

NOTES.

Preliminary Observations on the Behaviour of Rhenium and of the Complex Thiocyanates of Rhenium and Molybdenum with Toluene-3 : 4-dithiol. By CHRISTINA C. MILLER.

HAMENCE (*Analyst*, 1940, 65, 152) reported that molybdenum and tungsten form with toluene-3 : 4-dithiol ("dithiol") characteristic green complexes. Rhenium(VII) also forms a green complex very like that of molybdenum, but it differs from the latter in being decomposed by potassium thiocyanate.

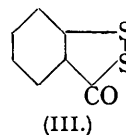
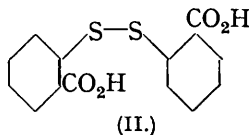
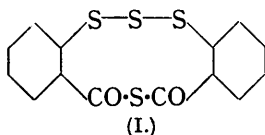
When one drop of a 1% solution of dithiol in *n*-sodium hydroxide was added to a hydrochloric acid solution (1 ml.) containing 5 γ of rhenium as perrhenate, no reaction was observed in the cold in 0.5*N*- or 2*N*-acid, but a pale green colour appeared soon in 11*N*-acid. Five mins.' heating developed a very pale green colour in the 2*N*-acid, and did not affect the others. Under the same conditions 5 γ of molybdenum(VI) developed a green colour in 0.5*N*- and 2*N*-acid in the cold, and a paler green in 11*N*-acid. Heating developed all slightly. 5 γ of tungsten(VI), which yielded no colour in any acid in the cold, soon developed a blue-green colour in the weakest acid on heating, and none in the most concentrated. The rhenium complex, like those of molybdenum and tungsten, was readily soluble in organic solvents, *e.g.*, *n*-butyl acetate, carbon tetrachloride, etc. Its colour in *n*-butyl acetate closely resembled that of the molybdenum complex, but it was a purer green, with $\frac{1}{2}$ — $\frac{1}{3}$ of the intensity for the same weight of metal.

The following interesting observation was made when the dithiol complexes of rhenium, molybdenum, and tungsten were produced by adding to hydrochloric acid solutions (1 ml.) 0.25 ml. of *n*-butyl acetate and 2—3 mg. of dithiol, which dissolved in the ester. In the cold, 5 γ of rhenium showed a pale green colour in 11*N*-acid in 1 min., and, on heating, full colour development in $\frac{1}{2}$ min. A feeble green colour was observed in 2*N*-acid on heating for 5 mins. Molybdenum and tungsten, which, in the absence of the ester, reacted least readily in concentrated acid, now reacted in the cold, molybdenum showing full colour development in 20 secs. A pale blue-green colour due to tungsten required several mins.' heating to reach its maximum intensity, which was, however, only one-half as great as that observed by adopting Miller and Lowe's procedure (*J.*, 1940, 1258) of gradually acidifying with phosphoric acid an alkaline tungstate solution containing dithiol.

In experiments with solutions in *n*-butyl acetate of the well-known orange-red thiocyanate complex of molybdenum, $\text{Mo}(\text{OH})_2(\text{SCN})_3$, and the corresponding orange-yellow complex of rhenium, probably $\text{ReO}(\text{SCN})_4$ (Geilmann, Wrigge, and Weibke, *Z. anorg. Chem.*, 1932, 208, 217; Hurd and Babler, *Ind. Eng. Chem., Anal.*, 1936, 8, 112), it was found that, if these were heated with hydrochloric acid and a little dithiol, the green dithiol complex of molybdenum was formed at once in concentrated acid, and, in a short time, in dilute acid. In acid ranging from 0.5 to 11*N* the colour of the ester layers containing rhenium showed no vestige of green, but a deepening to red-brown, which was probably associated with a reduction process. Conversely, when solutions of the green dithiol complexes of molybdenum, rhenium, and tungsten in *n*-butyl acetate were heated with 2*N*- or 11*N*-hydrochloric acid containing 20 mg. of potassium thiocyanate, the rhenium solutions changed to dark brown, while those of molybdenum and tungsten remained unaltered. This behaviour served to distinguish the rhenium-dithiol complex from that of molybdenum. The dark brown substance, deposited from the ester solution on evaporation, also dissolved readily in carbon tetrachloride and benzene, but not in ethyl alcohol.—THE UNIVERSITY, EDINBURGH, 9. [Received, July 4th, 1941.]

The Identity of Hinsberg's o-Trisulphidobenzoic Acid Thioanhydride with Smiles and McClelland's 2-Dithiobenzoyl. By ALEXANDER SCHONBERG and (MISS) AKILA MOSTAFA.

HINSBERG (*Ber.*, 1910, 43, 1874), by the pyrolysis of 2 : 2'-dicarboxydiphenyl disulphide (II), obtained a substance which he regarded as *o*-trisulphidobenzoic acid thioanhydride (I). We find it to be identical with the 2-dithiobenzoyl (III) described by Smiles and McClelland (*J.*, 1922, 121, 86).



We obtained 2-dithiobenzoyl, m. p. 77°, by the procedure of Smiles and McClelland (*loc. cit.*) (Found : C, 50.1; H, 2.5; S, 38.6. Calc. for $C_7H_4OS_2$: C, 49.9; H, 2.4; S, 38.1%).

The preparation of this compound by the thermal decomposition at 280° of 2 : 2'-dicarboxydiphenyl disulphide was carried out as described by Hinsberg (*loc. cit.*). The product was crystallised from dilute acetone and then steam-distilled. The crystals that separated from the distillate were distilled at about 200°/vac.; the pale yellow needles obtained had m. p. 77°, not depressed by 2-dithiobenzoyl (Found : *M*, cryoscopic in benzene, 162. Calc. : *M*, 168).—FOUAD I UNIVERSITY, CAIRO. [Received, September 26th, 1941.]

Studies in Aromatic Substitution. Part IV. The Action of Fuming Nitric Acid on 3-Fluoroanisole and 3-Fluoro-2-, -4-, and -6-nitroanisoles. By HERBERT H. HODGSON and JOSEPH NIXON.

FUMING nitric acid (*d* 1.5) nitrates 3-fluoroanisole and also 3-fluoro-4-nitroanisole to give 3-fluoro-4 : 6-dinitroanisole at both 0° and 50°; 3-fluoro-2-nitroanisole and 3-fluoro-6-nitroanisole each afford 3-fluoro-2 : 6-dinitroanisole at 0° but give 3-fluoro-2 : 4 : 6-trinitroanisole at 50°.

The replacement of all three chlorine atoms by nitro-groups when 3-fluoro-2 : 4 : 6-trichloroanisole is treated with fuming nitric acid at 0° (Hodgson and Nixon, *J.*, 1930, 1870) therefore appears to be in the sequence 6-, 2-, and 4-. If the 4-chlorine atom had been replaced first, the reaction should stop with the formation of 3-fluoro-2-chloro-4 : 6-dinitroanisole. That 6- rather than 2-chlorine is first replaced follows from analogy with 3-fluoro-2 : 4 : 6-tri-iodoanisole, in which only the 6-iodo-substituent is reactive.

General Procedure.—The substance (1 g.) was added gradually to ice-cold nitric acid (10 c.c., *d* 1.5) and the mixture was kept for 15 minutes and poured on ice; the resulting precipitate was washed free from acid and crystallised from 50% aqueous alcohol.

3-Fluoro-4 : 6-dinitroanisole, obtained from 3-fluoroanisole or 3-fluoro-4-nitroanisole, or by the action of methyl iodide on the silver salt of 3-fluoro-4 : 6-dinitrophenol, crystallised in long colourless parallelepipeds, m. p.'s of each preparation and mixed m. p. 99° (Found : N, 13.1. $C_7H_5O_5N_2F$ requires N, 13.0%).

3-Fluoro-2 : 6-dinitroanisole, obtained from 3-fluoro-2-nitroanisole and also from 3-fluoro-6-nitroanisole, crystallised in long colourless rectangular prisms, m. p.'s of each preparation and mixed m. p. 90° (Found : N, 13.1. $C_7H_5O_5N_2F$ requires N, 13.0%).

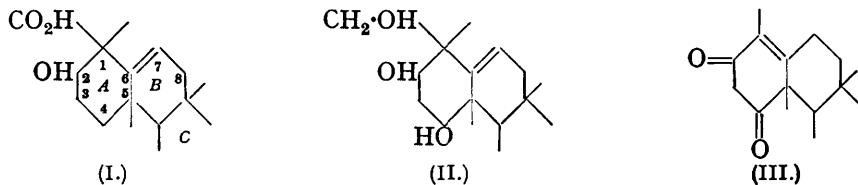
The authors thank Dr. D. E. Nicholson for making the micro-analyses and Imperial Chemical Industries (Dyestuffs Group) Ltd. for gifts of chemicals.—TECHNICAL COLLEGE, HUDDERSFIELD. [Received, August 21st, 1941.]

The Constitution of β -Boswellic Acid. By J. C. E. SIMPSON and GEORGE A. R. KON.

It has been suggested that the double bond of β -boswellic acid is situated in ring *B*, probably between C_6 and C_7 (partial formula I) (Simpson and Williams, *J.*, 1938, 1712). Since the acid has been converted into α -amyryn (Ruzicka and Wirz, *Helv. Chim. Acta*, 1939, 22, 948), the position of the double bond in this compound has acquired an additional interest.

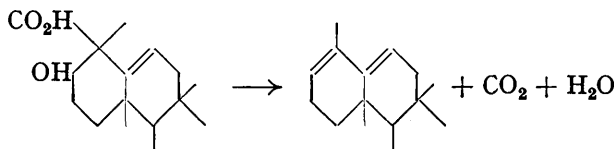
It has recently been shown that one of the double bonds of bassic acid (partial formula II) is situated in position 6 : 7 and can be made to migrate into the adjacent ring *A* when methyl

bassate is oxidised with copper bronze; the resulting $\alpha\beta$ -unsaturated diketone (III) is readily recognised by its characteristic absorption spectrum (Kon and Heywood, J., 1940, 713):



It was thought that β -boswellic acid should undergo a similar change, giving rise to a ketone analogous to (III) but without the additional carbonyl group at C_4 . The reaction proceeded smoothly, giving an unsaturated ketone, m. p. 186° , $[\alpha]_D + 182.6^\circ$, the spectrum of which showed no selective absorption in the region 2400 A. and its m. p. was not depressed by admixture of nor- β -boswellenone (m. p. 195 — 196°). The somewhat lower m. p. and higher rotation of the nor- β -boswellenone so obtained is attributable to the fact that we used β -boswellic acid of high rotation for its preparation (Simpson and Williams, *loc. cit.*, p. 1719). It can be concluded that the expected migration of the double bond did not take place; the process now described constitutes a considerable improvement on the method of preparation of nor- β -boswellenone originally employed.

The formation of a compound with conjugated double bonds would also be expected on elimination of water and carbon dioxide from β -boswellic acid to form β -boswellyene (Winterstein and Stein, *Z. physiol. Chem.*, 1932, 208, 9; Beaucourt, *Monatsh.*, 1929, 53/54, 897):



We have prepared β -boswellyene by the pyrolysis of both the acid and its acetyl derivative, but the hydrocarbon formed did not possess the expected selective absorption. Actually, both it and nor- β -boswellenone were found to have some absorption in the region 2800 A., but the intensity of this was only of the order of $E_{1\%}^{1\text{cm.}} = 100$; and a similar absorption was also found in methyl β -boswellate prepared from the acid used as a starting material. This suggests the presence of a small amount of impurity with a selective absorption in the region 2800 A., which is not removed in the ordinary course of purification of β -boswellic acid.

The present experiments are purely negative and cannot, therefore, be regarded as conclusive evidence against Simpson and Williams's formulation of β -boswellic acid; for the present they are placed on record until decisive evidence regarding the position of the double bond in the α -amyryn group of triterpenes becomes available.

Nor- β -boswellenone.—2 G. of β -boswellic acid were heated in a sausage flask with 9 g. of copper powder for 20 mins. by means of a nitrate bath kept at 340° . The flask was then evacuated with a mercury vapour pump, the yellow oil (1.4 g.) distilling into the side arm solidifying at once. Crystallisation from acetone gave sparkling flattened needles (0.8 g.) melting at about 180° , and constantly at 186° after two more crystallisations. The rotation, $[\alpha]_D + 182.6^\circ$, was determined in chloroform ($c = 1.835$) (Found: C, 85.2; H, 11.4. Calc.: C, 84.8; H, 11.3%).

β -Boswellyene.— β -Boswellic acid was heated at atmospheric pressure until decomposition was complete, and the product distilled in the vacuum of an oil-pump. The distillate was dissolved in light petroleum, freed from acid by shaking with sodium hydroxide, and percolated through a little alumina, the solution evaporated, and the residue crystallised three times from acetone, forming fine needles, m. p. 123° , $[\alpha]_D + 231.8^\circ$ ($c = 1.815$ in chloroform) (Found: C, 88.5; H, 11.5. Calc.: C, 88.3; H, 11.8%).

The authors are indebted to Dr. R. H. Kerlogue for measuring the absorption spectra.—
UNIVERSITY OF DURHAM AND IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W.7. [Received, August 18th, 1941.]

Œstrone Azobenzene-4-carboxylate. By F. BERGEL and A. COHEN.

THE publication by Coffman (*J. Biol. Chem.*, 1941, **140**, XXVIII) of a report on the preparation and chromatographic analysis of benzeneazo-*p*-benzoyl derivatives of androsterone, isoandrosterone, dehydroisoandrosterone, pregnanediol and cholesterol makes it desirable for us to publish the results of similar experiments undertaken some time ago in the field of the oestrogenic hormones. The object was to purify various grades of œstrone or even the total crystallisate of the oestrogenic hormones by chromatographic analysis of the azobenzene-4-carboxylates. Duschinsky and Lederer have described experiments on the chromatographic separation of free œstrone and equilenin (*Bull. Soc. Chim. biol.*, 1935, **17**, 1534).

Ladenburg, Fernholz, and Wallis (*J. Org. Chem.*, 1938, **3**, 294) showed that some sterols can be separated in the form of their azobenzene-4-carboxylates, and Reich (*Biochem. J.*, 1939, **33**, 1000) separated various sugars as poly-azobenzenecarboxylates.

When the azobenzene-4-carboxylates prepared from samples of œstrone of varying degrees of purity were submitted to chromatographic analysis, as described below, a sharp separation could not be effected, almost the whole of the material forming a deep diffuse band on the alumina column. The crystallisation of the coloured ester was, however, in itself a better means of purifying the œstrone than crystallisation from alcohol, as is shown in the following experiments.

Œstrone Azobenzene-4-carboxylate.—A mixture of œstrone (0.2 g.), m. p. 257.5—259.5,* and azobenzene-4-carboxylic acid chloride (0.4 g.) in anhydrous pyridine (10 c.c.) was warmed at 50° for 24 hours. A small quantity (0.03 g.) of the ester separated directly from this solution, which was filtered and poured into ice-water to precipitate the bulk of the product. The latter was dried (0.45 g.), dissolved in 36 c.c. of benzene, and shaken for a few seconds with activated alumina (1.5 g. Brockmann) and then filtered. The filtrate was concentrated, and the *œstrone azobenzene-4-carboxylate* precipitated by the addition of light petroleum and recrystallised from ethyl acetate, forming red rhombs (0.2 g.), m. p. 226.5—227.5° (Found: C, 77.6; H, 6.1; N, 5.9. $C_{31}H_{30}O_3N_2$ requires C, 77.8; H, 6.3; N, 5.9%).

Œstrone regenerated from this ester by hydrolysis with 2% alcoholic potassium hydroxide had m. p. 259.5—260.5° after crystallisation from alcohol, whereas recrystallisation of the original œstrone gave a specimen of m. p. 255.5—257.5°.

Attempted Chromatographic Analysis of "Azo-ester" of Œstrone Samples.—(a) Crude œstrone of m. p. 253.5° (0.2 g.) was esterified as described above. When the pyridine solution was chilled, 0.14 g. of the pure ester, m. p. 226.5°, was directly obtained. The mother-liquor yielded, on precipitation with water, 0.23 g. of orange solid. This was dissolved in 50 c.c. of benzene–light petroleum (b. p. 60—80°) (a 2 : 1 mixture was used in all the experiments) and run through a column of activated alumina about 14 cm. long and 22 mm. wide. The column was washed with 50 c.c. of benzene–light petroleum (2 : 1) and then developed with 300 c.c. of a 9 : 1 mixture. When about 150 c.c. of the developing solution had been added, a faint yellow colour appeared in the filtrate, which was collected separately as long as colour persisted, and evaporated to dryness, yielding a trace of crystalline material too small for further examination. At the end of development, a deep diffuse band was the main constituent of the chromatogram and extended over the lower half of the column. Elution with acetone yielded 0.15 g. of red crystalline solid, m. p. 209.5—211.5°, *i.e.*, still 17° lower than that of the pure ester. When recrystallised from ethyl acetate, however, the product (0.1 g.) had m. p. 226.5°.

A small coloured band which formed above the main band gave, on acetone elution, a very small amount of gummy material.

(b) In another experiment, 0.2 g. of œstrone of m. p. 253.5° yielded directly 0.24 g. of the azo-ester (68% yield), m. p. 225.5°, when only 5 c.c. of pyridine were used and the reaction mixture was cooled below 0° after 24 hours at 50°. Precipitation of the pyridine liquor with water yielded 0.22 g. of crude ester, m. p. 198.5—223.5°. A benzene solution of this was shaken for a few moments with activated alumina, filtered, and evaporated to dryness. The residue, recrystallised from ethyl acetate, yielded 0.05 g. of ester, m. p. 224.5—225.5°, raising the total yield of purified ester to 82%. On hydrolysis of this with 2% alcoholic potassium hydroxide, œstrone was obtained, m. p. 258.5—260.5° after crystallisation from alcohol.

(c) The starting material in this experiment was a "total crystalline oestrogenic hormone fraction" of m. p. 211—223°. It was esterified in the usual way and the product precipitated by water was dried and had m. p. 199—202°. A solution of 0.4 g. of this crude ester in 60 c.c. of benzene–light petroleum (2 : 1) was run through an alumina column, washed with 100 c.c.

* All m. p.'s are corrected.

of the solvent mixture (2 : 1), 100 c.c. (4 : 1) and 300 c.c. (9 : 1). Again the main band was deep and diffuse in the lower part of the column and gave, on elution with acetone, 0.3 g. of red crystalline material, m. p. 199—202°, so that no improvement in m. p. had been effected. One crystallisation of this material from ethyl acetate gave a product, m. p. 219.5—220.5°, which was hydrolysed to œstrone of m. p. 253.5—254.5° (one crystallisation from alcohol). A faint upper layer was again observed in the chromatogram.

The m. p.'s of various specimens of œstrone, including the International Standard, before and after purification through their azobenzene-4-carboxylates are compared in the following table :

	Before esterification.	After regeneration from azo-ester.
œstrone, purified technical	257.5—259.5°	259.5—260.5°
œstrone, technical	253.5	258.5—260.5
Total cryst. œstrogenic hormone	211—223	253.5—254.5
International Standard œstrone	261.5—263.5	262.5—263.5

A specimen of highly purified œstrone, kindly supplied by Dr. A. Winterstein of Messrs. Hoffmann-La Roche and Co., Basle, showed an even higher m. p. of 264—264.5°.

Azobenzene-4-carboxylic acid chloride is readily prepared by refluxing the acid with excess of thionyl chloride till solution occurs, or with a benzene solution of slightly more than the calculated quantity of thionyl chloride. The presence of anhydrous sodium carbonate (cf. Ladenburg *et al.*, *loc. cit.*) has not been necessary.

The authors are grateful to Dr. P. Hartley of the National Institute for Medical Research for providing the International Standard and to Messrs. Hoffmann-La Roche and Co., Basle, for the other samples of œstrone.—RESEARCH DEPARTMENT, ROCHE PRODUCTS LTD., WELWYN GARDEN CITY. [Received, September 10th, 1941.]