with methanol to give benzyl methyl carbonate; benzyl chloride does not react with methanol under these reaction conditions. The carbonate/(carbonate + chloride) ratio exceeded 96%.

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**Registry No.**—**1**, 1885-14-9; **2**, 13248-54-9; **3**, 108-88-3; **4**, 4351-54-6; ($n$-Bu)$_3$SnH, 688-73-3.

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# Carbon-13 Nuclear Magnetic Resonance Spectral Analysis Using Spin-Lattice Relaxation Data and Specific Deuteration. Thiamine Hydrochloride

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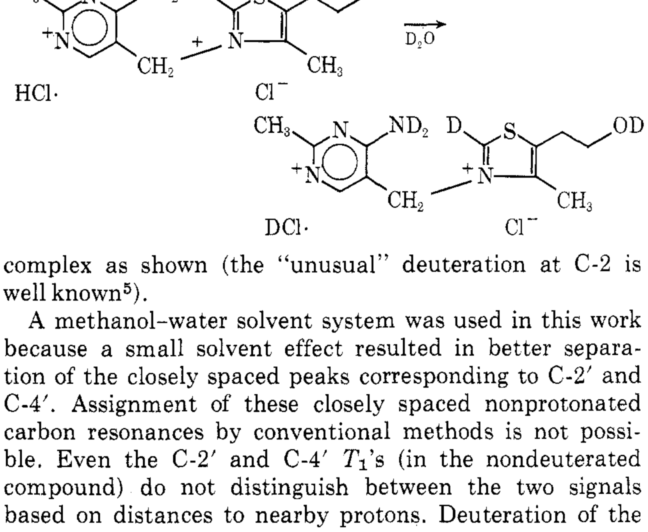
Carbon-13 spin-lattice relaxation data (the spin-lattice relaxation time, $T_1$, and nuclear Overhauser effect, NOE) can be useful parameters for organic spectral analysis.[2] In particular, $^{13}C$–$^{1}H$ dipolar $T_1$'s (which account for $^{13}C$ relaxation in large organic molecules) can indicate the degree of proton substitution for each carbon in the molecule.[1b] $^{13}C$ $T_1$'s for nonprotonated carbons in these molecules may also facilitate spectral assignments, since the efficiency of the dipolar relaxation mechanism for a given carbon depends strongly on the intermolecular distances between the carbon and nearby protons.[2c,d]

The sensitivity of $T_1^{DD}$ (the dipolar $T_1$) to internuclear distances can be exploited in another way. When a carbon bearing protons is selectively deuterated, the $^{13}C$ $T_1$ for that carbon increases because the deuterium nucleus has a smaller magnetic moment than the proton. If all attached protons are replaced by deuterium nuclei, then $T_1^{DD}$ for that carbon will increase by *ca.* tenfold (combining much less efficient $^{13}C$–$^{2}H$ dipolar relaxation with $^{13}C$–$^{1}H$ dipolar relaxation from nearby nonbonded protons). The effect of deuteration can also be seen on $T_1^{DD}$ for nearby *nonprotonated carbons,* which depend on nonbonded protons for their relaxation.

The $^{13}C$ nmr spectrum of vitamin $B_1$, thiamine hydrochloride, has been published[3] but many of the assignments were listed as tentative. We report here a $^{13}C$ nmr spectral study of this compound. Most of the present resonance assignments were made by use of model compounds and standard chemical shift correlations.[4] However several lines could not be assigned on that basis.

$^{13}C$ chemical shift and spin-lattice relaxation data for thiamine hydrochloride are given in Table I. Also in Table I are $T_1$ data for the partially deuterated compound separately prepared and redissolved in $CD_3OD$-$D_2O$. The exchange reaction results in pentadeuteration of the ion pair

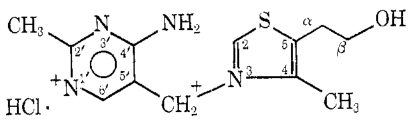


complex as shown (the "unusual" deuteration at C-2 is well known[5]).

A methanol-water solvent system was used in this work because a small solvent effect resulted in better separation of the closely spaced peaks corresponding to C-2′ and C-4′. Assignment of these closely spaced nonprotonated carbon resonances by conventional methods is not possible. Even the C-2′ and C-4′ $T_1$'s (in the nondeuterated compound) do not distinguish between the two signals based on distances to nearby protons. Deuteration of the amino group in the exchange reaction affords definitive assignments, however. $T_1^{DD}$ for the C-4′ carbon ($\alpha$ to the $ND_2$ group) increases by *ca.* 300% (see Table I) while the increase in $T_1$ for C-2′ is three times smaller. For the remaining carbons in the partially deuterated compound, smaller changes in $T_1^{DD}$ can be noted (however, note that $\Delta T_1$ is subject to considerable error since it is a difference between two derived quantities.).

The significant positive $\Delta T_1$ value for C-4 is interesting, but as yet we have no certain explanation for this. We also have no explanation for the substantial negative $\Delta T_1$ values observed for the two $CH_3$ carbons. Possibilities for the former effect include conformational considerations such as molecular stacking; the latter effect might indicate a reduced rate of $CH_3$ group rotation in the deuterated medium. Other, more easily interpreted molecular dynamics effects are indicated from the data in Table I. For example, $T_1$'s for the 2′-$CH_3$ and 4-$CH_3$ carbons indicate that both $CH_3$ groups are spinning rapidly. The 5-$\alpha$ and 5-$\beta$ $CH_2$ carbons and also the ring-bridging $CH_2$ group undergo some group segmental motion.[2c]

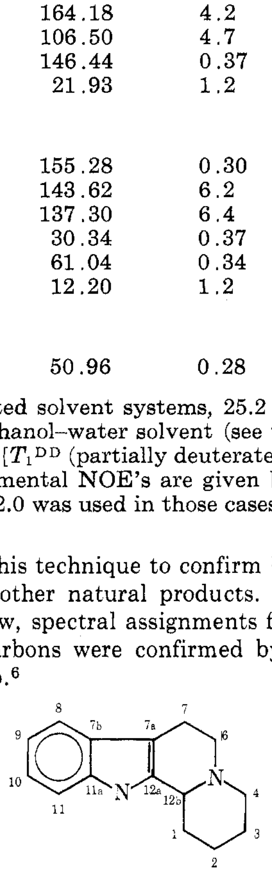
Table I
$^{13}$C Nmr Data for Thiamine Hydrochloride[a]



| | Chemical shift[b] | CH$_3$OH–H$_2$O[c] | | | CD$_3$OD–D$_2$O[c] | | | |
|---|---|---|---|---|---|---|---|---|
| | | $T_1$ | NOE | $T_1^{DD}$ [e] | $T_1$ | NOE | $T_1^{DD}$ [e] | $\Delta T_1^{DD}$, %[d] |
| | | | | Pyrimidine Ring | | | | |
| C-2′ | 163.78 | 4.7 | 1.7 | 5.5 | 7.1 | 1.3 | 10.9 | +98 |
| C-4′ | 164.18 | 4.2 | 1.7 | 4.9 | 9.8 | 1.0 | 19.6 | +300 |
| C-5′ | 106.50 | 4.7 | 1.8 | 5.2 | 4.5 | 1.9 | 4.7 | −10 |
| C-6′ | 146.44 | 0.37 | 2.0 | 0.37 | 0.31 | 2.1 | 0.31 | −16 |
| 2′-CH$_3$ | 21.93 | 1.2 | 2.1 | 1.2 | 0.8 | 1.9 | 0.8 | −33 |
| | | | | Thiazole Ring | | | | |
| C-2 | 155.28 | 0.30 | 2.0 | 0.30 | *f* | *f* | | |
| C-4 | 143.62 | 6.2 | 1.8 | 6.9 | 6.9 | 1.6 | 8.6 | +25 |
| C-5 | 137.30 | 6.4 | 1.9 | 6.7 | 6.4 | 1.9 | 6.7 | 0 |
| 5-α-CH$_2$ | 30.34 | 0.37 | 2.2 | 0.37 | 0.32 | 2.0 | 0.32 | −14 |
| 5-β-CH$_2$ | 61.04 | 0.34 | 2.1 | 0.34 | 0.34 | 1.9 | 0.36 | +6 |
| 4-CH$_3$ | 12.20 | 1.2 | 2.1 | 1.2 | 0.85 | 2.0 | 0.85 | −29 |
| | | | | Bridging CH$_2$ | | | | |
| | 50.96 | 0.28 | 2.0 | 0.28 | 0.24 | 2.0 | 0.24 | −14 |

[a] 1.2 *M* in stated solvent systems, 25.2 MHz, 38 ± 3°. [b] In parts per million downfield from TMS (internal dioxane δ 67.40). [c] 1:1 methanol–water solvent (see text). Estimated errors: $T_1$ (sec) ±5–10%, NOE ($\eta$) ±0.1–0.2, $T_1^{DD}$ (sec) ±10–20%. [d] $\Delta T_1^{DD} = [T_1^{DD}\,(\text{partially deuterated}) - T_1^{DD}\,(\text{protio})]/T_1^{DD}\,(\text{protio}) \times 100$. [e] $T_1^{DD}$ calculated from $(T_1)(1.99)/\text{NOE}$ observed. Experimental NOE's are given but (physically impossible) NOE's larger than 2.0 were not used in calculations of $T_1^{DD}$; instead 2.0 was used in those cases. [f] Not measured.

We are using this technique to confirm $^{13}$C nmr spectral assignments for other natural products. For example, in the alkaloid below, spectral assignments for the nonprotonated olefinic carbons were confirmed by deuteration at carbons 7 and 12b.[6]



Dideuteration at C-7 increased $T_1$ for the resonance assigned to carbon 7a by *ca.* 100% while the other nonprotonated carbon $T_1$'s were increased by only 30–40%. Deuterium substitution at 12b lengthened the 12a carbon $T_1$ by 45% while not appreciably affecting the other carbons (all $T_1$'s were predominantly dipolar).

## Experimental Section

The $T_1$ values in Table I were obtained with an inversion–recovery pulse sequence. Both direct and indirect NOE's were obtained; the values reported in Table I are averages of several runs. Direct NOE's were measured on $^1$H decoupled spectra using pulse-modulated decoupling. NOE's of 1.7–1.8 indicate minor but probably significant contributions from other relaxation mechanisms.

In the pulse-modulated {$^1$H} experiments, $^{13}$C pulse intervals > ~4$T_1$ for all carbons were used. Wideband {$^1$H} decoupling (*ca.* 15 W) was gated on *only* during tha data acquisition periods (typically 0.8 sec). The nuclear Overhauser effect does not grow in during an individual free induction decay acquisition, even if $T_1$ is much less than 1 sec (*e.g.*, for the protonated CH and CH$_2$ carbons); the long delays between pulses eliminate previously generated NOE through $^{13}$C–$^1$H relaxation processes.

**Registry No.**—Thiamine hydrochloride, 67-03-8.

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# The Specific Introduction of an Isopropylidene Group in the Synthesis of the Monoterpene Terpinolene and the Sesquiterpene (±)-α-Curcumene

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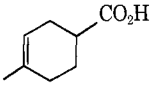
The isopropylidene group is a commonly occurring structural feature found in naturally occurring products.[2] In order to demonstrate the application of a simple procedure for the introduction of this grouping in synthetic routes to natural products, we wish to report the conversions of the carboxylic acid 1 into the monoterpene terpinolene (2) and the aldehyde 3 into the sesquiterpene (±)-α-curcumene (4). The overall transformations introduce



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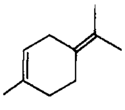

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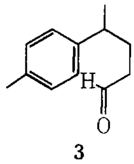

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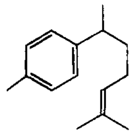

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