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^{13}C Nuclear Magnetic Resonance Assignments for α- and β-Carbons of Thiacycloalkanes using α,α-Dideutero Derivatives[1]

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The ^{13}C nuclear magnetic resonance chemical shifts for α- and β-carbons of simple thiacycloalkanes, namely thietane, thiolane, thiane and thiepane, have been completely and unambiguously assigned by using α,α-dideutero compounds; the α-carbon signal, except for thietane, always appeared at lower field than that of the β-carbon.

Keywords——^{13}C NMR; thiacycloalkanes; thietane; thiolane; thiane; thiepane; lithium aluminum deuteride; α,α-dideuterothiacycloalkanes

Generally, in carbon-13 nuclear magnetic resonance (NMR) spectra, it has been well established that increased s-orbital character of a carbon atom caused a lower field chemical shift when recorded in the complete proton noise decoupling mode and a larger coupling constant, J_{C-H} of the carbon-hydrogen bond, normally using the NOE mode,[2] Hitherto, by utilizing these basic criteria, the chemical shifts of various 5- and 6-membered heteroaromatics[3] were fully established that except for thiophene, α-carbon signals in general appear in the lower field than β-carbon signals, whereas in case of the corresponding saturated counterparts[3] some aza- and oxacycloalkanes were easily assigned since the α-carbons to heteroatoms resonated at a by far lower field than the β-carbons, in accordance with their electronegativities.[4] However, in thiacycloalkanes, especially in the thiolane and thiane series, the problem that the extremely small difference in electronegativity[4] between sulfur and carbon atoms, unfortunately, have made only the "tentative" chemical shift assumption possible continues to be puzzling, so that this situation prompted us to present our unambiguous carbon-13 assignments of thiacycloalkanes.[3a,5]

Assignments were performed on the following important and well-known effects when hydrogen atom attached to the carbon in question is replaced by a deuterium atom.[6] 1)

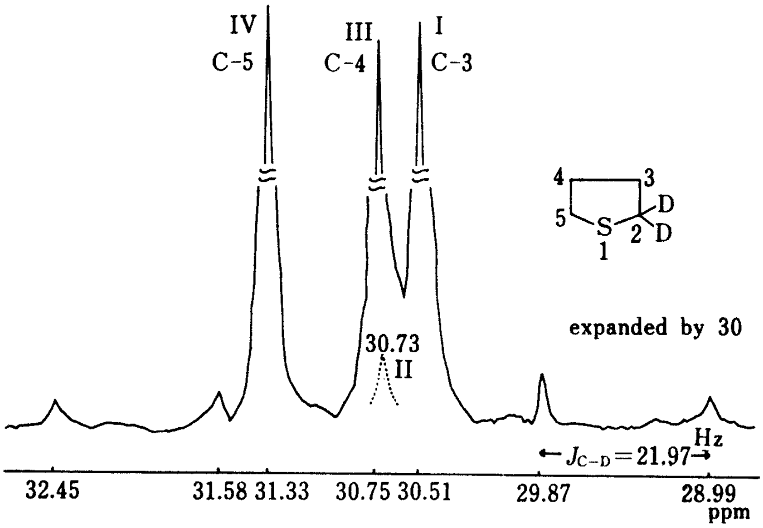
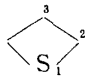
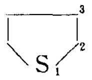
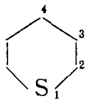
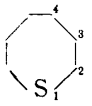


Fig. 1. ^{13}C NMR Spectrum of 3 M Solution in $CDCl_3$ of 2,2-Dideuterothiolane using Complete Proton Noise Decoupling Mode at 25.0 MHz, 22°C

Disappearance of the original carbon-13 signal. 2) Appearance of a characteristic carbon-13 splitting pattern due to the magnetic moment of deuterium atom. 3) For mono-deuterated carbon and the adjacent carbon, carbon-13 chemical shifts show upfield shifts by 0.29 ppm and 0.1 ppm, respectively, which are so-called α- and β-deuterium isotopic effects.

As shown in Fig. 1 for 2,2-dideuterothiacyclopentane (thiolane), according to non-equivalency by inducing deuterium atom, there appeared three normal intensity singlet signals I (30.51 ppm), III (30.75 ppm) and IV (31.33 ppm) and also the very small and broad quintet, II centered at 30.73 ppm (calculated). These newly appeared signals I and II (quintet) were assigned to carbon-3 and carbon-2 since the chemical shift differences between II and IV and I and III were 0.60 ppm and 0.24 ppm, respectively, which are well consistent with the isotopic effects expected for two deuterium atoms (see effect 3 above), as shown in Table I. Moreover, taking account of both nuclear spin or angular momentum and the coupling constant between carbon-13 and deuterium which generally lies in around 21 Hz,7) the quintet, II should arise from carbon-2. In a similar manner, other thiacycloalkanes were thus completely assigned and the results are summarized in Table I.

Table I. Chemical Shifts and Coupling Constants for α,α-Dideuterated Thiacycloalkanes in $CDCl_3$ a)

Compound	Carbon atom	δ_C		Δ b)	J_{C-D}
		Original	Deuterated		
 Thietane	C-2	25.34	24.75	0.59	21.97
	C-3	27.38	27.14	0.24	
 Thiolane	C-2	31.33	30.73	0.60	21.97
	C-3	30.75	30.51	0.24	
 Thiane	C-2	28.80	28.20	0.60	20.75
	C-3	27.48	27.24	0.24	
	C-4	26.22	26.22		
 Thiepane	C-2	33.33	32.74	0.59	20.69
	C-3	31.19	30.95	0.24	
	C-4	26.61	26.61		

a) Chemical shifts are given in ppm (δ_C) relative to internal TMS and coupling constants in Hz.

b) Differences (ppm) between oirginal δ_C and deuterated δ_C.

In conclusion, the α-carbon signal in the carbon-13 NMR spectra except in the case of thietane, always appeared at lower field than the β-carbon signal in a series of simple thiacycloalkanes.

Experimental

All complete proton noise-decoupled ^{13}C NMR spectra were recorded in $CDCl_3$ (3 M solution) at 22±0.1°C on a JEOL JNM-FX 100 spectrometer operating at a frequency of 25.0 MHz by the Fourier transform technique. The chemical shifts are expressed in parts per million relative to internal TMS with an accuracy of at least 0.06 ppm and a pulse width of 3 μs was found to be adequate for a frequency range of 5000 Hz. All starting chemicals (β-propiolactone, γ-butyrolactone, δ-valerolactone and ε-caprolactone) were of commercial source and were distilled shortly prior to use. Lithium aluminum deuteride (min. 98%) was purchased from E. Merck, Darmstadt. All boiling points are uncorrected and the procedures described below are representative of those used in the preparation of all the deutero compounds listed in Table I.

2,2-Dideuterothiacyclopentane (2,2-Dideuterothiolane): General Procedure[8]——(1) The γ-butyrolactone (0.2 mol) in dry tetrahydrofuran (20 ml) was dropwise added to an ice-cold tetrahydrofuran suspension (140 ml) of lithium aluminum deuteride (0.1 mol) over a period of 30 min and then the resulting suspension was refluxed for 3 h with vigorous stirring. The suspension was chilled down to ice temperature, and to this were carefully added in small portions H_2O (4.2 ml), 15% aq. NaOH (4.2 ml) and H_2O (12.5 ml) successively. The filtered tetrahydrofuran solution was dried ($MgSO_4$) and concentrated *in vacuo* and distillation of the residual viscous oil under diminished pressure furnished colorless pure 1,1-dideuterobutane-1,4-diol (0.17 mol, 85%), bp 132°C (17 Torr).

(2) Phosphorus tribromide (0.16 mol) was dropwise added to 1,1-dideuterobutane-1,4-diol (0.16 mol) under ice-cooling with stirring, and then the whole mixture was heated at 100°C for 3 h, during which time hydrogen bromide gas was violently evolved. Distillation under aspirator pressure gave a small first fraction of excess phosphorus tribromide, followed by colorless pure 1,4-dibromo-1,1-dideuterobutane (0.145 mol, 91%), bp 81°C (17 Torr).

(3) Both finely ground sodium sulfide nonahydrate (0.13 mol) and 1,4-dibromo-1,1-dideuterobutane (0.13 mol) were dissolved in crude dimethyl sulfoxide (60 ml) (a little exothermic) and the resulting greenish-yellow solution was heated at 150°C for 30 min with vigorous stirring to yield the steam-distillate, which was separated, dried ($MgSO_4$) and evaporated under ordinary pressure to afford colorless pure 2,2-dideuterothiacyclopentane (0.117 mol, 90%), bp 121—122°C (760 Torr), n_D^{20} 1.5046.

The properties of the dideutero compounds prepared by this method were as follows.

2,2-Dideutero compounds	Overall yield (%)	bp(760 Torr)	n_D^{20}
Thietane	53	95—96°C	1.5096
Thiolane	70	121—122°C	1.5046
Thiane	61	140°C	1.5066
Thiepane	24	175°C	1.5136

References and Notes

1) Presented in part at the 101st Annual Meeting of the Pharmaceutical Society of Japan, Kumamoto, April, 1981.

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