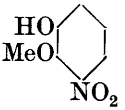
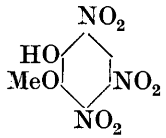
CCLXVIII.—*New Derivatives of Guaiacol and Veratrole substituted in the 3- and 6-Positions.*

By ALBERT EDWARD OXFORD.

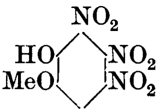
3-NITROGUAIACOL (I), hitherto the only unknown mononitro-derivative of guaiacol, has now been prepared. Benzoyl nitrate at −15° is an excellent agent for nitrating phenols and their ethers * in the ortho-position (Francis, J., 1906, **89**, 1; *Ber.*, 1906, **39**, 3798), and by means of it 3-nitro-2-methoxyphenyl acetate was obtained in minute yield from *o*-methoxyphenyl acetate, 5-nitro-2-methoxyphenyl acetate being the main product. At −40°, two-thirds of the original acetate were recovered, but the remaining third had been nitrated chiefly in the 3-position. Acetyl nitrate at −15° proved a much more satisfactory reagent, 3- and 5-nitro-2-methoxyphenyl acetates being formed in almost equal proportions, but the difficulty of effecting a complete separation of 3- from 5-nitroguaiacol somewhat diminished the final yield of the 3-isomeride. The constitution of the new nitroguaiacol follows from the fact that it yields 3-nitroveratrole on methylation and that it is not identical with 6-nitroguaiacol (Klemenc, *Monatsh.*, 1912, **33**, 701).



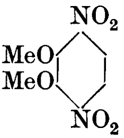
(I.)



(II.)



(III.)



(IV.)

3-Nitroguaiacol, on further nitration in acetic acid solution, gave 3 : 4- and 3 : 6-*dinitroguaiacols* in about equal proportions, together with a small amount of 3 : 4 : 6-trinitroguaiacol (II), which can be obtained in excellent yield by the direct nitration of 3-nitroguaiacol by concentrated nitric acid, and also by the further nitration of 3 : 6-dinitroguaiacol. In the same way, 4 : 5 : 6-trinitroguaiacol (III), recently prepared (Kohn and Löff, *Monatsh.*, 1925, **45**, 605) by the partial hydrolysis of 3 : 4 : 5-trinitroveratrole, can readily be obtained by the direct nitration of 5-nitroguaiacol.

The necessary proofs of the constitution of the two new dinitroguaiacols are obtained from the observations that the one yields

---

* Francis's statement that veratrole is converted quantitatively into 3-nitroveratrole by this method of nitration obviously contains a clerical error, since the melting point quoted is that of 4-nitroveratrole. The present author, repeating the experiment, obtained an almost quantitative yield of 4-nitroveratrole identical in every respect with a specimen prepared from veratrole by the action of aqueous nitric acid.

3 : 4-dinitroveratrole on methylation, whilst the other yields 3 : 6-*dinitroveratrole* (IV), the diamine from which will not condense with phenanthraquinone to a derivative of phenazine. All the mono-, di,- and tri-nitro-derivatives of guaiacol and veratrole are therefore now known, with the single exception of 3 : 4 : 5-trinitroguaiacol (compare Pollecoff and Robinson, J., 1918, **113**, 647).

EXPERIMENTAL.

3-*Nitroguaiacol* (I).—Since the use of pure benzoyl nitrate, as recommended by Francis (*loc. cit.*), involves a troublesome preparation, it is much more convenient to produce the acyl nitrate *in situ*.

A mechanically stirred solution of *o*-methoxyphenyl acetate (30 g.) and redistilled acetyl chloride (25 c.c.) in pure dry carbon tetrachloride (60 c.c.), cooled in a freezing mixture and protected from moisture, is treated during 2 hours with 31 g. (a slight excess) of dry, very finely-powdered silver nitrate,* and stirring is continued one hour longer. The red liquid is then filtered from silver chloride, shaken twice with water, dried over anhydrous sodium sulphate, and, after evaporation of the solvent, distilled in a vacuum, three fractions being collected: (i) (140—170°/20 mm.), 6 g. of a yellow liquid; (ii) (170—190°/20 mm.), 18 g. of an orange liquid; (iii) (190—200°/20 mm.), 8 g. of an orange liquid.

(i) contains all the unchanged *o*-methoxyphenyl acetate, mixed with a considerable amount of 3-nitro-2-methoxyphenyl acetate; (ii) is chiefly this acetate, whilst (iii), being almost pure 5-nitro-2-methoxyphenyl acetate, solidifies on standing, and crystallises from alcohol in long, lustrous, colourless needles, melting at 101—102°, either alone or mixed with a genuine specimen prepared from *o*-methoxyphenyl acetate by Paul's method of nitration (*Ber.*, 1906, **39**, 2779).

The first two fractions are warmed on the steam-bath with 2*N*-sodium hydroxide (10 vols.), and since the success of the preparation depends upon the rapidity with which hydrolysis is carried out, the flask is corked and shaken vigorously until all the oil has dissolved (10—15 minutes). After acidification, extraction with ether and evaporation of the solvent, the crude 3-*nitroguaiacol* † is crystallised

---

* It is essential that the silver nitrate should be in the finest possible state of division, and this is most satisfactorily ensured by heating the finely powdered salt at 100° for several hours and repulverising immediately before use.

† Experiments with metallic nitrates other than silver nitrate gave the following results: lead and potassium nitrates were entirely inert; mercurous nitrate ($HgNO_3,2H_2O$) nitrated about 25% of the *o*-methoxyphenyl acetate, chiefly in the 3-position; cupric nitrate [$Cu(NO_3)_2,2H_2O$] gave rise to an oil, b. p. 140—150°/14 mm., which, when hydrolysed by sodium hydroxide solution free from chloride, yielded a deep red solution containing much sodium

first from light petroleum, and then thrice from carbon disulphide; it forms long, slender, very pale yellow, lustrous needles, m. p. 68·5—69·5°. The author is indebted to Mr. H. E. Buckley of the Crystallography Department of this University for the following description of these crystals (Fig. 1).

FIG. 1.

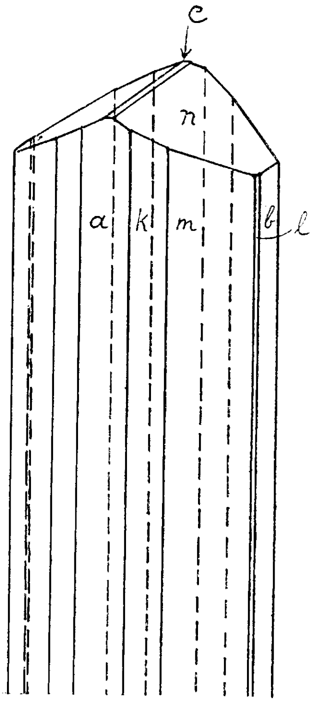
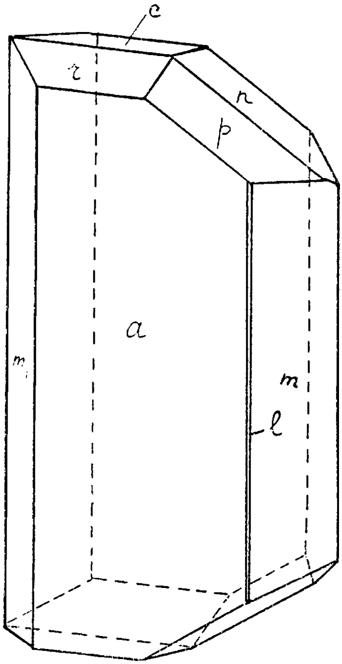


FIG. 2.



Symmetry : Rhombic, prismatic.

Axial ratios : $a : b : c = 0{\cdot}934 : 1 : 0{\cdot}584$.

Forms developed : $a = 100$, $k = 210$, $m = 110$, $l = 120$, $b = 010$, $c = 001$, $n = 011$.

Habit : Acicular, parallel to zone axis (001).

Mean angular values : *am* 43°2′, *ak* 25°7′(25°6′), *ml* 18°59′(18°47′), *bn* 59°43′, *mn* 69°25′(69°52′), *kn* 77°35½′(77°39′) (calculated values in brackets).

Cleavage : 010 perfect, 001 rare.

The crystals deposited from light petroleum (above) and from

---

chloride. Menke (*Rec. trav. chim.*, 1925, **44**, 146) has succeeded in simultaneously nitrating and chlorinating phenol to 4 : 6-dichloro-2-nitrophenol by the action of acetyl chloride and cupric nitrate at −14°.

carbon disulphide are identical in habit. They are readily soluble in the cold in all the usual solvents with the exception of water, carbon tetrachloride, and the two named above (Found : C, 49·6; H, 4·1; N, 8·7. $C_7H_7O_4N$ requires C, 49·7; H, 4·1; N, 8·3%).

3-Nitroguaiacol is perceptibly volatile in steam and gives a violet coloration with ferric chloride. The very soluble *sodium* salt separates as a jelly of dull red, microscopic threads when concentrated sodium hydroxide is added to a solution of the nitrophenol in saturated aqueous sodium carbonate. The *acetyl* derivative, obtained by heating the nitrophenol with acetic anhydride, is a pale yellow, uncrystallisable oil, b. p. 168—169°/12—13 mm. The *benzoyl* derivative * crystallises from alcohol in colourless, glistening plates, m. p. 88—89°. It is sparingly soluble in cold methyl alcohol. The methyl ether is identical with 3-nitroveratrole and was obtained in 96% yield from the sodium nitrophenoxide and an excess of methyl iodide in boiling methyl alcohol; after crystallisation from aqueous methyl alcohol, it had m. p. 64—65°.

3-Aminoguaiacol, obtained in small yield when 3-nitroguaiacol is reduced by hot aqueous sodium hyposulphite or by zinc and aqueous-alcoholic hydrochloric acid, crystallises from light petroleum in colourless needles, m. p. 95—96°, which rapidly become straw-brown on exposure to the air. Jona (*Centr.*, 1912, II, 1113) describes it as forming straw-coloured needles, m. p. 97—100°. It gives a brown coloration with ferric chloride.

6-*Aminoguaiacol*, obtained in excellent yield by reducing 6-nitroguaiacol † (Klemenc, *loc. cit.*) with boiling aqueous sodium hyposulphite, crystallises from light petroleum in colourless, rectangular leaflets with a silvery lustre, melting at 83·5°, and not appreciably darkening on exposure to the air (Found : C, 60·5; H, 6·9. $C_7H_9O_2N$ requires C, 60·4; H, 6·5%). It gives a port-wine colour with ferric chloride, and when boiled with excess of acetic anhydride for 4 hours appears to yield a *triacetyl* derivative, which crystallises from light petroleum in colourless, pointed needles, m. p. 122—124°

---

* There can be little doubt that Meldola's benzoyl-*o*-nitroguaiacol, m. p. 88—89° (P., 1896, **11**, 127; 5-nitro-2-methoxyphenyl benzoate has m. p. 102—103°), obtained in very small yield by the action of fuming nitric acid on a solution of *o*-methoxyphenyl benzoate in acetic acid, is the 3-nitro-isomeride. There is, however, no record of any subsequent investigation of this product, apart from a brief note on its reduction (J., 1898, **73**, 690). The present author found that *o*-methoxyphenyl benzoate yields a considerable proportion, but the corresponding carbonate very little, of the 3-nitro-isomeride when nitrated by acetyl chloride and silver nitrate.

† No trace of 6-nitroguaiacol could be isolated from the product from the nitration of guaiacol by acetyl chloride and silver nitrate, most of the guaiacol entirely escaping nitration at −15°. Acetyl nitrate is also without action on 6-nitro-2-methoxyphenyl acetate.

(Found : N, by micro-Dumas method, 5·5. $C_{13}H_{15}O_5N$ requires N, 5·3%).

3 : 6-*Dinitroguaiacol.*—A stirred solution of 3-nitroguaiacol (20 g.) in acetic acid (66 c.c.), cooled in ice-water, was treated with nitric acid (27 c.c.; *d* 1·42) dissolved in acetic acid (13 c.c.), the first half being added during 10 minutes and the second portion during 2 minutes. Water was added immediately, and the oil thrown down solidified on partial neutralisation of the liquid. The dry solid (7 g.) was crystallised from carbon disulphide, several times from water, and finally from light petroleum, from which it separated in yellow prisms, m. p. 69—70° (Found : C, 39·0; H, 3·1. $C_7H_6O_6N_2$ requires C, 39·2; H, 2·8%). It crystallises from water in small, thick rods, and is readily soluble in the cold in all the usual organic solvents except carbon disulphide and light petroleum. Its solution in aqueous sodium carbonate is orange-red, changing to yellow on acidification. Addition of concentrated sodium hydroxide precipitates orange-red rods of the *sodium* salt. When reduced by zinc and aqueous-alcoholic hydrochloric acid, it yields a solution of the hydrochloride of the corresponding diamine, which gives an intense permanganate colour with ferric chloride.

The *acetyl* derivative crystallises from ethyl alcohol, in which it is sparingly soluble in the cold, in very pale yellow needles, m. p. 56°. It is moderately easily soluble in cold methyl alcohol. Like 6-nitroguaiacol, 3 : 6-dinitroguaiacol could not be made to yield a benzoyl derivative by the ordinary Schotten-Baumann method and gave no coloration with ferric chloride.

3 : 6-*Dinitroveratrole* (IV), obtained in moderate yield from the above nitrophenol by the xylene–methyl sulphate–potassium carbonate method, about 30% of the nitrophenol being recovered after 3 hours' boiling, crystallises from alcohol in pale yellow, slender, flat needles, m. p. 56°, which are moderately easily soluble in cold methyl alcohol but very sparingly soluble in light petroleum (Found : C, 42·3; H, 4·0. $C_8H_8O_6N_2$ requires C, 42·1; H, 3·6%).

3 : 6-*Diaminoveratrole*, obtained by reducing the above dinitroveratrole by zinc and aqueous-alcoholic hydrochloric acid, crystallises from light petroleum in colourless needles, m. p. 82°, which turn grey almost immediately on exposure to the air (Found : C, 57·4; H, 7·3. $C_8H_{12}O_2N_2$ requires C, 57·1; H, 7·2%). It is very soluble in water, and gives an intense permanganate colour with ferric chloride. When boiled with acetic anhydride (10 parts) for 4 hours, it appears to yield a *triacetyl* derivative, which crystallises from light petroleum in clusters of colourless prisms, m. p. 96—97° (Found : N, by the micro-Dumas method, 9·5; *M*, in camphor, 308. $C_{14}H_8O_5N_2$ requires N, 9·5%; *M*, 294).

3 : 4-*Dinitroguaiacol*.—The aqueous mother-liquor from the filtration of crude 3 : 6-dinitroguaiacol was extracted with ether, yielding 9·5 g. of impure 3 : 4-isomeride. This was boiled with 120 c.c. of carbon disulphide to dissolve any 3 : 6-isomeride and then recrystallised from carbon tetrachloride several times, finally separating in colourless, microscopic plates, m. p. 109·5—110° (Found : C, 39·3 ; H, 2·8. $C_7H_6O_6N_2$ requires C, 39·2 ; H, 2·8%). It is sparingly soluble in the cold in water, carbon disulphide, carbon tetrachloride, or light petroleum, and definitely less soluble in other organic solvents than the 3 : 6-isomeride. It gives a reddish-brown colour with ferric chloride, and its *sodium* salt is precipitated in yellow, hair-like needles when sodium hydroxide is added to its solution in aqueous sodium carbonate.

The *acetyl* derivative, colourless leaflets from alcohol, melts at 99—100·5°, and the *benzoyl* derivative, colourless prisms from aqueous alcohol, at 132—133°. Both are moderately easily soluble in cold methyl alcohol, while the acetate is very sparingly soluble in cold ethyl alcohol. The *methyl* ether is identical with 3 : 4-dinitroveratrole (m. p. 91° ; compare Pollecoff and Robinson, *loc. cit.*), and is readily obtained by means of the xylene–methyl sulphate–potassium carbonate method.

Both 3 : 4-dinitroguaiacol and its methyl ether, when reduced by zinc and aqueous-alcoholic hydrochloric acid, yield diamines which condense with the bisulphite compound of phenanthraquinone to give the corresponding ethers of 1 : 2-dihydroxyphenanthraphenazine; these exhibit a green fluorescence in benzene solution, and a dull magenta tint with concentrated sulphuric acid. 3 : 4-Diaminoguaiacol gives a permanganate colour with ferric chloride only slightly less intense than that given by the 3 : 6-isomeride.

3 : 4 : 6-*Trinitroguaiacol* (II).—3-Nitroguaiacol (2 g.), cooled by running water, was nitrated with 9 c.c. of nitric acid (*d* 1·42) ; the product crystallised after a few minutes and was collected after the addition of water (yield 1·5 g.).

This trinitroguaiacol was obtained in small quantity by extracting the mother-liquor of the dinitroguaiacols with ether, and also by the further nitration of 3 : 6-dinitroguaiacol : 0·1 g. of the latter dissolved in 0·5 c.c. of cold concentrated nitric acid slowly deposited crystals of the trinitroguaiacol.

3 : 4 : 6-Trinitroguaiacol is dimorphous : one modification, pale yellow leaflets, m. p. 108—109°, is obtained by crystallisation from water or by slow deposition from carbon tetrachloride solution, and the higher-melting form, very pale yellow, flat needles, m. p. 113·5°, by rapid crystallisation from a hot concentrated carbon tetrachloride solution or from benzene containing a little light

petroleum. Well-formed crystals (Fig. 2) can be obtained by very slow crystallisation from the last-named solvents, and the author is indebted to Mr. H. E. Buckley for the following description of them:

System: Monoclinic sphenoidal (digonal polar). Axial ratios: $a : b : c = 1{\cdot}429 : 1 : 0{\cdot}622$, $\beta = 97°35'$. Habit, somewhat tabular on $a(100)$. The following forms are usually present: $a = 100$, $m = 110$, $r = 101$, $c = 001$, $n = 011$, $p = 111$ and less frequently $l = 210$. Mean angular values: *ar* 72°59′, *rc* 24°36′, *am* 54°47′, *ap* 75°41′(75°26′), *an* 96°41′(96°27′), *np* 20°56′(21°1′), *al* 35°17′(35°19′), *cn* 32°5′(31°40′) (calculated values in brackets). Cleavage: good parallel to *c*, fair parallel to *a*.

Optical properties: there is a straight extinction parallel to edge $a : m$ and to edges $c : n$ and $c : r$ in accordance with the symmetry, but no sign of an interference figure could be obtained in any of the expected directions. This would indicate the possibility of a still lower class of symmetry, *viz.*, anorthic pedial.

The two modifications also differ as regards decomposition point. The higher-melting form always begins to evolve gas at 131°, but the decomposition point of the lower-melting form varies with the rate of heating and may lie anywhere between 145° and 175°. Below 131°, the melt always resolidifies to the higher-melting modification. In combustions a high result was always obtained for carbon, and even a micro-Dumas estimation gave a slightly low result for nitrogen (Found: N, 15·9. $C_7H_5O_8N_3$ requires N, 16·2%).

This trinitroguaiacol, which is but sparingly soluble in cold water to a pale yellow solution, dissolves in aqueous sodium carbonate with evolution of carbon dioxide and, as might be predicted from its constitution, is much more sensitive to caustic alkalis than either of its known isomerides.

Addition of concentrated sodium hydroxide to its solution in aqueous sodium carbonate precipitates a yellow *sodium* salt, which redissolves almost immediately to give a deep red solution. A solution of the trinitroguaiacol in 10% aqueous sodium hydroxide, yellow at first, becomes rose-red in 2 minutes, and a very deep shade of red in 30 minutes. The solution then contains sodium nitrite and yields no precipitate on acidification.

Its solution in ammonia or in aqueous sodium carbonate also develops a permanent red colour on boiling.

When boiled with methyl sulphate and potassium carbonate in xylene solution, 3 : 4 : 6-trinitroguaiacol entirely escapes methylation and is slowly decomposed.

The *benzoyl* derivative crystallises from aqueous alcohol in nearly colourless, short needles, m. p. 146—147°. It is moderately soluble in cold alcohol.

The *quinoline* salt is immediately precipitated when a solution of quinoline sulphate in very dilute sulphuric acid is added to a dilute aqueous solution of the trinitroguaiacol. It crystallises from chloroform–light petroleum in intensely yellow, minute prisms which soften at 185° and decompose at 190° (Found: N, by the micro-Dumas method, 14·1. $C_7H_5O_8N_3,C_9H_7N$ requires N, 14·4%). This derivative was also isolated from the original nitric acid solution from which the crude 3 : 4 : 6-trinitroguaiacol was separated, the proof of identity being the comparison of decomposition points under simultaneous heating. Hence, 3 : 4 : 6-trinitroguaiacol is the only trinitroguaiacol produced by the direct nitration of 3-nitroguaiacol.

The *pyridine* salt, yellow, ill-defined prisms from methyl alcohol, softens at 146° and melts at 150—153° (decomp.).

4 : 5 : 6-*Trinitroguaiacol* (III).—5-Nitroguaiacol (9 g.) nitrated exactly as described in the preparation of 3 : 4 : 6-trinitroguaiacol (above), except that the beaker was cooled in ice, yielded 4·5 g. of the crude trinitroguaiacol, which crystallised from chloroform–light petroleum in small, very pale yellow needles, m. p. 144—147° (decomp.) (Found: N, by the micro-Dumas method, 16·3%). The benzoyl derivative melts at 140—143°, and the quinoline salt, small, yellow, elongated, rectangular plates from chloroform–light petroleum, at 207—209° (decomp.), with darkening at 203°. Kohn and Löff (*loc. cit.*) quote m. p.'s 143—149° (decomp.), 146°, and 201° (decomp.), respectively.

This trinitroguaiacol is sparingly soluble in water to a distinctly orange solution, and dissolves momentarily in saturated aqueous sodium carbonate with evolution of carbon dioxide, after which a copious yellow precipitate of the sodium salt is thrown down.

I wish to thank Professor R. Robinson, F.R.S., for his interest in this work.

THE UNIVERSITY, MANCHESTER. [*Received*, *May* 10*th*. 1926.]