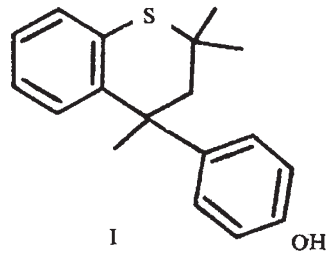
Clathration as a Practical Method for Handling Dimethylmercury

THE interest in dimethylmercury in connexion with studies of environmental pollution prompts us to report a convenient and comparatively safe method for handling this volatile and extremely toxic compound. We have found that dimethylmercury may be stored, until ready for release, in the form of an inclusion compound, the organometallic guest being accommodated in the relatively large, approximately hour-glass shaped, cavity[1,2] formed by the clathrate[3] host, 4-*p*-hydroxyphenyl-2,2,4-trimethylthiochroman (Structure I). This represents the first successful attempt to prepare a stable inclusion compound containing dimethylmercury, although diethylmercury and longer chain mercury dialkyls have been reported[4] to form inclusion compounds with urea; diethylmercury has also been included[5] in the tri-*o*-thymotide chanel structure.



The highly crystalline adduct, prepared by recrystallization of unsolvated[3] (Structure I) from neat liquid dimethylmercury (cation), is found by NMR analysis to have a molecular ratio of host to guest of 6:1 (microanalysis requires 10.35% Hg; found 10.42% Hg). This host-to-guest ratio corresponds to single occupancy[1-3] of the clathrate voids.

The crystals suffer no detectable loss of guest (NMR analysis) even when pumped for several days under vacuum, the closed nature of the clathrate cage[3] preventing escape of dimethylmercury. Grinding the crystals does, however, liberate sufficient guest to be detectable by mass spectrometry. Thus when crystals of the adduct in an evacuated flask attached to the inlet of a mass spectrometer are finely ground by using a magnet to agitate a small steel ball in the flask, the mass spectrum of dimethylmercury is observed. The minimal interference found from the spectrum of the host makes this an attractive method for obtaining mass spectra of guest molecules in clathrates.

The dimethylmercury 4-*p*-hydroxyphenyl-2,2,4-trimethylthiochroman clathrate is very convenient for preparing solutions of known concentration in dimethylmercury, preweighed quantities of the adduct merely being dissolved in the appropriate solvent.

Controlled release of organometallic guests from Structure I and other host lattices promises to be of considerable value in, for example, organic synthesis—especially where guest materials are difficult, or hazardous, to handle in the free state.

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BIOLOGICAL SCIENCES

Inhibitory Effect of Potent Interferon Preparations on the Regeneration of Mouse Liver after Partial Hepatectomy

INTERFERON exhibits a marked antitumour effect in mice inoculated with allogeneic or syngeneic transplantable tumours[1-3], but comparable interferon preparations did not affect the growth or development of newborn mice[4]. It is important from both a theoretical and a practical point of view to determine whether interferon can inhibit normal cell division in the animal. It has been shown that interferon preparations inhibited the multiplication of normal adult allogeneic spleen cells and syngeneic bone marrow cells injected into heavily X-irradiated mice[5]. Jahiel and his coworkers demonstrated that three interferon inducers, Newcastle disease virus (NDV), polyinosinicpolycytidylic acid and statolon, inhibited the mitotic response of liver cells after partial hepatectomy[6], but that administration of interferon itself did not inhibit this response[7]. Now that potent and relatively purified mouse interferon preparations are available, we have used this experimental system, and report here a marked inhibition by interferon of liver regeneration after partial hepatectomy.

Three-month-old male Ajax mice were subjected to partial hepatectomy[8]. By determining the mean weight of the $\frac{2}{3}$ of liver removed, one can estimate the weight of the residual $\frac{1}{3}$ of liver and therefore also estimate the total RNA and DNA of the residual liver[8]. Two hours after hepatectomy and at intervals thereafter, mice were injected with an interferon preparation, mock interferon or left untreated. Mouse interferon was prepared from mouse sarcoma C-243 cells[9] inoculated with NDV. The interferon preparation was concentrated and purified by ammonium sulphate fractionation and its activity assayed on L cells inoculated with vesicular stomatitis virus[2]. Omitting the interferon inducer NDV, mock interferon was prepared, concentrated and purified in a manner identical to that used in the preparation of interferon. The time and the amount of interferon inoculated are presented in the legend of Table 1. (One unit of interferon as expressed in the text is the equivalent of 4 mouse reference units.) Forty-eight hours after hepatectomy, mice were injected with 20 μCi of ^{3}H-thymidine (CEA, France) and were killed 1 h thereafter. Liver weight at 48 h is not a reliable criterion for an inhibitory effect on cell division because of varying degrees of steatosis[8], so the criteria of regeneration were: total RNA and DNA; specific activity of DNA; and the number of labelled cells (autoradiography) on microscopic examination. Determination of RNA and DNA was based on the technique of Schmidt and Thannhauser as modified by Moulé[10].

Repeated injections of partially hepatectomized mice with potent interferon preparations did not result in any increased postoperative mortality. Two experimental findings indicated that treatment of mice with interferon resulted in a marked inhibition of the synthesis of both total RNA and DNA. (1) The total amount of RNA and DNA present in the livers of control mice had increased at 48 h after operation, whereas the amount of RNA and DNA present in the livers of mice treated with interferon did not increase (comparison of the mean values at 0 h and 48 h: Table 1). (2) After a pulse of 1 h with ^{3}H-thymidine the specific activity of DNA of the livers of control mice was much higher than that of mice treated with interferon (Table 1). (The finding that the amount of radioactivity present in the acid-soluble fraction was virtually the same for both control and interferon treated mice indicates that the block was in synthesis of DNA and not in precursor incorporation.) Synthesis of RNA precedes

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