455. *Steroids. Part XXVI.* Virtual Allylic Coupling in the 60 Mc. n.m.r. Spectrum of 7,7-Ethylenedithiocholest-4-en-3-one*

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7,7-Ethylenedithiocholest-4-en-3-one (III) was prepared in order to isolate an allylic spin system of three protons [$H_{(4)}$ and the methylene protons at C-6]. The 60 Mc. n.m.r. spectrum of (III) indicates that virtual coupling between $H_{(4)}$ and equatorial $H_{(6)}$ is taking place; this effect is absent in the essentially first-order, 100 Mc. spectrum of (III).

THE steric requirements for effective allylic coupling have been established by studies of coupling between $H_{(4)}$ and $H_{(6)}$ in a series of 6-substituted cholest-4-en-3-ones.[1-5] With compounds unsubstituted at C-6, the signals due to $H_{(4)}$ appear as unresolved [2,3] multiplets instead of the expected doublets, and this has been rationalised [2,3] in terms of virtual coupling [6,7] of the $H_{(4)}$ proton with the equatorial proton at C-6. However, owing to the overlap of the signals due to the methylene protons at C-6 by other signals, and to further coupling between protons on C-6 and C-7, this spin system could not be analysed. In order to isolate the three-spin system [$H_{(4)}$ and methylene at C-6], we have synthesised 7,7-ethylenedithiocholest-4-en-3-one (III).

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* Part XXV, C. W. Shoppee, F. P. Johnson, R. E. Lack, and S. Sternhell, preceding Paper.

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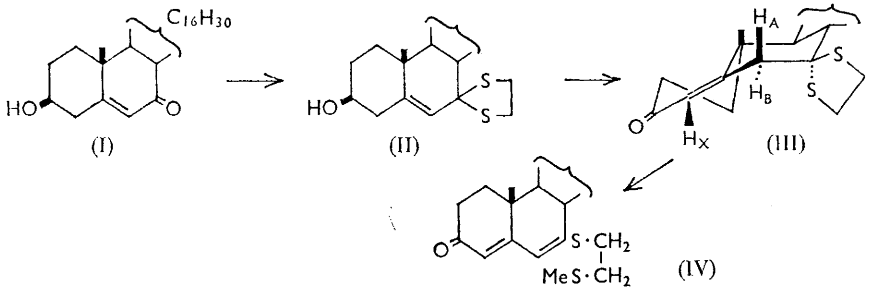
Treatment of 7-oxocholesterol (I) with boron trifluoride etherate and ethanedithiol gave the thioketal (II), converted by Oppenauer oxidation into 7,7-ethylenedithiocholest-4-en-3-one (III). The 60 Mc. n.m.r. spectra of (I) and (II) both showed unresolved multiplets for the vinylic protons, whilst the signals assigned to the methylene protons at C-4 were observable as two signals downfield from the bulk of the resonance due to the remaining protons. In each case, the upfield signal was assigned to the axial $H_{(4)}$ proton,[8] and, in confirmation, this signal was broader [large axial–axial coupling with axial $H_{(3)}$ proton] than that assigned to the equatorial $H_{(4)}$ proton.



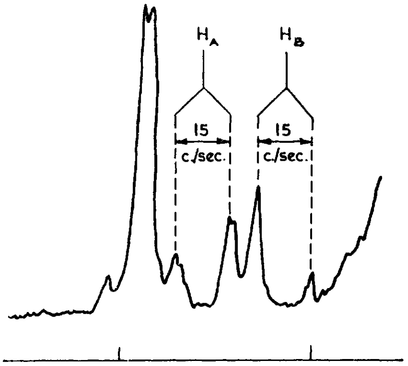


FIGURE 1. A portion of the 60 Mc n.m.r. spectrum of 7,7-ethylenedithiocholest-4-en-3-one (III)

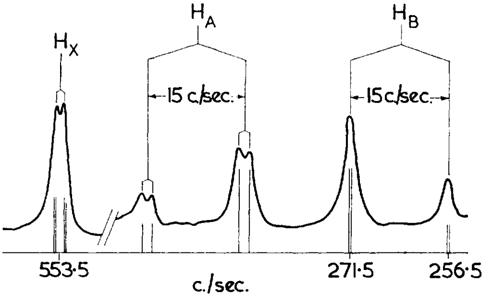


FIGURE 2. A portion of 100 Mc. n.m.r. spectrum of 7,7-ethylenedithiocholest-4-en-3-one (III). The calculated spectrum is shown below the experimental spectrum [Frequencies are c./sec. from tetramethylsilane]

The 60 Mc. n.m.r. spectrum of (III) showed the signal assigned to the vinylic proton (H_X) as an unresolved multiplet at τ 4·50 with W_H 2·7 c./sec., and the signals due to the methylene protons at C-6 as a multiplet, partially overlapped by signals due to the ethylenedithio-group and the main resonances of the other steroid protons (Figure 1). The assignment shown in Figure 1 is based on the expectation of larger allylic coupling between the axial proton at C-6 and $H_{(4)}$ (J_{AX}) than between the equatorial proton at C-6 and $H_{(4)}$ (J_{BX}); it is interesting to note that this leads to the assignment of the upfield portion of the signal to the equatorial protons, *i.e.*, the reverse of the usual order.[8] A similar phenomenon has been noted with a number of α-halogenoketones.[9,10]

The 100 Mc. spectrum of (III) (Figure 2) showed the vinylic proton (H_X) as a doublet, and

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in addition revealed all the resonances due to the methylene protons at C-6. This spectrum, which is essentially first-order, is a good fit (Figure 2) with an ABX pattern calculated[11] by use of the following parameters: J_{AB} 15 c./sec.; ν_{AB} 28 c./sec.; J_{AX} 1·5 c./sec.; ν_{AX} 288 c./sec.; J_{BX} 0. In particular, the calculated X part consists of four lines of approximately equal intensity with the separation between the inner pair of 1·3 c./sec. and the separation of the outer pair of 1·5 c./sec. Using these parameters, adjusted for change of frequency, to calculate the 60 Mc. spectrum of (III) gives the X part as four lines with separation of the inner pair of 1·1 c./sec. and the separation of the outer pair of 1·5 c./sec. Clearly, this pattern would be more difficult to resolve, and thus it is not unexpected that the 60 Mc. spectrum of (III) shows the signal due to the vinylic proton (H_X) as an unresolved multiplet.

We therefore consider the 60 Mc. spectrum of (III) as an example of virtual coupling, and, by analogy, this is the most likely cause of the unresolved nature of the signals due to $H_{(4)}$ in cholest-4-en-3-one[2] and related compounds.[3]

In an attempt to prepare 7,7-ethylenedithio-4-methylcholest-4-en-3-one and so to isolate the corresponding homoallylic system,[5,12,13] the ketone (III) was treated with potassium t-butoxide and methyl iodide.[14] However, opening of the thioketal ring occurred, to give (IV).

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus. Ultraviolet spectra (in ethanol) and infrared spectra (in carbon tetrachloride) were measured with Perkin-Elmer 4000 A and Perkin-Elmer 221 spectrophotometers, respectively. 60 Mc. n.m.r. spectra were obtained for deuteriochloroform solutions on a A Varian 60 spectrometer using tetramethylsilane as internal reference; the 100 Mc. spectrum of compound (III) was obtained for a carbon tetrachloride solution on a DP 100 spectrometer calibrated by the usual sideband technique.

7,7-*Ethylenedithiocholest*-5-*en*-3β-*ol* (II).—7-Oxocholesterol[15] (I) (1·5 g.) was triturated with ethanedithiol (1·5 ml.) and boron trifluoride etherate (1·5 ml.). After 5 min., methanol was added and the resulting solid, after filtration and drying, introduced on to alumina (40 g.) in ether–benzene (1 : 9). Elution with ether–benzene and ether–chloroform gave the *product* (II) (1·3 g.), m. p. 189° (from ethanol), whose n.m.r. spectrum showed: a singlet for 3 protons at τ 9·00 (C-19 Me); a singlet for 3 protons at τ 9·30 (C-18 Me); a multiplet at τ 6·67 (protons of thioketal group); a multiplet at τ 4·42, peak width at half height (W_H) 2·6 c./sec. (olefinic 6-proton) [Found (after drying at 90°/0·01 mm. for 48 hr.): C, 72·8; H, 10·1. $C_{29}H_{48}OS_2$ requires C, 73·05; H, 10·15%].

7,7-*Ethylenedithiocholest*-4-*en*-3-*one* (III).—The alcohol (II) (1 g.) was dissolved in toluene (75 ml.) and cyclohexanone (25 ml.), and toluene (25 ml.) was distilled off under reduced pressure to dry the system. Aluminium isopropoxide (1·5 g.) was added, and the solution refluxed for 20 min. Rochelle salt solution was added, and solvents removed by steam-distillation. Ether extraction gave an oil, which was introduced on to alumina (35 g.) in hexane. Elution with ether–benzene (1 : 1) gave the *product* (III) (670 mg.), m. p. 154° (from ethanol), $\nu_{max.}$ 1676 cm.$^{-1}$. The n.m.r. spectrum showed: a singlet for 3 protons at τ 8·81 (C-19 Me); a singlet for 3 protons at τ 9·26 (C-18 Me); a multiplet at τ 6·80 (protons of thioketal group); a multiplet at τ 4·50, W_H 2·7 (olefinic 4-proton) [Found (after drying at 20°/0·1 mm. for 12 hr.): C, 73·3; H, 9·8. $C_{29}H_{46}OS_2$ requires C, 73·35; H, 9·8%].

7-(2′-*Methylthioethyl*)*thiocholesta*-4,6-*dien*-3-*one* (IV).—The ketone (III) (496 mg.) was dissolved in benzene (15 ml.), and solutions of potassium (150 mg.) in t-butyl alcohol (5 ml.), methyl iodide (1·5 ml.) in benzene (40 ml.), and t-butyl alcohol (40 ml.) were added.[13] After refluxing for 3 hr., solvents were removed under reduced pressure; ether extraction gave an oil, which was introduced on to silica gel (40 g.) in benzene. Elution with ether–benzene (1 : 19) gave the *product* (IV) (250 mg.), m. p. 121° (from ethanol), $\lambda_{max.}$ 244, 345 (log ε 3·72, 4·41), $\nu_{max.}$

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1642, 1580 cm.$^{-1}$. The n.m.r. spectrum showed a singlet for 3 protons at τ 8·92 (C-19 Me); a singlet for 3 protons at τ 9·23 (C-18 Me); a singlet at τ 7·84 (protons of thiomethyl group); two narrow multiplets at τ 4·10 and 4·40 (olefinic protons) [Found (after drying for 4 hr. at 70°/0·5 mm.): C, 73·25; H, 10·25%; *M* (mass spectrometry), 488. $C_{30}H_{48}OS_2$ requires C, 73·75; H, 9·95%; *M*, 488].

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