bonylverbindungen übergeführt werden. Gesättigte Alkoholgruppen wurden dabei nicht angegriffen.

Überraschenderweise gelang die selektive Oxydation der Benzylalkoholgruppe auch, wenn die *p*-Stellung durch Hydroxyl substituiert war. Hierin erweist sich das DDB dem für die selektive Oxydation von Benzylalkoholen ebenfalls verwendbaren aktiven Mangandioxyd überlegen, da letzteres auch die phenolische Hydroxylgruppe angreift [4].

Tabelle 1 gibt eine Übersicht über die von uns vorläufig untersuchten Reaktionen. Diese wurden, wie für Allylalkohole beschrieben [3], in trockenem Dioxan ausgeführt. Vom auskristallisierten 2,3-Dichlor-5,6-dicyan-hydrochinon (DDH) wurde abgesaugt und die Lösung über eine Säule von Al_2O_3 filtriert, worauf mit Äther nachgewaschen wurde. Aus den vereinigten Filtraten kristallisierten beim Eindunsten die entsprechenden Carbonylverbindungen; sie wurden durch Vergleich der IR-Spektren mit authentischem Material identifiziert.

Früher war bereits die Oxydation von Benzylalkoholen mit Tetrachlor-*o*-benzochinon von Braude und Mitarb.[5] untersucht worden, jedoch waren die Ausbeuten hierbei unbefriedigend.

Über die Verwendung von 2,3-Dichlor-5,6-dicyan-1,4-benzochinon zu analytischen Untersuchungen am Lignin soll später berichtet werden.

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1. Braude, E. A., Brook, A. G. und Linstead, R. P. *J. Chem. Soc.* **1954** 3569.
2. Burn, D., Kirk, D. N. und Petrow, V. *Proc. Chem. Soc. (London)* **1960** 14.
3. Burn, D., Petrow, V. und Weston, G. O. *Tetrahedron Letters No.* **9** (1960) 14.
4. Freudenberg, K. und Grion, G. *Chem. Ber.* **92** (1959) 1355.
5. Braude, E. A., Linstead, R. P. und Wooldridge, K. R. *J. Chem. Soc.* **1956** 3070.

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The Sulfonation of Iodobenzene

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The anhydride of the *p*-iodobenzenesulfonic acid, pipsan, labelled with ^{131}I or ^{35}S, has become an invaluable tool in the determination of steroid hormones in submicrogramme quantities [1-3].

The preparation of the pipsan by conventional methods [1] has proved impractical from the point of view of radiation protection. It was therefore found of interest to study the formation of arylsulfonic acid anhydride from aryl halide and oleum at room temperature. This type of reaction has been known for many years [4,5], and recently Lukashevich [6] has worked out approximate conditions for separation of such compounds.

The original method of recovering the anhydride is to pour the sulfonation mixture on to ice, whereby the insoluble anhydride precipitates. The present paper describes a method of isolating pipsan from the sulfonation mixture without the use of ice or water. The modification proves of benefit, especially in a remote handling procedure [7]. Further, the conditions for optimal separation of the pipsan have been studied in detail.

Sulfonations of iodobenzene conducted on a semi-micro scale with varying amounts of oleum containing varying amounts of SO_3 revealed that within a rather narrow range of conditions the sulfonic acid anhydride separated rapidly in a yield of 50–60 %, which is at least as good as the yield reported by Lukashevich [6].

Experimental. The samples of oleum were prepared by mixing "60 % free SO_3" (p.a.) oleum and conc. sulfuric acid (p.a.), and the contents of total SO_3 in the mixtures were determined by titration according to Rosin [8]. The iodobenzene was a British Drug Houses preparation, "not less than 98 %". Weighed amounts of the components (0.5 g of iodobenzene and 0.5—4 g of oleum) were mixed in 10 ml centrifuge tubes and kept at 0° for 3 h, whereupon the precipitate, if any, was centrifuged down and the supernatant removed. The precipitate was washed consecutively with 5 ml of acetic acid anhydride, 2 × 4 ml of

ether and 4 ml of pentane, dried in a stream of nitrogen and weighed. The yield is calculated as per cent of the theoretical from iodobenzene.

The dried crude product melts rather unsharp at 190—205° and is insoluble in cold water and only slowly soluble in boiling water. A quick way to effect hydrolysis is to expose the anhydride to steam.

In all instances the products were completely soluble in water after hydrolysis, indicating absence of any sulfone. By titration with 0.1 N NaOH, the crude, hydrolyzed product was found to have a neutralization equivalent weight of 280 ± 5 (calc. 275).

The crude product may be recrystallized from pure acetic acid anhydride, acetonitrile, nitromethane and chloroform. By dissolving in hot, purified and anhydrous chloroform and reprecipitating with four volumes of pentane, the acid anhydride separates in 70—80 % yield, m.p. 207—213°, previously reported: 220—221° [1], eqiv.wt. 280.

On comparison of the infra-red spectra of the recrystallized material with a specimen prepared according to Bojesen [1] it was concluded that the product prepared in oleum contained about 95 % of the *para* isomeride. Neither sulfone nor sulfonic acid could be detected, but an isomeric anhydride may be present as a contaminant.

Anhydrous *p*-iodobenzenesulfonic acid was prepared by hydrolysis of the anhydride and drying *in vacuo* at 100°. It is very hygroscopic, readily soluble in cold water and has a m.p. of about 70°.

Results and discussion. On the arbitrary assumption that oleum consists of 100 % H_2SO_4 and free SO_3, the mole ratios H_2SO_4/C_6H_5I and free SO_3/C_6H_5I have been calculated for each experiment. From Fig. 1 it is seen that regardless of the H_2SO_4/C_6H_5I ratio, the maximum yields are obtained with a free SO_3/C_6H_5I ratio of 1.0—1.6.

Free SO_3/C_6H_5I: 0 — 1.0. In this range the iodobenzene dissolves in the oleum and the mixture takes on a faintly yellow colour, but hardly any precipitation of anhydride occurs. After some minutes, however, colourless needles start to appear, and with low contents of H_2SO_4 the mixture soon solidifies to a mass of crystals soluble in acetic anhydride and water. These crystals are probably iodobenzenesulfonic acid.

Free SO_3/C_6H_5I: 1.0 — 1.6. This is the range for optimal yields of acid anhydride. The mixture is instantaneously coloured deeply yellow-brown, and after a while the colourless anhydride starts precipitating. With stirring, the precipitation seems to be complete after half an hour.

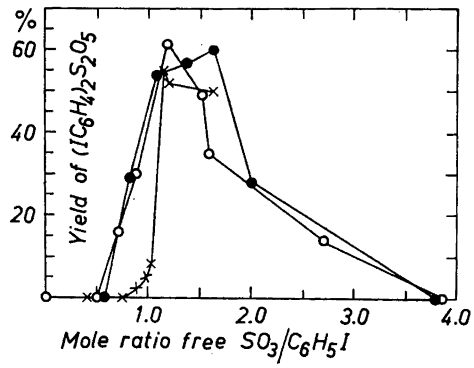

Fig. 1. Yields of iodobenzenesulfonic acid anhydride formed by sulfonation of iodobenzene with oleum (100 % H_2SO_4 + free SO_3), 3 h at 0°. × = 0.6—1.2, ● = 1.8—3.6 and ○ = 5.2—8.2 moles of H_2SO_4 pr mole of C_6H_5I.

Free SO_3/C_6H_5I: 1.6 — 4.5. With increasing contents of SO_3 the reaction mixture becomes a dark violet or black tar and the yield of anhydride decreases. The reason for the colour-formation is apparently not destruction of iodobenzene, since on dissolving the tar in acetic acid anhydride an orange gel is formed. If the tar is poured on to ice the colour disappears completely, *cf.* also observations by Willgerodt *et al.*[11] It should be noticed that the stoicheiometric equation $3SO_3 + 2C_6H_5I \rightarrow (IC_6H_4)_2S_2O_5 + H_2SO_4$ demands a ratio of 1.5. The reason why the yields do not exceed 60 %, even at the ratio 1.5, is probably competitive reactions. With increasing SO_3/C_6H_5I-ratios these reactions may become predominant. Under analogous conditions the formation of pyrosulfonic acids, disulfonic acids and SO_3-adducts has been described by various authors [9,10].

The restricted yield cannot be wholly explained by solubility of the sulfonic acid anhydride in the cold oleum. When the supernatants from the sulfonation mixtures were poured on to ice-water, only a slight turbidity was formed. It is also noteworthy in this respect that maximum yields of 60 % are obtained regardless the size of the reaction volumes (as defined by the H_2SO_4/C_6H_5I ratio).

Iodine-131-labelled pipsan, prepared after this method, has now for one year been successfully applied by The Institute of Experimental Medicine, University of Copenhagen, for making indicators used in routine analyses of steroid hormones.

1. Bojesen, E. *Scand. J. Clin. Lab. Invest.* **8** (1956) 55.
2. Bojesen, E. and Degn, H. *Advance Abstr. short Comm. 1st Intern. Congr. Endocrinol.* Copenhagen 1960, p. 1057.
3. Svendsen, R. *Acta Endocrinol.* **35** (1960) 161.
4. Rosenberg, J. *Ber.* **19** (1886) 652.
5. Neumann, G. S. *Ann.* **241** (1887) 33.
6. Lukashevich, V. O. *Doklady Akad. Nauk S.S.S.R.* **99** (1954) 995; *Chem. Abstr.* **50** (1956) 217.
7. Christensen, N. H. *Proc. Conf. Use Radioisotopes Phys. Sci. and Ind. Copenhagen.* IAEA Vienna 1961, no. 244. *In press.*
8. Rosin, J. *Reagent Chemicals and Standards,* 3rd Ed., van Nostrand Co., New York 1955, p. 458.
9. Lukashevich, V. O. *Proc. Acad. Sci. U.S.S.R., Sect. Chem.* **112** (1957) 133, (English translation).
10. Courtot, C. and Bonnet, J. *Compt. rend.* **182** (1926) 855.
11. Willgerodt, E. and Waldeyer, O. *J. prakt. Chem.* **59** (1899) 194.

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On the Reaction of 2,4-Dihydroxy-1,4-benzoxazin-3-one to 2(3)-Benzoxazolinone

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In earlier papers [1,2] from this laboratory it was confirmed that the aglucone, 2,4-dihydroxy-1,4-benzoxazin-3-one, isolated from crushed rye seedlings and its 7-methoxy derivative [3] from wheat and maize plants undergoes a reaction by heating in aqueous solution, upon which 2(3)-benzoxazolinone (or its 6-methoxy derivative) is formed by simultaneous liberation of formic acid. Later a similar reaction was found to occur also by heating of 4-hydroxy-1,4-benzoxazine-2,3-dione (III)[4], carbon dioxide being split off.

Theoretically there are two possibilities for the formation of the formic acid: from carbon atom 2 or 3. To solve this problem an aglucone (II) labelled with ^{14}C at the position 2 was synthesized by an analogous procedure as in the case of the syntheses of the normal aglucone [5] from *o*-methoxymethoxyphenylhydroxylamine (I) and dibromoacetyl-2-^{14}C chloride. The needed dibromoacetyl-2-^{14}C chloride was prepared by the following reactions from diethyl-(malonate-2-^{14}C).

After heating the aqueous solution of II, the radioactivity was found in the formic acid, and we conclude that the formic acid originates from carbon atom 2 in II. Nothing certain can be said about the reaction mechanism. A prerequisite for this reaction seems to be the easy rupture of the bond between the oxygen and carbon atom 2 and the presence of the N-hydroxyl group. The compound IV [4] which has a simple ether linkage and the compound V[5] which has no N-hydroxyl group are quite stable in boiling aqueous solution.

Dibromoacetyl-2-^{14}C chloride. A mixture of 1.85 mg (0.025 mC) of diethyl-(malonate-2-^{14}C)* and 500 mg of diethylmalonate in 10 ml of 2 N hydrochloric acid was heated for 24 h at 50°C. The solution was then evaporated to dryness under reduced pressure. The residue was dissolved in 1 ml of 2 N hydrochloric acid, the solution cooled below +5°C, and 350 μl of bromine were added. After standing for 2 h the solvent was evaporated in vacuum. The residue (dibromomalonic acid) was then decarboxylated to dibromoacetic acid by heating for 1 h at 130°C. Two ml of thionyl chloride were added after cooling, and the mixture was boiled for 1 h on a water bath. The excess of thionyl chloride was then removed under reduced pressure, and the residue was used without further purification for the following reaction.

2,4-Dihydroxy-1,4-benzoxazin-3-one-2-^{14}C. A solution of the above dibromoacetyl-2-^{14}C chloride in 10 ml of dry ether was added under cooling to a solution of *o*-methoxymethoxyphenylhydroxylamine prepared from 0.5 g of *o*-

* A product of The Radiochemical Centre.