

spectrum of the T_3 model compound (2) were of approximately equal intensity (Fig. 3), indicating an almost equal population of distal and proximal conformations. This represents the first experimental evidence indicating the existence of two conformations of T_3 or one of its analogues in solution. In extrapolating these low temperature results to biological temperature, it was necessary first to determine the variation of the weighted average chemical shifts of the 2' and 6' protons of (2) with temperature in the absence of changes in conformer population. Graphical plots showed that all protons in compounds (1-4) suffered chemical shift changes due to the influence of a common solvent effect. The results for compounds (3) and (4) are of particular interest since they involve only one conformation. The chemical shift of the proximally positioned¹⁹, 6' proton of the 2'-methyl derivative (4) showed a shift towards low field of only 5 Hz over the range +40 to -110 °C. The average chemical shift of the 2' and 6'-protons of (3) showed a similar change. We can conclude from these results that both proximal (2',6') and distal (2',6') protons show conformationally independent chemical shift changes with temperature, but these changes are likely to be (a) small compared with the chemical shift difference between 2' (or 6') proximal and distal protons and (b) similar for proximal and distal protons, that is, the chemical shift difference ($\Delta\nu$) is largely temperature independent. These results enable us to calculate distal-proximal ratios at different temperatures from the equation

$$n_D = \frac{(v_{W2'H} - v_{W6'H}) + (v_{D6'H} - v_{P2'H})}{(v_{D6'H} - v_{P6'H}) + (v_{D2'H} - v_{P2'H})} \quad (1)$$

where n_D = mole fraction of distal form, and v_D , v_P and v_W refer respectively to distal, proximal and weighted average

chemical shifts. v_D and v_P were obtained from the single spectrum of (2) at -108 °C (Fig. 3) and n_D is calculated at any higher temperature by measuring $v_{W2'H} - v_{W6'H}$ at that temperature. On substituting $v_{W2'H} = 427.3$, $v_{W6'H} = 393.7$, $v_{D6'H} = 435$, $v_{P6'H} = 367$, $v_{D2'H} = 463$ and $v_{P2'H} = 390$ Hz into the above equation, n_D (40 °C) is calculated to be 0.56 (range 0.5-0.6 after taking account of experimental error); this indicates that there is very little change in the conformer ratio over the temperature range studied.

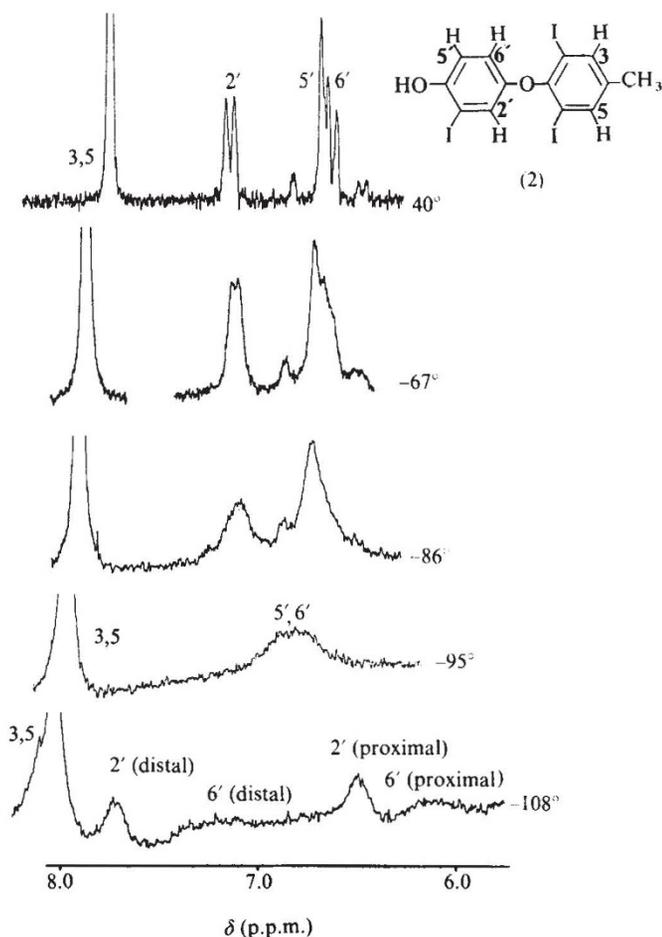
In summary, these results indicate that the barrier to rotation around the ether oxygen in thyroid hormones is in the range 7-9 kcalorie mol⁻¹, in reasonable agreement with a calculated⁴ barrier (11 kcalorie mol⁻¹) for T_3 . Furthermore, the observation of approximately equal populations of distal and proximal forms of the T_3 analogue (2) is not incompatible with an 'active' distal form, as suggested previously^{2,3}.

A recent communication by Camerman *et al.*²⁰ reported the observation of a single species of 3,5,3'-triiodothyropropionic acid in a mixture of diethanolamine, urea and methanol, but claimed to have shown the presence of two non-interconvertible conformations in a 2:1 mixture of ethanol-1 N HCl at room temperature. We believe that this work is in error as, first, the reported shift difference (1.7 Hz) between the 2' proximal and distal protons is negligible compared with those observed by us and other workers¹¹ and, second, the barrier to rotation, reported to be in excess of 20 kcalorie mol⁻¹, is far higher than expected. These apparently anomalous results are readily explained, however, if one assumes partial esterification of the acid by the acidic ethanol used as solvent.

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Fig. 3 Variable temperature NMR spectra of compound (2).



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Errata

In the article "Eccentricity-specific dissociation of visual functions in patients with lesions of the central visual pathways" by E. Pöppel *et al.* (*Nature*, **256**, 489; 1975) Fig. 1 and its legend should have been deleted and do not refer to the paper as published.

The title of the article (*Nature*, **256**, 750; 1975) by B. Donzel *et al.* should have read "Synthesis and conformations of hypothalamic hormone releasing factors: two TRF-analogues containing backbone N-methyl groups" and not as printed.