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Nuclear Magnetic Resonance of Semicarbazones and Thiosemicarbazones of an Aliphatic Aldehyde[1]

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In the previous report,[3,4] it was described that leucomycin A_3, a family of macrolide antibiotic, contains an aliphatic aldehyde group such as $-CH_2CHO$, from the value of the ultraviolet absorption and nuclear magnetic resonance (NMR) spectra of the thiosemicarbazone of leucomycin A_3. Evans and Gillam[5] studied the ultraviolet absorption spectra of aldehydes, and those of their semicarbazones and thiosemicarbazones, and showed that the thiosemicarbazones of saturated aldehydes exhibit absorption bands near 270 mμ which are some 500 times more intense than those of the parent carbonyl compound. It would therefore seems necessary that simple type of thiosemicarbazones of saturated aldehydes have absorption at around 230 and 270 mμ. Table I shows the corresponding ultraviolet absorption data on the thiosemicarbazones of leucomycin A_1 and A_3, magnamycin B,[6] and spiramycin B,[7] and it is clear from these data that the results closely parallel those of analogous saturated aldehydes.

On the other hand, our interest in the problems of NMR on the multiplicity and coupling constant of the aldehyde proton of luecomycin A_3[3,4] have led us to examine the NMR spectra of the thiosemicarbazones and semicarbazones of aliphatic aldehydes. Because of a very small coupling constant of the aldehyde itself (1—3 cps),[8] these derivatives are suitable not only for calculating the coupling constant by the enlargement of the coupling constant to 4—7 cps, but also give bands in the region of 7—8 ppm[9] by the shielding effect of derivatives. Bhacca and Williams[10] indicated the aldehyde proton resonance in the NMR spectrum of 20-formylprogn-4-en-3-one, and its chemical shift and 9.58 ppm and the coupling constant to C-20 methine hydrogen was 3 cps. Karabatsos and his co-workers[8,9,11] studied the conformation and configuration of several aldehydes and ketones, and their oxime O-methyl ethers, and N-methylphenylhydrazones.

In the present investigation, the coupling constant of the aldehyde proton to hydrogens attached to the neighboring carbon atom was studied in the NMR spectra of saturated aliphatic aldehydes, and their thiosemicarbazones and semicarbazones. The obtained data are summarized in Tables I and II.

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Kuehne and Benson[12] have recently reported that magnamycin A and B had shown a singlet aldehyde proton (9.50 ppm), while spiramycins had shown a doublet at 9.65 ppm. This observation initially suggested the structure of magnamycin would require an aldehyde function attached to a quaternary carbon atom, and spiramycin would require an aldehyde attached to a secondary carbon atom. In the case of leucomycins, the expected aldehyde proton triplet could not be observed and was indicated as a poor split in Table I. However, conversion of leucomycin A_1 and A_3, and magnamycin B to their thiosemicarbazones resulted in the splitting appearing as the expected triplet at 7.00, 7.62, and 7.12 ppm (J=5.0—5.1 cps), respectively.

The NMR spectrum of spiramycin B shows a doublet at 9.80 ppm (J=3.0 cps). The thiosemicarbazone of spiramycin B shows the band at 7.28 ppm (J=5.4 cps) in dioxan.

The thiosemicarbazone of chloral had already been shown to have the true hydrate structure from its infrared spectral studies.[13] This was confirmed from the NMR spectra.

Table I. Uutraviolet Absorption and NMR Spectra of Aldehydes and Their Thiosemicarbazones

Compound Secondary aldehyde ($R\cdot CH_2CHO$) R	Thiosemicarbazone mp (°C)	Ultraviolet absorption λ_{max}^{EtOH} mμ (log ε)	NMR (ppm, cps) Aldehyde in CCl_4	Thiosemicarbazone in Me_2SO	in dioxan
H	148—149	241 (3.98), 269 (4.04)	9.66 q. 2.8[a]	7.49 q. 5.2	7.30 q. 5.4
CH_3	155—156	229 (3.88), 270 (4.38)	9.70 t. 1.5	7.48 t. 4.2	7.28 t. 5.4
C_2H_5	109—110	230 (3.89), 270 (4.74)	9.69 t. 1.5	7.42 t. 5.1	7.27 t. 5.1
n-C_3H_7	66	230 (3.98), 271 (4.47)	9.66 t. 1.8	7.47 t. 5.1	7.28 t. 5.1
iso-C_3H_7	48	230 (3.99), 270 (4.44)	9.72 t. 1.8	7.47 t. 5.1	7.24 t. 4.5
n-C_5H_{11}	89— 90	230 (3.93), 271 (4.40)	9.67 t. 1.5	7.46 t. 5.1	7.28 t. 5.1
n-C_6H_{13}	65— 66	230 (3.98), 271 (4.37)	9.61 t. 1.5	7.45 t. 5.4	7.29 t. 5.1
n-C_7H_{15}	77— 78.5	230 (4.01), 271 (4.45)	9.68 t. 1.5	7.46 t. 5.1	7.26 t. 5.4
Leucomycin A_1	158—162	228 (4.48), 269 (4.33)			7.00 t. 5.1
Leucomycin A_3	138—141	232 (4.54), 271 (4.37)	9.56 poor split		7.62 t. 5.0
Magnamycin B	135—138	235 (3.98), 273 (4.60)	9.58 poor split		7.12 t. 5.1
Tertiary aldehyde $\left(\begin{matrix}R\\R\end{matrix}\!\!>\!CHCHO\right)$					
CH_3	86— 87	230 (3.85), 270 (4.28)	9.54 d. 0.6	7.40 d. 5.4	7.26 d. 5.4
C_2H_5	92— 93.5	230 (3.83), 270 (4.32)	9.46 d. 1.2	7.31 d. 6.6	7.20 d. 6.0
Spiramycin B	151—155	230 (4.55), 270 (4.35)	9.80 d. 3.0		7.28 d. 5.4
Quaternary aldehyde $\left(\begin{matrix}R\\R\text{-}CCHO\\R\end{matrix}\right)$					
CH_3	113—114	228 (3.81), 270 (4.33)	9.37 s.	7.33 s.	7.13 s.
Cl	122—123[b] (decomp.)	245 (4.02)	8.96 s.	7.40 d. 5.4	not soluble

a) in deuteriochloroform b) reported[13] mp 104—105° (decmp.)

Table II. Ultraviolet Absorption and NMR Spectra of Aldehydes and Their Semicarbazones

Compound	mp (°C)	Ultraviolet absorption λ_{max}^{EtOH} mμ (log ε)	NMR (ppm, cps) Aldhyde in CCl_4	Semicarbazone in Me_2SO	in dioxan
CH_3CHO	160—161	230 (4.08)	9.66 q. 2.8	7.11 q. 5.4	not soluble
$CH_3(CH_2)_4CHO$	109—110	230 (4.07)	9.67 t. 1.5	7.13 t. 5.4	7.01 t. 5.4
$(CH_3)_2CHCHO$	123—124	234 (4.09)	9.54 poor split	7.06 d. 4.8	6.97 d. 5.4
$(CH_3)_3CHO$	194	228 (4.08)	9.37 s.	7.33 s.	7.13 s.

12) M.E. Kuehne and B.W. Benson, *J. Am. Chem. Soc.*, **87**, 4660 (1965).
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Chloral itself showed the expected aldehyde proton singlet at 8.96 ppm, but the chloral thiosemicarbazide showed the elusive splitting as a doublet at 7.40 ppm (J=5.4 cps).

Experimental[14]

Semicarbazones and Thiosemicarbazones——Derivatives were prepared by the usual procedures.[15] Their melting point, ultraviolet absorption, and NMR spectral data are summarized in Tables I and II.

14) All melting points are uncorrected. The NMR spectra were obtained with Hitachi H-60 spectrometer at 60 Mc and tetramethylsilane was used as an internal reference.
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Studies on the Azasteroids and Related Compounds. IV.[1] Reactions of 1,2,3,4,6a,7,8,9,10,10a-Decahydro-6*H*-benzo[*c*]quinolizin-6-one

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In continuation of our synthetic studies on 14-azasteroids,[1,3,4] which included preparation and some reactions of B/C *trans* fused dodecahydro-6*H*-benzo[*c*]quinolizin-6-one (I), we now describe angular methylation at C-4a position of I and attempt to prepare the benzo[*c*]quinolizine derivatives with functional group at C-4 position which corresponds to C-17 position in natural steroid structure, from the compound (I).

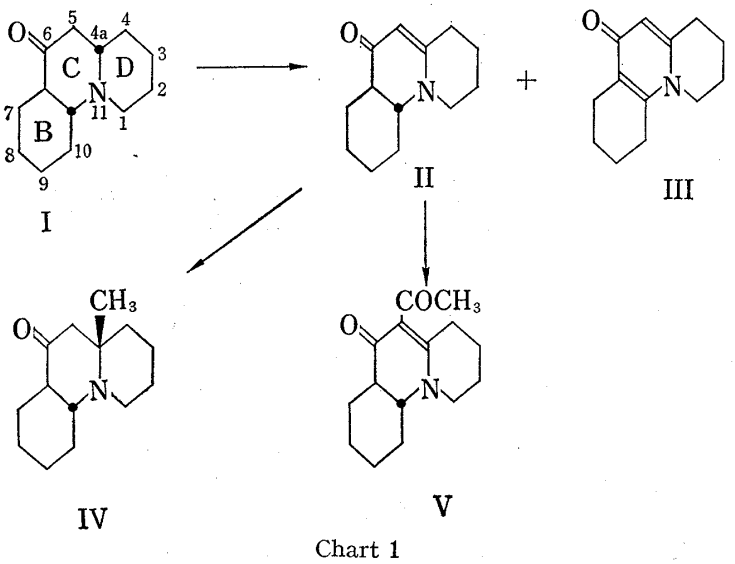

Chart 1

Dehydrogenation of the quinolizidinone (I) with mercuric acetate in 35% acetic acid solution afforded a mixture of decahydrobenzo[*c*]quinolizin-6-one (II) and the γ-pyridone (III). The former was methylated at the angular position

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