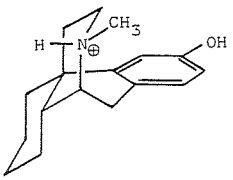
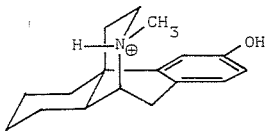
03.4–2 CRYSTAL STRUCTURES OF TWO INTERMEDIATES IN THE SYNTHESIS OF SULFONIUM ANALOGS OF LEVORPHANOL AND ISOLEVORPHANOL. By F.R. Ahmed, Division of Biological Sciences, National Research Council of Canada, Ottawa, Canada K1A 0R6.

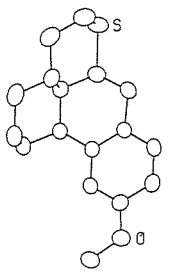
B. Belleau, of McGill University, is investigating the exact role of the N-proton and its directionality in the opiate receptor's response to agonists and antagonists. To conduct this study he has elected to synthesize sulfonium analogs of the potent narcotic analgesics levorphanol 1 and isolevorphanol 2, the rationale being that whereas N-quaternary salts are not stereoelectronically equivalent to tertiary amine salts, sulfonium cations are virtual isosteres of the latter as ion pair-forming entities except for their complete inability to accept a proton. Pharmacological tests on these analogs would therefore aid in the evaluation of the separate roles of ion pairing and of H-bond complex formation at the acceptor site level of the receptor. The synthetic procedure yielded two intermediates which could not be identified except through an X-ray crystallographic analysis, which showed them to be compounds 3 and 4. Their crystal structures are the subject of this presentation.



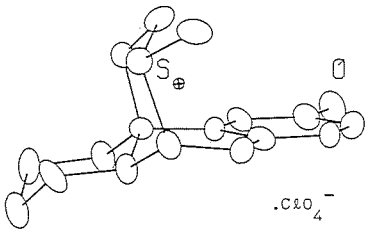
1 Levorphanol



2 Isolevorphanol



3 $C_{17}H_{22}OS$



4 S-Methyl isosulforphanol perchlorate, $C_{17}H_{23}OS^{+}.ClO_4^{-}$

Compound 3, M_r = 274.4, is produced as the minor component and forms tabular crystals which are monoclinic, $P2_1/a$, a = 17.080(2), b = 9.372(1), c = 9.327(1) Å, β = 108.67(1)°, V = 1414.44 Å^3, Z = 4, D_c = 1.288 g cm^{-3}. The structure was determined by the symbolic addition procedure and refined by block-diagonal least squares to R = 0.034 for 2542 observed reflections. The S–C bonds are 1.813(2) and 1.822(2) Å with C–S–C = 98.6(1)°.

Compound 4, M_r = 374.9, is the major component and forms small crystals resembling a fish bone. The unit cell is orthorhombic, $Pna2_1$, a = 10.934(1), b = 9.219(1), c = 17.131(1) Å, V = 1726.8 Å^3, Z = 4, D_c = 1.442 g cm^{-3}. The structure was solved by the heavy-atom method, and refined to R = 0.07 (excluding the H atoms) for 1017 observed reflections. Further refinement is in progress. The S–C bonds are 1.85(1), 1.84(2) and 1.76(2) Å, and the endocyclic C–S–C = 99.5(6)°. The hydroxyl group and the perchlorate are interlinked through a hydrogen bond, O···O = 2.79(2) Å.

03.4–3 METAL ION INTERACTIONS WITH VITAMINS. BIOTIN-SILVER(I) COMPLEXES CONTAINING VERSATILE METAL BONDING MODES. By K. Aoki and W. Saenger, The Institute of Physical and Chemical Research, Wako-shi, Saitama 351, Japan and Institut für Kristallographie, Freie Universität Berlin, Takustrasse 6, D-1000 Berlin 33, F.R.G.

Biotin (vitamin H) dependent-carboxylases require divalent metal ions such as Mg^{2+}, Mn^{2+}, Co^{2+}, Zn^{2+}, or Cu^{2+} for carboxylation of biotin with HCO_3^- and ATP. In order to gain basic stereochemical informations on metal ion interactions with biotin that could bear on the mechanism of biotin's biochemical actions, we have undertaken an X-ray study of metal complexes of biotin (J. Inorg. Biochem. (1983), 19, 269-273). We compare here various metal bonding modes observed in the three silver(I)-biotin complexes, $[Ag(biotin)(NO_3)]\cdot 0.5H_2O$ (1), $[Ag_{0.5}(biotin)]\cdot(PF_6)_{0.5}$ (2), and $[Ag(biotinato)]\cdot 1.5H_2O$ (3), the first of metal ion-biotin complexes, and discuss possible roles of metal ions in enzymatic processes.

The complex (1) is a two-dimensional polymer, where the Ag^+ atom is tetrahedrally bonded to three different biotin molecules via two thioether S1 atoms in cis and trans direction with respect to the ureido ring and via one ureido carbonyl O2' atom, and also bonded to a nitrate oxygen. The complex (2) is two-dimensionally polymeric with the Ag^+ atom tetrahedrally bonded to four biotin molecules through two S1 atoms with only cis arrangement and through two carboxyl oxygens. The complex (3) is a three-dimensional polymer, in which the Ag^+ atom is five-coordinated to four biotin molecules via cis and trans S1 atoms, one carbonyl O2', and via two deprotonated carboxylate oxygens of one molecule. The most interesting structural feature common to these complexes is the cis metal bonding to the thioether S1 atom, because such a bonding has been believed to be unfavorable due to the bulkiness of the metal ion. The attachment of the metal ion to the ureido carbonyl O2' reveals the nucleophilic nature of O2'

As possible roles of metal ions in the carboxylation reaction catalized by carboxylases the following should be considered: i) metal ion-carbonyl O2' bonding activates N1', a site of carboxylation, via polarization mechanism, and/or fixes the substrate HCO_3^- near to N1' through the O2'-metal-HCO_3^- ternary complex formation, ii) metal ion-thioether S1 cis bonding fixes HCO_3^- near to N1', or iii) metal ion-thioether S1 trans bonding fixes the biotin moiety to the active site of the enzyme through the S1-metal-enzyme ternary complex formation, and/or regulates the conformation of the valeric acid chain through interligand interactions (the conformational change of this side chain has been postulated to be essential for CO_2 translocation) Research supported in part by the Alexander von Humboldt Foundation.