

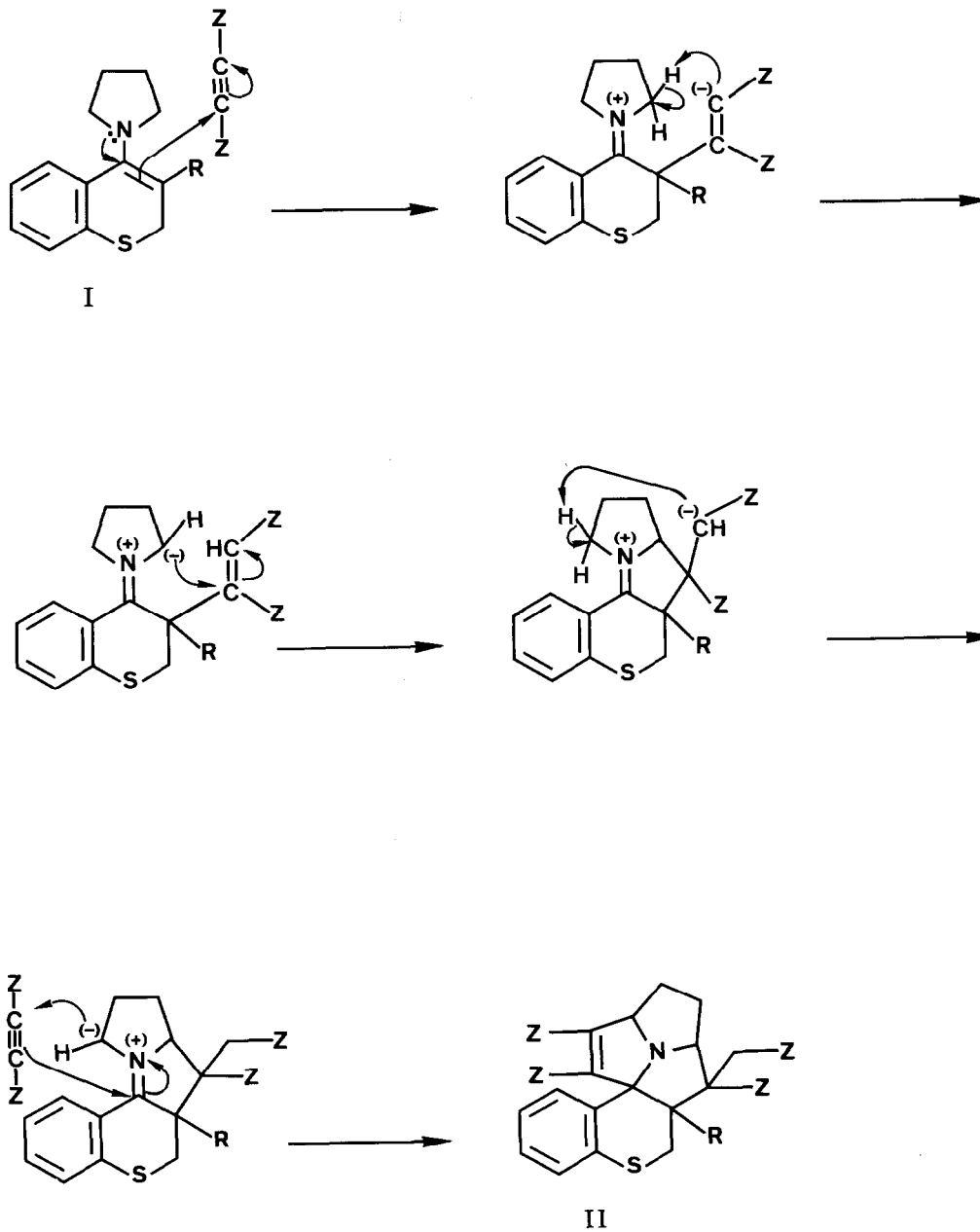
STRUCTURE OF THE 2 : 1 ADDUCT OF DIMETHYL
ACETYLENEDICARBOXYLATE AND THE PYRROLIDINE
ENAMINE OF 3-METHYLTHIOCHROMAN-4-ONE: A
NOVEL PENTACYCLIC SYSTEM

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Abstract: The structure of the 2 : 1 adduct of dimethyl acetylenedicarboxylate and 3-methyl-4-(1-pyrrolidinyl)-2H-thiochromene has been determined by single-crystal X-ray diffraction.

In previous work, the [2+2] cycloaddition of dimethyl acetylenedicarboxylate (DMAD) to the pyrrolidine enamine of thiochroman-4-one was described.¹ Electrocyclic rearrangement of the cyclobutene adduct initially formed leads to an eight-membered ring compound, 4,5-bis-methoxycarbonyl-6-(1-pyrrolidinyl)-2H-benzo[b]thiocin. We now report the unexpected outcome of the reaction between DMAD and 3-methylthiochroman-4-one pyrrolidine enamine. In tetrahydrofuran (THF) solution, a compound with the molecular composition corresponding to a 2 : 1 adduct, C₂₆H₂₉NO₈S, was obtained in 23 % yield. The 270 MHz ¹H NMR spectrum gave some clues to the structure, but the final solution was provided by X-ray crystallography.

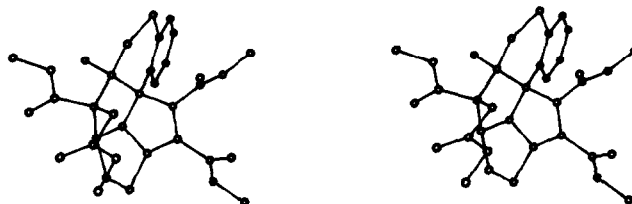
A formation route, the details of which have been inspired by recent work by other groups,^{2,3} is shown in the Scheme. Nucleophilic attack of the enamine on DMAD yields a zwitterionic intermediate. Rather than forming a cyclobutene ring, the vinylic carbanion abstracts one of the pyrrolidine α protons. Michael addition of the negative terminal of the ylid thus formed on the unsaturated ester side chain gives a pyrrolizine system. A second proton transfer from the opposite α position of the pyrrolidine ring gives a



new ylid. The latter, resonance stabilized by the adjacent π bond, undergoes 1,3-dipolar cycloaddition with a second molecule of DMAD to yield the stable final product, 1,2a,3,3a,4,11a-hexahydro-3-(2-methoxy-2-oxoethyl)-3a-methyl-2H-[1]benzothiopyrano[3,4-b]pyrrolo[2,1,5-cd]pyrrolizine-3,10,11-tricarboxylic acid trimethyl ester. A stereographic picture of one molecule is provided in the Figure. The molecule is chiral, and furthermore, the edge containing the dimethyl succinate part and the adjacent bridgehead methyl group could, in principle, give rise to diastereoisomerism. It is seen that the methoxycarbonyl group on carbon 3 and the methyl group on carbon 3a are on the same side of the ring periphery.

Literature procedures were followed to prepare 3-methylthiochroman-4-one⁴ and its pyrrolidine enamine.⁵ A solution of 14.2 g (100 mmol) of DMAD in 20 ml of dry THF was added during 1 h at 0 °C under nitrogen to a solution of 20.7 g (90 mmol) of enamine in 80 ml of dry THF. After 24 h at room temperature, the solvent was evaporated at reduced pressure, and ether was added. A solid product separated, which was recrystallized from acetonitrile to give 6 g (23 %) of colourless needles, m.p. 264-265 °C, ¹H NMR (270 MHz, CDCl₃): δ vs. TMS 1.04 (3H, s), 1.21-1.29 (1H, m), 1.85-1.90 (1H, m), 2.34-2.47 (2H, m), 2.87 (1H, d, J 11.4 Hz), 3.18 (2H, AB, J 17.5 Hz), 3.63 (3H, s), 3.69 (3H, s), 3.70 (3H, s), 3.73 (3H, s), 3.89 (1H, d, J 11.4 Hz), 4.63 (1H, d, J 5.9 Hz), 5.06 (1H, m), 7.01-7.11 (3H, m) and 7.34-7.37 (1H, m). The MS parent peak was at 515.1595, calc. for C₂₆H₂₉NO₈S: 515.1614.

The crystal chosen for X-ray study had the dimensions 0.3 x 0.05 x 0.03 mm. It was triclinic, space group P $\bar{1}$, $a = 8.246(3)$, $b = 11.115(6)$, $c = 14.035(7)$ Å, $\alpha = 88.98(5)$, $\beta = 104.84(4)$, $\gamma = 91.62(4)^\circ$, $U = 1243(1)$ Å³, $F(000) = 544$, $Z = 2$, $D_c = 1.38$ Mg m⁻³, $\mu(\text{Mo K}\alpha) = 1.86$ cm⁻¹. The data, collected on a Syntex P2₁ diffractometer, gave 3015 independent reflections with $I > 3\sigma(I)$. The structure was solved with the program MULTAN 80 which revealed the positions of all non-hydrogen atoms.⁶ The atomic positions of 27 hydrogen atoms were found after least-squares refinement and difference Fourier syntheses. The final refinement cycle included isotropic and anisotropic thermal parameters for the hydrogen and non-hydrogen atoms, respectively. The final R-value was 0.054 (R_w 0.055). The atomic coordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW.



Stereographic picture of one molecule of
2 : 1 adduct.

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