mixture. When allowed to react with sulphite ion 1 Mol of the 'monosulfoxide' produced 0.5 Mol of thiol as measured by amperometric titration with mercuric chloride[14]. This is difficult to explain on the basis of structure (II) but can be reconciled with the assumption that the product is an equimolar mixture of (I) and (III), since (III) does not yield thiol under these conditions[3]. The hypothesis that the 'monosulfoxide' is an equimolar mixture of (I) and (III) agrees with the figures[12] for elementary analyses and equivalent weight; and the specific rotation ($[\alpha]_D^{24} = -111°$)[12] is approximately the mean of the rotations of I (– 213°) and III (– 22°). Contrary to the previous report[12] it is now found that in the region 7–10 μ the infra-red spectra[15] of the 'monosulfoxide' and of an equimolar mixture of I and III are indistinguishable. Simple aliphatic and aromatic thiolsulfinates are unstable and readily disproportionate into a mixture of the corresponding disulfide and thiolsulfonate[16,17] and it is possible that 'cystine monosulfoxide' decomposes in this way as soon as it is formed in the acidic solution (HCl + KI).

To further investigate possible intermediate oxidation products of cystine, the performic acid oxidation method[5] has been studied using varying amounts of oxidant (1–5 Mol). The products of these oxidations were analysed quantitatively using the iodometric reduction method of TOENNIES and LAVINE[4] and also qualitatively by the combination of paper electrophoresis and paper chromatography[13]. The reaction course is found to be markedly affected by the presence of HCl, presumably because the effective oxidant in this case is chlorine, formed *in situ*. In the presence of HCl large amounts of the two intermediate oxidation products III and VI are formed[18] whereas in the absence of HCl the final oxidation stage cysteic acid (VII), is reached with only minor amounts of III and VI; and VII is the ultimate product when excess of performic acid is used either in the presence or absence of HCl. It is noteworthy that there is no evidence for intermediates other than III and VI whereas the whole range of products from R–S–SO–R to R–SO_2–SO_2–R can be prepared in the simple aliphatic and aromatic series[19,20]. Recent work has shown that although apparently simple, the oxidation of thiols to disulfides[21] and of thiolsulfinates to thiolsulfonates[22] may involve complex reaction mechanisms[23].

Zusammenfassung. Die früher als «Cystinmonosulfoxyd» beschriebene Verbindung (Thiosulfinat II) verhält sich wie eine äquimolekulare Mischung von Cystin (I) und dem entsprechenden Thiosulfonat (III). Oxydation von Cystin mit Perameisensäure führt, besonders in Gegenwart von HCl, über die Zwischenprodukte Thiosulfonat (III) und Sulfinsäure (VI) zu Cysteinsäure (VII).

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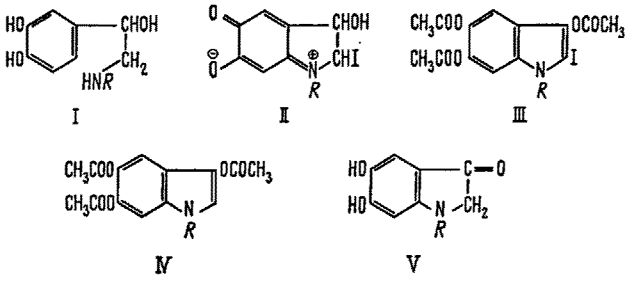
Noradrenolutin

It has been known for many years that fluorescent substances can be obtained from the oxidation products of adrenaline (I: $R = CH_3$) and noradrenaline (I: $R = H$) by treatment with alkali and this phenomenon has been widely used in the fluorometric estimation of these catecholamines in body fluids (for references see HEACOCK[1], VON EULER[2], and PERSKEY[3]). The fluorescent derivative of adrenaline, known as adrenolutin (5,6-dihydroxy-N-methylindoxyl (V: $R = CH_3$))[4] was isolated and characterized several years ago[6]; however isolation of the fluorescent oxidation product of noradrenaline in the solid state has not yet been reported. BU'LOCK and HARLEY-MASON failed to obtain any crystalline material from the alkaline rearrangement products of solutions of noradrenaline, which had been oxidized with potassium ferricyanide[7]. An alternative unsuccessful route attempted by these authors[7] has been reexamined and crystalline noradrenolutin (i.e. 5,6-dihydroxyindoxyl (V: $R = H$)) has now been obtained.

2-Iodonoradrenochrome (II: $R = H$) can be obtained from the oxidation of noradrenaline hydrochloride with potassium iodate[7,8]. (The procedure described by BU'LOCK and HARLEY-MASON gives a poor yield of crystalline product and only after removal of much tarry material[7].) However, a moderate yield of crystalline 2-iodonoradrenochrome with minimal formation of tarry



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byproducts was obtained by treating a solution of noradrenaline hydrochloride (0.5 g) in water (150 ml) with potassium iodate (0.8 g); stirring the reaction mixture for $1^1/_2$ h; adjusting the pH to 2 (with hydrochloric acid) and finally allowing the solution to stand at 4° overnight. Direct acetylation of 2-iodonoradrenochrome (II: R = H) with acetic anhydride and dry pyridine gave 3,5,6-triacetoxy-2-iodoindole (III: R = H) (m.p. 207–208°) (Found: C, 40.32; H, 2.92; N, 3.14; I, 30.53. $C_{14}H_{12}O_6NI$ requires C, 40.30; H, 2.89; N, 3.36; I, 30.43%) which on deiodination with zinc and acetic acid gave 3,5,6-triacetoxyindole (IV: R = H) (m. p. 123–124°) (Found: C, 57.79; H, 4.53; N, 4.81. $C_{14}H_{13}O_6N$ requires C, 57.73; H, 4.50; N, 4.82%). These two compounds had previously been described as 3,5,6-triacetoxy-N-acetyl-2-iodoindole (III: $R = COCH_3$) and 3,5,6-triacetoxy-N-acetylindole (IV: $R = COCH_3$) respectively[7], however identification was based on carbon and hydrogen analysis alone, which in these cases does not give a sufficiently clear cut differentiation between the tri- and tetra-acetyl derivatives. In neither case does the infrared spectrum show any amide carbonyl bands, however both show definite N–H stretching peaks[9] at 3450 cm^{-1} and 3470 cm^{-1} respectively. BU'LOCK and HARLEY-MASON failed to obtain any crystalline fluorescent product from the alkaline hydrolysis of the deiodinated acetyl derivative[7], however, hydrolysis of 3,5,6-triacetoxyindole with 1 N sodium hydroxide in the presence of a small quantity of sodium hydrosulphite gave, in our hands, after acidification with glacial acetic acid, a yellow-orange solid, which afforded noradrenolutin (5,6-dihydroxyindoxyl, V: R = H) in bright yellow needles (m.p.—totally decomposed by 248°) on recrystallization from hot water (containing a small quantity of sodium hydrosulphite). (Found: C, 58.43; H, 4.49; N, 8.48. $C_8H_7O_3N$ requires C, 58.18; H, 4.27; N, 8.48%). No crystalline product could be isolated when the hydrolysis was carried out in the absence of sodium hydrosulphite[7]. Noradrenolutin obtained by the method described above dissolves in water or methanol to give intensely fluorescent solutions. The ultraviolet and visible absorption spectra were measured in water (λ_{max}: 248; 284; 315; 368 mμ). The fluorescence characteristics[10] of noradrenolutin were also measured in aqueous solution and showed that maximum fluorescence apparently occurred at 490–500 mμ with excitation at 380–390 mμ.

These studies which form part of a comprehensive study of the chemistry of aminochromes are continuing and further details will be published elsewhere.

Zusammenfassung. Herstellung und einige Eigenschaften von kristallinem Noradrenolutin (5,6-Dioxyindoxyl), dem gelbgrün fluoreszierenden Oxydationsprodukt von Noradrenalin, werden beschrieben.

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[9] The infrared spectra were measured in chloroform solution.

[10] Measured on an Aminco-Bowman spectrophotofluorometer, through the courtesy of Dr. V. WOODFORD.

Uncoupling of Oxidative Phosphorylation in Antigen-Antibody Reactions

It is now an accepted fact that cells are damaged by antigen-antibody reactions, probably by intervention of complement.

Although the exact mechanism by which the damage is produced is so far unknown, we can infer, from indirect data and by comparison with the phenomena observed in sensitized erythrocites, that the lesion begins in the cell membrane.

It is usually accepted that blood vessel endothelia and mesenchymal cells are the site of the antigen-antibody reaction; parenchymal injury is thought to be secondary, caused by toxic substances liberated by the cells at the site of reaction. Numerous data bear out this hypothesis, but one cannot entirely reject the possibility that parenchymal cells may be site of antigen-antibody reaction, either in abnormal conditions or because the antigen, having first been modified by the cells of the reticuloendothelial system, then passes into the cells of the parenchyma.

It is not known which cellular structures take part in the antigen-antibody reaction, nor whether it takes place at the cell surface or inside the cell itself. It seems logical to suppose that the antigen penetrates into those cells which produce the antibodies, as this is the only way protein syntheses may be stimulated and directed according to the chemical structure of the antigen; it is also possible that the antigen may be adsorbed at the surface of cells which are not directly involved in antibody production. The fact that lesions in serum sickness begin as soon as antibodies appear in the blood stream (HAWN and JANEWAY[1]; GERMUTH[2]; GERMUTH, PACE, and TIPPETT[3]) while the antigen is still present, is in accordance with this hypothesis. Adsorption of the antigen at the cell surface and its subsequent binding to the antibody appears therefore to be the damaging factor of cell structures.

In this study I have considered oxidative phosphorylation, which is a most precise and sensitive index of the function and structure of mitochondria, which are concerned with some of the most important aspects of cellular life.

Investigations were carried out in three directions, i.e.: (1) Action of specific antiserum on oxidative phosphorylation in mitochondria obtained at various intervals from animals injected with corresponding antigen. (2) Influence of the antigen-antibody complex on oxidative phosphorylation after removal of the precipitate. (3) Behaviour of oxidative phosphorylation in mitochondria after antigen adsorption and subsequent treatment with corresponding serum.

Methods. Animals: Albino rats weighing on the average 100–120 g were used. The rats were fed on a standard diet and were killed by decapitation.

Isolation of mitochondria: Mitochondria were obtained by centrifugation (Servall SSI centrifuge) from 10% homogenate of liver and kidney prepared in a cold room at + 2°C with 0.25 M sucrose and 0.02 M Tris-HCl buffer pH 7.4. The mitochondrial sediment was then resuspended in 0.25 M sucrose and 0.02 M Tris buffer. The system used for the study of oxidative phosphorylation consisted of: 0.013 M Na_2HPO_4-KH_2PO_4 pH 7.4; 0.01 M Tris buffer pH 7.4; 0.005 M $MgCl_2$; 0.01 M KCl; 0.00001 M $MnCl_2$; 0.02 M ATP; 0.02 M KF; 0.02 M glucose; 0.03 M sucrose;

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