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THE NITROGEN FUNCTION OF LACCAIC ACID A_1

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Recently we described (1) the isolation and purification of laccaic acid A_1, the major component of laccaic acid. We now report experiments which establish the nature of the nitrogen function in laccaic acid A_1. These and other experiments lead us to modify the molecular formula adopted earlier (1) to $C_{26}H_{17}NO_{11}.H_2O$.

Hydrolysis of laccaic acid A_1 with 2N-sodium hydroxide gave acetic acid (identified as S-benzyl thiouronium acetate) and desacetyl-laccaic acid A_1. The latter, a highly insoluble red compound, was purified by precipitation with acid from its solution in dilute alkali. Analysis indicated the molecular formula $C_{24}H_{15}NO_{10}.2H_2O$ (Titration equivalent, 500). Prolonged drying removed a molecular equivalent of water, and analysis then corresponded to the formula $C_{24}H_{15}NO_{10}.H_2O$.

Methylation of desacetyl-laccaic acid A_1 (dimethyl sulphate/potassium carbonate/acetone) gave four products, which were separated by chromatography on silicic acid. The major one (45% of the crude mixture) formed yellow-orange needles, m.p. 290°, from chloroform-methanol. It was soluble in water, gave a precipitate with potassium iodide solution, contained sulphur, and was clearly a quaternary methosulphate. Analysis suggested the composition $C_{33}H_{35}NO_{14}S$.

This quaternary salt, when boiled with 2N-sodium hydroxide gave trimethylamine (isolated as the hydrochloride and identified as its picrate) and an orange compound which was re-methylated under the conditions used for the parent compound. The product, called "the methylated Hofmann product", formed yellow needles, m.p. 260° , from acetone. Analysis agreed with the formula $C_{29}H_{22}O_{10}$ (M.Wt. in chloroform by vapour pressure osmometry, 538).

Treatment of the methylated Hofmann product with osmium tetroxide and potassium meta-periodate in aqueous dioxan, purification of the product by chromatography on silicic acid, and crystallisation from acetone gave yellow needles, m.p. 265° (the infrared spectrum showed a peak at 1693 cm.$^{-1}$). Analysis agreed with the formula $C_{28}H_{20}O_{11}$. (M.Wt. in chloroform by vapour pressure osmometry, 542). Formaldehyde (identified as the 2,4-dinitrophenylhydrazone) was isolated from the oxidation liquor.

N.m.r. spectroscopy provides strong support for the following interpretation of this sequence of reactions:

$$\mathrm{Ar.CH_2.CH_2.NH.COMe} \longrightarrow \mathrm{Ar.CH_2.CH_2.NH_3^+}$$

Laccaic acid A_1 . Desacetyl-laccaic acid A_1 .

$$\mathrm{Ar.CH_2.CH_2.\overset{+}{N}Me_3\ (MeSO_4^-)} \longrightarrow \mathrm{Ar.CH{:}CH_2} \longrightarrow \mathrm{ArCHO + H.CHO}$$

Methylation product . Methylated Hofmann product.

The n.m.r. spectrum of laccaic acid A_1 in deuterodimethyl sulphoxide includes signals at 8.06 τ (singlet; 3H; MeCO), 7.20 τ (multiplet; 2H; Ar.CH_2.), and 6.65 τ (multiplet; 2H; CH_2 adjacent to NH.COMe). These signals are in excellent agreement with those given by N-acetyl-β-phenethylamine (2). The spectrum of desacetyl-laccaic acid A_1 showed no signal from an acetyl group. In deuterodimethyl sulphoxide + D_2O it contained a broad band at 6.90 τ (4H; Ar.CH_2.CH_2.$\overset{+}{N}\equiv$). In the spectrum of the methylation product there were signals at 6.80 τ (broad singlet; 4H; Ar.CH_2.CH_2.$\overset{+}{N}\equiv$), and 6.56 and 6.60 τ (2 singlets; 12H; $\overset{+}{N}Me_3$ + $MeSO_4^-$). The pertinent feature of the spectrum of the methylated Hofmann product was a doublet of doublets at 3.15 τ (J_{cis} 11.4, J_{trans} 17.4 c.p.s.; 1H; Ar.CH=) and two doublets at 4.26 and 4.72 τ (J_{trans} 17.4 and J_{cis} 10.8, respectively; $J_{gem} < 0.8$ c.p.s.; each doublet 1H; $=CH_2$) (3).

The infrared spectrum of laccaic acid A_1 (1) contains a band at 1677 cm.$^{-1}$ hitherto attributed to a non-quinonoid carbonyl group. The band is absent from the spectrum of desacetyl-laccaic acid A_1, and clearly is to be assigned to the N-acetyl group.

We have reported (1) that the nitrogen in laccaic acid A_1 could be estimated by the van Slyke method, and this is true of the nitrogen in desacetyl-laccaic acid A_1. Hydrolysis of the N-acetyl group of laccaic acid A_1 must, therefore, occur under the conditions (aqueous acetic acid at 90°) of the van Slyke estimation.

The laccaic acids isolated by us (1) resemble in many respects the mixture described by Venkataraman and his co-workers (4). An important difference seems to be that all three laccaic acids (A_1, A_2, and B) (making up 85% of crude laccaic acid) isolated by us contain nitrogen. Laccaic acid A_1 resembles the laccaic acids of the Indian workers in containing a purpurin unit (1,4) and, as now shown, the unit $Ar.CH_2.CH_2X$.

References

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3) Ibid., spectrum No. 498.

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