibid.*, 1943, **64**, 1363; 1944, **65**, 582; *Chem. Abs.*, 1947, **41**, 3774) has obtained both solid dimerides by treating *isosafole* with hydrogen bromide, hydrogen chloride, and with the chlorides of aluminium, chromium, iron, and zinc.

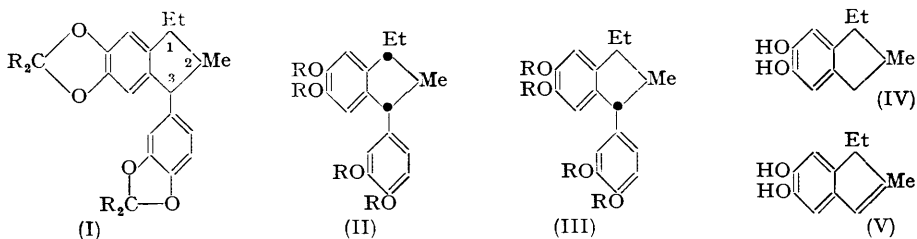
A liquid dimeride of *isosafole* was obtained as one product of the action of ethanolic hydrogen chloride. Its structure was shown to be 1:3-bis-(3:4-methylenedioxyphenyl)-2-methylpent-1-ene (Imoto, *loc. cit.*; Pailer, *Monatsh.*, 1947, **77**, 45) corresponding to that of *isoanethole*. Degradative studies on the solid dimerides have indicated that they are almost certainly dimorphic or stereoisomeric forms of 1-ethyl-2-methyl-5:6-methylenedioxy-3-(3:4-methylenedioxyphenyl)indane (I; R = H) (Pailer, *loc. cit.*; Pailer, U. Müller, and Porschinski, *Monatsh.*, 1948, **79**, 620; Baker, Haksar, McOmie, and Ulbricht, *J.*, 1952, 4310). Recently the structure and configuration of the solid dimerides of anethole and of 3:4-dibenzoyloxypropenylbenzene were established by converting them into *diisoeugenol* dimethyl ether (II; R = Me) whose structure and stereochemistry were already known (Baker *et al.*, *loc. cit.*). We have now been able to extend this correlation by converting the two solid dimerides of *isosafole* into the stereoisomeric *diisoeugenol* dimethyl ethers (cf. Baker *et al.*, *loc. cit.*, p. 4312).

The preparation of the higher-melting dimeride has been studied with the object of avoiding the use of sealed tubes. When *isosafole* was heated with hydrogen chloride in cyclohexanol or *n*-butanol, the dimeride of m. p. 144° was obtained in 1—2.5% yield; with toluene-*p*-sulphonic acid in *n*-butanol at 150° the yield was 1%; with orthophosphoric acid at 180° an even lower yield of the two solid dimerides was obtained. Winter (Thesis, Bristol, 1950) showed that *isosafole* with zinc chloride at 120° gave a 1.5% yield of the dimeride, m. p. 144°, and by altering the conditions of this reaction the yield has now been raised to 8%.

The conversion of the solid *diisosafoles* into the corresponding *diisoeugenol* dimethyl ethers was achieved by using a modification of Barger's method of demethylenation (*J.*,

^{*} Hoering and Baum (*Ber.*, 1908, **41**, 1914) heated *isosafole* with phosphorus trichloride and pentachloride, and, after adding water, isolated a crystalline product, m. p. 140—141°, which they regarded as *diisosafole*, in spite of the facts that it contained phosphorus and gave analytical figures some 25% low in carbon and 2% low in hydrogen. Phosphorus pentachloride is known to react readily with methylenedioxybenzenes (Barger's method of demethylenation used in the present work) and it is most unlikely, therefore, that Hoering and Baum obtained *diisosafole*; we have been unable to obtain any *diisosafole* by this method.

1908, 93, 563). The diisosafroles (I; R = H) were heated with phosphorus pentachloride in dry benzene and the resulting bisdichloromethylenedioxy-compounds (I; R = Cl) were hydrolysed to the cyclic carbonates (I; R₂ = O) by cold water. The carbonates were then hydrolysed and methylated simultaneously in nitrogen, thus avoiding the isolation of the unstable tetrahydroxy-compounds (II and III; R = H). In this way the *iso*safrole dimeride of m. p. 92° yielded the α -racemate of diisoeugenol dimethyl ether (II; R = Me) which is known to have the *trans-trans*-configuration (A. Müller, Mészáros, Körmeny, and Kucsman, *J. Org. Chem.*, 1952, 17, 787). Similarly the dimeride of m. p. 144° yielded the γ -racemate (III; R = Me) which has the *cis-trans*-configuration. Thus the solid dimerides of *iso*safrole are stereoisomers of structure (I; R = H) and they differ only in the configuration at position 1. This possibly explains why we have not been able to convert the lower- into the higher-melting form of diisosafrole by distillation at 150° (Baker *et al.*, *loc. cit.*, p. 4311), contrary to the claim by Mayer (*loc. cit.*).



The present result also appears to contradict the work of Pailer, U. Müller, and Porschinski (*loc. cit.*) who degraded the diisosafrole, m. p. 146°, by ethylmagnesium iodide followed by hydriodic acid to 1-ethyl-5 : 6-dihydroxy-2-methylindane (IV) and catechol; similarly diisoeugenol dimethyl ether (α -racemate) with hydriodic acid gave the same indane (IV). It is possible that the degradations proceed *via* 1-ethyl-5 : 6-dihydroxy-2-methylindene (V) with subsequent reduction of the double bond. In this way original differences in configuration at positions 2 and 3 would disappear. Our attempts to realise this degradation of diisoeugenol dimethyl ether to the dihydroxyindane (IV) have not been successful, although catechol was isolated.

EXPERIMENTAL

Diisosafrole, m. p. 92°.—This was prepared in 69% yield by heating *iso*safrole with formic acid according to Glichitch (*loc. cit.*) who, however, stated that the method gave the higher-melting isomeride.

Diisosafrole, m. p. 142°.—*iso*Safrole (50 g.) was heated with powdered anhydrous zinc chloride (10 g.) for 5 hr. at 140–150°. An ethereal solution of the product, after being washed with water and dried, deposited crystals. After 24 hr. two crops (total 5.2 g.), m. p. 130–140°, were obtained, which, when recrystallised from light petroleum (b. p. 80–100°), gave diisosafrole, m. p. 142° (4.03 g.). The ethereal solution also yielded the other isomeride (4.37 g.), m. p. 85–87°.

Conversion of Diisosafrole, m. p. 92°, into *Diisoeugenol Dimethyl Ether*, m. p. 105–106° (α -*Racemate*).—*Diisosafrole*, m. p. 92° (5 g.), in benzene (15 c.c.) was added to a hot solution of phosphorus pentachloride (15 g.) in dry benzene (60 c.c.). The mixture was heated on a steam-bath for 1½ hr., during which the colour changed from red to green and finally to a deep Prussian-blue. After cooling, the solution was poured into ice and water, the benzene layer (now yellow-green) washed with water and dried, and the benzene removed under reduced pressure in nitrogen; the solution again became deep blue. Methanol (30 c.c.), methyl sulphate (10 c.c.), and aqueous sodium hydroxide (20% ; 20 c.c.) were then added in turn, with mechanical stirring, in nitrogen. More methyl sulphate (10 c.c.) and sodium hydroxide solution (20 c.c.) were added, and once again after heating under reflux for ½ hr. After a further 2½ hours' heating, the methanol was removed under reduced pressure, and the solution was made alkaline and extracted with ether. The dried ethereal solution yielded a yellow oil (3.8 g.), b. p. 195–210°/0.5 mm. The oil was dissolved in the minimum quantity of ethanol and filtered through a column of alumina, which was eluted successively with light petroleum (b. p. 60—

80°) and methanol. The product slowly crystallised (one week; this is characteristic of the α -racemate), as needles, m. p. 88—90° (0.9 g.). Recrystallisation from methanol gave diisoeugenol dimethyl ether (α -racemate), m. p. alone or mixed with an authentic specimen, 105—106°.

On addition of a few drops of bromine in acetic acid to a 1% solution of the product in acetic acid no purple colour was obtained, whereas the β - and the γ -racemate give a strong and a weak purple-violet colour respectively (A. Müller *et al.*, *loc. cit.*).

Conversion of Diisosafrole, m. p. 142°, into Diisoeugenol Dimethyl Ether, m. p. 100° (γ -Racemate).—The procedure was as above, until the methylation, which was carried out in acetone (30 c.c.). Methyl sulphate (10 c.c.) and aqueous potassium hydroxide (30%; 15 c.c.) were added in turn, with mechanical stirring, in nitrogen. After addition of similar quantities of the reagents, the mixture was heated for $\frac{1}{2}$ hr., then made alkaline with potassium hydroxide solution (45 c.c.), and more methyl sulphate (10 c.c.) was added. After a further $\frac{1}{2}$ hour's heating, the solution was again made alkaline with potassium hydroxide (40 c.c.) and heated under reflux for 2 hr. After being worked up as before, a yellow oil, b. p. 200—210°/1 mm. (3.6 g.), was obtained. The oil was filtered through a column of alumina and it then crystallised from methanol as prisms, m. p. 90—96° (0.63 g.). Recrystallisation gave diisoeugenol dimethyl ether (γ -racemate), m. p. 98—100°, not depressed by admixture with an authentic sample kindly supplied by Professor A. Müller.

With both specimens, bromine in acetic acid gave a definite, but not intense, purple colour.

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