π-Complexes with Biologically Significant Materials.

I. Estrone Chromium Tricarbonyl

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The possible significance of π-bonding in biological media was pointed out recently by one of us 1. We would now like to report the first synthesis of an organometalllic π-complex of a hormone, estrone. Estrone has an aromatic ring and can be regarded as a derivative of phenol. A number of chromium tricarbonyl π-complexes of aromatic compounds have been prepared 2–5. Phenol has been shown 4 to form an unstable chromium tricarbonyl π-complex which has been isolated 5 in relatively low yield. Estrone was heated at reflux with an excess of chromium hexacarbonyl in di-n-butyl ether and the greenish-yellow crystals obtained were purified by recrystallization. The purified yellow ring compound was shown to have the composition, estrone-Cr(CO)3 (I). Strong absorption at 1855 and 1950 cm⁻¹ in the infrared spectrum of compound (I) showed clearly that the chromium tricarbonyl group was incorporated into the phenol nucleus of estrone. The presence of hands at 3150 and 1748 cm⁻¹ in the infrared showed the presence of phenolic hydroxyl and five-membered ring ketone groups, respectively. In the ultraviolet region, the compound showed an absorption maximum at 315 μ (log ε: 3.38) and an increasing absorption towards shorter wavelengths. It has been reported that arene chromium tricarbonyls generally have an absorption maximum at 319 μ (log ε: 4). 4

The following structure is proposed for the compound (I):

The stereochemical problem of whether the chromium tricarbonyl group is attached on the α or β side of the molecule is not settled. Probably the compound (I) is a mixture of both α and β isomers. The compound (I) is rather unstable at room temperature on standing in air, changing to a green solid. On heating at 140 – 150° in air, it decomposes to a brown solid without melting. The compound (I) is soluble in dilute aq. alkali, but decomposition occurs with evolution of a gas in an hour. In polar solvents, such as methanol, acetone, and chloroform, the compound (I) is soluble, but likewise decomposes on standing in air to give green amorphous precipitates. In ethyl acetate, however, a solution of the compound (I) is relatively stable as compared to the other solvents. Non-polar solvents, such as n-hexane, do not dissolve the compound.

Estrone-3-methyl ether analogously yielded a similar yellow chromium tricarbonyl complex (II) and the structure was confirmed by its infrared spectrum.

Experimental

1. Estrone chromium tricarbonyl (I)

Estrone (1.5 g, 5.5 mmole) was heated at gentle reflux under nitrogen with chromium hexacarbonyl (5.2 g, 24 mmole) in 50 ml of di-n-butyl ether and 12 ml of n-hexane. The addition of n-hexane as a solvent is to prevent sublimation of the chromium hexacarbonyl during the reaction. The reflux was continued for 72 hours and ca. 300 ml of a gas (12 mmole) was evolved. A part (1.0 g) to the greenish-brown solid (2.4 g) obtained on cooling was taken out and was reacted again with chromium hexacarbonyl (1.0 g) for 20 hours in a similar manner to complete the conversion of unreacted estrone to the π-complex. The solid obtained on cooling was removed by filtration, dried and the excess of chromium hexacarbonyl was then removed by sublimation at 60 – 80°/1 mm for 3 hours. The greenish-brown sublimation residue was for the most part dissolved in cold acetone – n-hexane mixture and the resulting yellow solution was filtered. The clear yellow filtrate was slowly evaporated under nitrogen with reduced pressure below room temperature to give yellow crystals (I) (ca. 0.7 g or 78% yield). These crystals were purified by recrystallization from cold ethyl acetate in a similar way to give an analytical sample.

Analysis: found C, 63.21; H, 5.89; Cr, 11.6%. Calculated for estrone-Cr(CO)3, C21H22Cr05 requires C, 62.06; H, 5.45; Cr, 12.79%. Molar weight: found (in CH2Br2) 485 calculated 406.4. [α]D = 154° (ethyl acetate).

The molecular weight found in dibromomethane may be indicative of some association of the molecule by hydrogen bonding, evidenced by the infrared OH stretching frequency.

2. Estrone-3-methyl ether chromium tricarbonyl (II)

Compound (II) was prepared in almost the same way as described for compound (I) and was obtained as a yellow semisolid decomposing in air at 210 – 230°. Although compound (II) was more stable in air and in solution than compound (I), it has not been obtained in nice crystalline form. It was partly crystalline and these crystals dissolved at 120 – 3°.

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