229. *Volume Effects of Alkyl Groups in Aromatic Compounds. Part I. Influence of 2 : 6-Dinitration on a Group* CR_1R_2Alk.

By R. J. W. Le Fèvre.

An inspection of scale diagrams * of compounds (I) and (II) (data from *Ann. Reports*, 1931, 402; Dadieu and Kohlrausch, *Monatsh.*, 1931, **58**, 428) shows that in (I) interference occurs

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* A scale drawing of (I) is reproduced in a preliminary note in *Nature*, 1933, **131**, 655.

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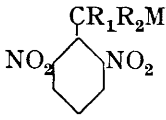
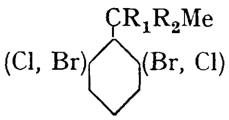
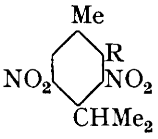
between the central carbon atom, its peripheral hydrogen atoms, and the oxygens of the nitro-groups, and in (II) between the methyl hydrogen atoms and the halogen atoms. Although no overlapping of the methyl carbon atom and the nitrogen atoms of the nitro-groups (I), or the chlorine or bromine atoms (II), is indicated, the successful resolution of 2 : 2′-difluoro-6 : 6′-diamino-3 : 5 : 3′ : 5′-tetramethyldiphenyl (*J. Amer. Chem. Soc.*, 1931, **53**, 1575), in which a similar situation exists in that the fluorine atoms do not touch the amino-nitrogen atoms (but can collide with the amino-hydrogen atoms), shows that inhibition of free rotation of $-CR_1R_2Me$ in compounds of types (I) and (II) is not impossible.



(I.)



(II.)



(III.)

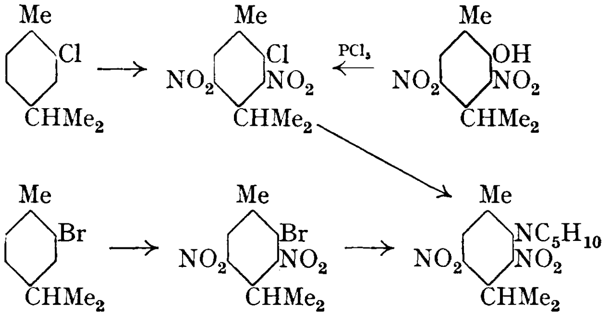
If this were to occur, then all 3 : 5-dinitro-2-substituted-*p*-cymenes (III) should each exist in three geometrically isomeric optically resolvable modifications. The racemic isomerides, having the physical differences associated with *cis-trans-amphi* triads, should be readily detectable.

However, no isomerides have been found for the cases in which R = OH, O·CO·Me, O·CO·Ph, Cl, or Br. 4 : 6-Dinitrocarvacrol (III, R = OH) was easily obtained by direct nitration; fractional crystallisation of this substance, its acetate, and benzoate (Mazzara, *Gazzetta*, 1891, **21**, 157) afforded no separation, and microscopic examination of the various crops of crystals revealed no heterogeneity.

The cases where R = Cl or Br were of particular interest since Fileti and Crosa (*Gazzetta*, 1888, **18**, 289; cf. Beilstein, " Handbuch," 4th edtn., p. 425) state that nitration of these halogeno-hydrocarbons gave two dinitro-derivatives : a solid and a liquid in each instance. Since it was possible that these isomerides were examples of the type sought in the present work, the nitrations were repeated on pure specimens specially prepared.

The halogeno-compounds both underwent nitration by fuming nitric acid to yield the solid dinitro-derivatives previously described. These contained labile halogen and gave a common *piperidinodinitrocymene* with piperidine. Further, these solids were formed in practically quantitative yields, and the small amounts of oily material obtained from the crystallisation mother-liquors had lower nitrogen contents. No formation of isomerides such as Fileti and Crosa describe has therefore been detected. Their results can be explained by contamination of their initial 2-halogenocymenes by the corresponding 3-isomerides, which can only be removed by careful fractionation. They prepared their compounds by direct halogenation of *p*-cymene and do not record any such purification.

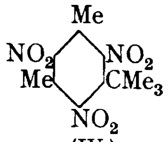
As a verification of the conclusion reached from the use of piperidine, the solid chlorodinitrocymene has been obtained from dinitrocarvacrol by the method used by Ladenburg and Engelbrecht (*Ber.*, 1877, **10**, 1220) in the analogous case of dinitrothymol:

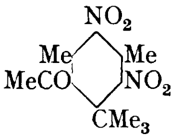


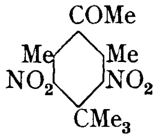
Both 3 : 5-dinitro-2-halogenocymenes behaved as uniform substances on repeated crystallisation.

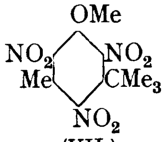
Were free rotation of CR_1R_2Alk prevented by two vicinal nitro-groups, then 2 : 4 : 6-trinitro-1 : 3 : 5-triethylbenzene should exist in several geometrically isomeric forms, but we found no evidence of heterogeneity on recrystallising our preparation of this substance (Gattermann, Fritz, and Beck, *Ber.*, 1899, **32**, 1124) from dilute alcohol.

At the outset it was hoped to investigate the commercial artificial musks for restriction of free rotation of the *tert.*-butyl group by attempting optical resolution of suitable derivatives. Neither of the nuclear methyl groups of "musk xylol" (IV), however, could be oxidised to carboxyl groups. Aromatic aldehydes (*e.g.*, benzaldehyde, salicylaldehyde, piperonal, vanillin) would not condense with (IV) (to give an oxidisable stilbene) under the conditions (8 hours' heating at 180° in presence of a trace of piperidine) which suffice to transform 2 : 4 : 6-trinitrotoluene into trinitrostilbene (Ullmann and Gschwind, *Ber.*, 1908, **41**, 2291). "Musk ketone" (V) was unaffected by boiling sodium hypochlorite solution, did not give indigotin with *o*-nitrobenzaldehyde (Le Fèvre and Pearson, *J. Soc. Chem. Ind.*, 1932, **51**, 433), and was but slightly destroyed by potassium permanganate or chromic acid in acetic acid.


(IV.)


(V.)


(VI.)


(VII.)

In view of the conclusion of Tschitschibabin (*Bull. Soc. chim.*, 1932, **51**, 1436) that this compound has the structure (VI), work on it was discontinued, since the resulting acid, even if rotation of $-CMe_3$ were restricted, would have a plane of symmetry and thus be optically inactive.

Demethylation of "musk ambrette" (VII), with a view to the synthesis of esters containing optically active acyloxy-groupings, also failed. Boiling piperidine reacted slowly to give the *piperidino*-derivative, whereas with 2 : 4 : 6-trinitroanisole its reaction is violent, indicating that (VII) is very inert.

The chemical inertness of (IV), (VI), and (VII) is surprising. In contrast, it is now shown that 2 : 4 : 6-trinitro-*m*-xylene condenses readily with benzaldehyde under the conditions used above with (IV). The reactions essayed with (IV) and (VII) depend upon the combination of the activating nitro-groups with the reagent (Kenner, J., 1914, **105**, 271; Powell and Dehn, *J. Amer. Chem. Soc.*, 1917, **37**, 1717; Marcellino, Giua, and Curti, *Gazzetta*, 1920, **50**, 50; Brewin and Turner, J., 1928 334), but when all six positions of the benzene ring are filled, this addition is hindered. The non-interaction of benzaldehyde with trinitromesitylene or 2 : 4 : 6-trinitro-1 : 3 : 5-triethylbenzene under the conditions used with (IV) is in accord with this explanation. Deactivation should be, and is, especially marked when one of the groups is exceedingly large, *e.g.*, the CMe_3 radical in the artificial musks.

EXPERIMENTAL.

Purification of Carvacrol.—All carvacrol used in these experiments was completely soluble in alkali and had been prepared from an Origanum oil imported from Asia Minor. It did not freeze at −20° and distilled over the range 230—240°. It appeared likely (Gildemeister, "The Volatile Oils," 1916) that the chief impurity was thymol (b. p. 233°). Purification was effected by repeated partial freezing (carbon dioxide and ether), draining, and melting. After four repetitions of this process, about one-fifth of the original oil remained; m. p. *ca.* −1° (Jahns, *Ber.*, 1882, **15**, 817, gives 0·5—1·0°).

Carvacryl methyl ether. The following is easier than the method of Paternò (*Gazzetta*, 1881, **5**, 20). Methyl sulphate (72 c.c.) was added, 5 c.c. at a time, to a solution of sodium hydroxide (30 g.) in water (210 c.c.) containing carvacrol (90 g.), the temperature being kept below 50°. The whole was then heated on the steam-bath for 2 hours. Dilution with water, etc., gave the methyl ether (84 g.), b. p. 215—216°/757 mm. (Paternò, 216·8°/761·3 mm., corr.).

Carvacryl p-*nitrobenzoate.* To carvacrol (15 g.) in ethyl alcohol (250 c.c.) with sodium hydroxide (8 g.), *p*-nitrobenzoyl chloride (17 g.) was added, and the mixture heated for 1 hour.

Dilution with water, extraction with light petroleum (b. p. 40—60°), etc., gave an oil which solidified after some months; it crystallised from dilute alcohol as plates, m. p. 50° (Found : N, 4·8. $C_{17}H_{17}O_4N$ requires N, 4·7%).

Carvacryl acetate. Carvacrol (71 g.) and acetyl chloride (120 c.c.) were refluxed together for ½ hr. and then distilled. On redistillation the acetate had b. p. 242°/756 mm.; yield, 65 g. (Paternò, *Ber.*, 1875, **8**, 71, gives b. p. 245·8°/758·3 mm.).

Dinitration of Carvacrol.—A solution of carvacrol (5 g.) in acetic acid (50 g.), as cold as was consistent with the solvent not freezing, was nitrated by the addition of nitric acid (*d* 1·42, 10 c.c.) in acetic acid (25 c.c.) during 1 hour. Dilution with ice–water gave a thick oil which solidified over-night, m. p. (crude) 113—116° (yield 5 g.). Repeated recrystallisation from light petroleum failed to raise the m. p. above 121—122° (Found: N, 12·0. Calc. for $C_{10}H_{12}O_5N_2$: 11·5%). The highest recorded m. p. is 117° (Mazzara, *Gazzetta*, 1890, **20**, 185).

4 : 6-Dinitrocarvacryl acetate (Mazzara and Plancher, *Gazzetta*, 1891, **21**, 157) had m. p. 74—75° after repeated recrystallisation from ligroin (lit. 72—73°) (Found: N, 10·0. Calc. for $C_{12}H_{14}O_6N_2$: N, 9·9%). Similar results were obtained with the benzoate (*idem, ibid.*), the m. p. being 100—101° instead of 98—100°.

Nitration of 2-Chloro- and 2-Bromo-cymenes.—The halogeno-compound (10 g.) was added to nitric acid (*d* 1·5, 100 g.) cooled below 0°. The mixture was at once poured on ice, and the solid separated. Yields of crude products : 10·2, 10 g.; m. p.'s 98—100°, 85—90° respectively. Recrystallisation from dilute methyl alcohol gave 8·5 g., m. p. 109—110°, and 9 g., m. p. 96—97° (Fileti and Crosa, *loc. cit.*, give m. p. 95—96° for the latter compound).

3 : 5-*Dinitro*-2-*piperidino*-p-*cymene.*—The halogeno-nitrocymenes (1 g.) were heated with piperidine (10 c.c.) for 1 hour; after being worked up as usual and crystallised from dilute alcohol, the *product* formed bright yellow needles, m. p. 123—124° (Found: N, 13·8. $C_{15}H_{21}O_4N_3$ requires N, 13·7%).

Attempted Oxidation of "Musk Xylol."—Ordinary reagents having failed, the following was tried : musk (10 g.) was added to chromic anhydride (14 g.) in sulphuric acid (80 c.c.). A gentle reaction started at 60°, but after 2 hours, dilution, etc., afforded largely unchanged material. Above 60° the reaction becomes explosive.

Condensation of Benzaldehyde and 2 : 4 : 6-*Trinitro*-m-*xylene.*—A mixture of benzaldehyde (10 c.c.) and the nitro-compound (5 g.) became warm on addition of a few drops of piperidine. After 1 hour's boiling the crude mass was extracted with alcohol. The solid residue of 2 : 4 : 6-*trinitro*-1 : 3-*distyrylbenzene*, on crystallisation from acetic acid, formed yellow needles, m. p. 145—146° (Found : N, 10·2. $C_{22}H_{15}O_6N_3$ requires N, 10·1%).

Interaction of Piperidine and "Musk Ambrette."—When the musk (2 g.) and piperidine (6 c.c.) were mixed they slowly became yellow, and reaction was completed by 1½ hours' heating on the steam-bath. After the usual treatment, the *piperidino*-derivative formed daffodil-yellow needles, m. p. 184° (Found : N, 14·7. $C_{16}H_{22}O_6N_4$ requires N, 15·3%), from alcohol.

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