68. *Synthesis and Proton Magnetic Resonance Spectrum of Deuterated γ-Picoline.*

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Deuterated γ-picoline was prepared by catalytic exchange between γ-picoline and deuterium oxide. The proton magnetic resonance spectrum of a nearly fully deuterated sample was measured and compared with that of γ-picoline. From the spectra a proton–proton coupling constant of 14.5 ± 0.4 c./sec. was calculated for the methyl group and hence a value of $108.2° \pm 1°$ for the HCH bond angle in the methyl group of γ-picoline. The spectrum also shows that deuteration proceeds more easily in the α-position than in the β-position and more easily in the ring than in the methyl group.

The nuclear magnetic resonance spectrum of γ-picoline has been observed and found [1] to consist of a pair of doublets due to the ring protons and, at higher field, a single methyl-group line. The present investigation is concerned principally with the absorption spectrum of the residual hydrogen nuclei in nearly fully deuterated γ-picoline. It is known [2] that " massive " deuteration of a compound often simplifies the proton spectrum

[1] (a) Baker, *J. Chem. Phys.*, 1955, **23**, 1981; (b) Bernstein and Schneider, *ibid.*, 1956, **24**, 469; (c) Rao and Venkateswarlu, *Proc. Indian Acad. Sci.*, 1961, **54**, *A*, 305; (d) Brügel, *Z. Electrochem.*, 1962, **66**, 159.
[2] Garnett, Henderson, Sollich, and Tiers, *Tetrahedron Letters*, 1961, **15**, 516.

considerably. The residual hydrogen atoms in the molecule will, in general, be spin-coupled only to deuterium atoms, and, since the ratio of the spin-coupling constants $J(HD)/J(HH)$ is equal to 0·154, the spectrum of the ring protons of γ-picoline will show greatly reduced splitting. The distribution of protons in the nearly fully deuterated γ-picoline can be determined from the intensities of the lines in the proton resonance spectrum.

<div align="center">EXPERIMENTAL</div>

Materials.—The γ-picoline was a N.C.L. standard sample with a purity of 99·90 moles %, as determined by freezing-point measurements.

Deuterated γ-picoline was prepared by a method similar to that used for [²H₅]pyridine,[3] *viz.*, by catalytic exchange in the vapour phase between γ-picoline and deuterium oxide. The exchange was carried out in the apparatus shown in Fig. 1 and comprising a boiler A, packed with capillary tubes, heated column B containing the catalyst, cold-finger condenser C, liquid-return line D, drying tube E packed with anhydrous calcium sulphate and surrounded with an external heater, and cold trap F. The apparatus could be evacuated through G, and deuterium from an electrolytic cell could be introduced at H.
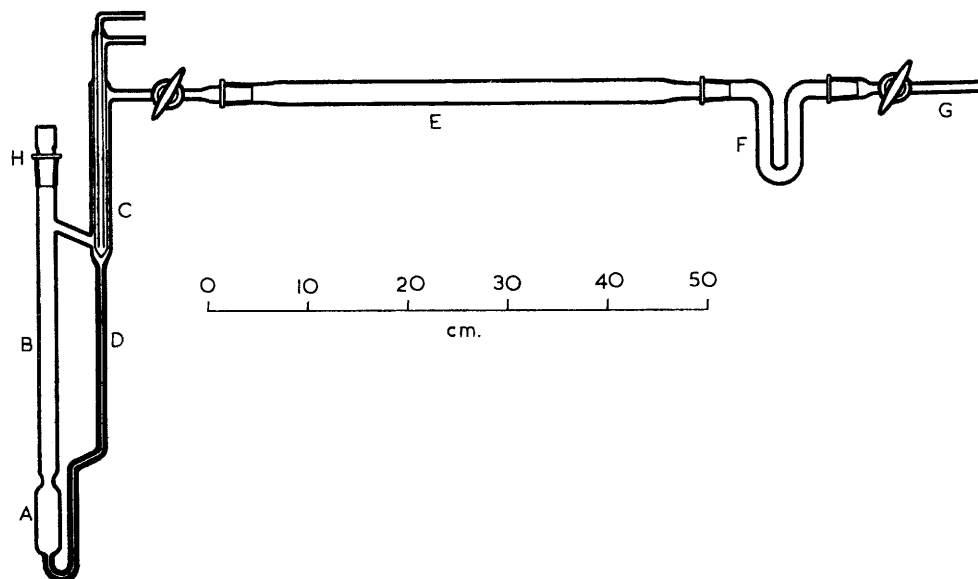

FIG. 1. Apparatus for H–D exchange. (A—H: see text.)

Equal volumes of γ-picoline and deuterium oxide (99·7% D₂O) were placed in the boiler and frozen by means of liquid nitrogen. The apparatus was evacuated and then filled with deuterium to atmospheric pressure. A palladium–charcoal catalyst, prepared by the method used by Linstead and Thomas [4] for the preparation of palladium–asbestos, was placed in column B and activated by treatment with deuterium at 240° for 4 hr. The temperature of the catalyst was measured by a thermocouple on the outside of the column and kept constant with a controller. The liquid was boiled and the vapours were passed over the catalyst at 200° and condensed. The condensate was returned to the boiler. The exchange was continued for periods up to 24 hr., after which the partly deuterated γ-picoline was separated from water by passage of the mixture in the vapour phase over anhydrous calcium sulphate. The dehydrated product was collected in the trap, F, which was cooled in liquid nitrogen. The partly deuterated product from one experiment was used as a starting material for the next. The drying agent was regenerated *in vacuo* at 230°, and the recovered water, containing deuterium, could be used for the preliminary treatment of further samples of γ-picoline. Fourteen

[3] Corrsin, Fax, and Lord, *J. Chem. Phys.*, 1953, **21**, 1170.
[4] Linstead and Thomas, *J.*, 1940, 1127.

successive exchange experiments were required to obtain about 98% deuteration. The replacement of hydrogen by deuterium was measured by a mass spectrometer, similar in design to that described by Graham, Harkness, and Thode.[5]

The compositions of the mixtures were estimated by measurement of the peak heights of masses 93—100. The sample of deuterated γ-picoline used for proton magnetic resonance spectral measurements was obtained by combination of the products of several series of exchange experiments. Parts of the mass spectra of this sample and of γ-picoline are given in Table 1. It was only possible to obtain an analysis of the mixture from the spectra if it was assumed that the mixture contains only γ-[$^2H_7$]- and γ-[$^2H_6$]-picolines, because the spectra of the pure components are not known. The peaks at m/e 100 and 99 corrected for ^{13}C and ^{15}N contributions gave some measure of the concentration of these components. It was reasonable to assume on statistical grounds that the concentration of components containing more than one hydrogen atom will be small. The approximate composition of the sample was γ-[$^2H_7$]picoline 88% and γ-[$^2H_6$]picoline 12%, and 98% of the hydrogen atoms were replaced by deuterium.

TABLE 1.

Mass spectra of γ-picoline (A) and deuterated γ-picoline (B).

m/e	102	101	100	99	98	97	96
Rel. intensity: (B)	0·6	7·9	**100**	14·9	17·4	2·6	1·3

m/e	95	94	93	92	91	90	
Rel. intensity: (A)	0·3	8·1	**100**	24·6	1·6	0·1	
(B)	0·3	0·2	0·7	0·1	—	—	

Proton Magnetic Resonance Spectra.—The spectra were obtained at 60·0 Mc./sec., with an Associated Electrical Industries Ltd. RS2 spectrometer, with flux stabilisation and a spinning sample tube 4·5 mm. in diameter. The resolution of the spectrometer (1 part in 10^8) would produce a line width of 0·6 c./sec. The temperature of measurement was ∼20°. The deuterated sample was distilled into the sample tube *in vacuo*; the non-deuterated sample was degassed by the freeze–pump–thaw technique. Both samples were examined as undiluted liquids, but about 10% by volume of cyclohexane was added to the non-deuterated γ-picoline, as an internal reference.

The positions of the lines in the γ-picoline spectrum were measured by the sideband technique of Arnold and Packard;[6] cyclohexane was assumed to have a τ value[7] of 8·56. The audio-oscillator used to generate the sidebands (Muirhead type D880A) had been calibrated against a frequency meter (Venner type 3336).

RESULTS AND DISCUSSION

The methyl-group absorption line had a τ value of 7·77 ± 0·01 (all errors quoted are standard deviations of the mean), and the centres of the two doublets had τ values of 2·92 ± 0·02 and 1·43 ± 0·02. Of the two doublets, the one occurring at lower field has been ascribed[1] to the α-protons, the one at higher field to the β-protons. The separation between the lines agreed with previous determinations (Table 2).

TABLE 2.

Chemical shift (in p.p.m.) between the methyl group and the ring protons of γ-picoline.

Shift between Me and α-H	6·2	6·23	6·46	6·45	6·34
,, ,, β-H	4·7	4·78	4·91	4·94	4·85
Reference	1a	1b	1c	1d	This work

The spectrum of the residual hydrogen nuclei in deuterated γ-picoline is illustrated in Fig. 2. It has been shown above that the proton concentration is small so that each residual hydrogen atom will be spin-coupled only to deuterium atoms in general. The ring protons will now give rise to sharp, single peaks. Because of the coupling to the

[5] Graham, Harkness, and Thode, *J. Sci. Instr.*, 1947, **24**, 119.
[6] Arnold and Packard, *J. Chem. Phys.*, 1951, **19**, 1608.
[7] Tiers, *J. Phys. Chem.*, 1958, **62**, 1151.

deuterium nuclei, which have a quadrupole moment, the lines will be slightly broadened, and are, in fact, about 2 c./sec. wide at half-height. The absorption due to the CHD_2 group consists of a set of five lines, with intensities in the ratio $1 : 2 : 3 : 2 : 1$. This is the pattern expected for a proton coupled equally to two deuterium nuclei, each with spin $I = 1$. The small peak lying between the quintet and the ring-proton peaks (see Fig. 2) is attributed to a small amount of water present as an impurity.

A method different from that employed for γ-picoline was used to measure the positions of the lines in the spectrum of the deuterated γ-picoline. The use of an internal reference was undesirable, as it would have contaminated the specimen and might have created problems of H–D exchange. An external reference in a capillary would have reduced still further the very weak signal from the small number of protons in the sample. The
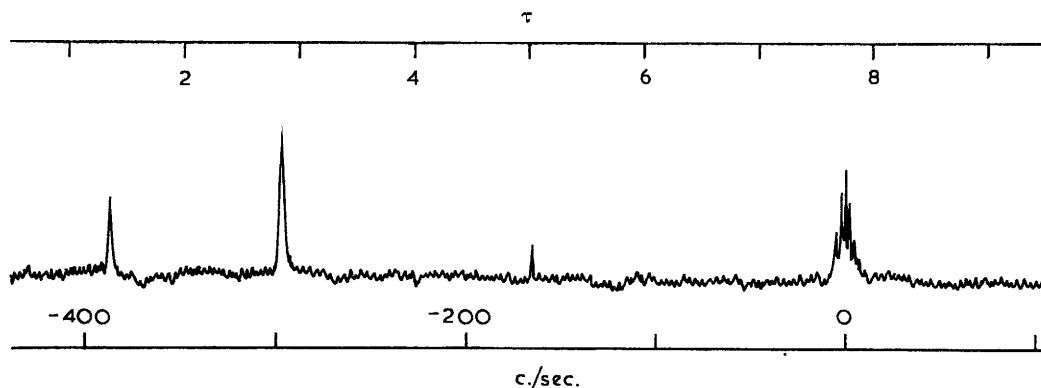

Fig. 2. Proton magnetic resonance spectrum showing residual hydrogen in deuterated γ-picoline.

spectra of the deuterated γ-picoline and of γ-picoline were recorded alternately, under conditions of increasing magnetic field. Since the spectrum of γ-picoline had been calibrated with reference to the cyclohexane line, the separation between the lines in the spectrum of the deuterated compound could in this way be measured. Each spectrum was swept six times, and the separations between the centre of the quintet and each ring-proton peak were calculated. The α-proton peak was found to be $6·39 \pm 0·11$ p.p.m., and the β-proton peak $4·87 \pm 0·03$ p.p.m. from the central line of the quintet. These values are in good agreement with the values 6·34 and 4·85 p.p.m. found in the present work for the separations between the ring-proton peaks and the methyl-group peak of non-deuterated γ-picoline. Any shift due to deuterium " isotope effect "[8] is too small to be measurable. Because of this agreement, it was assumed that both spectra have the same τ values, and these are shown in Fig. 2.

The splitting of the quintet in the deuterated γ-picoline permits a measurement of the spin-coupling constant in the methyl group to be made. Because the three protons in the methyl group of γ-picoline are chemically and magnetically equivalent, coupling of their spins produces no observable effects on the spectrum, and a single peak results. Substitution of deuterium destroys this equivalence, and coupling with the deuterium splits the proton-resonance line. The separation of the lines in the quintet gives J(HD), the proton-deuteron coupling constant, as $2·22 \pm 0·04$ c./sec. Since J(HH) $= J$(HH) $\times$ γ_H/γ_D, where γ_H, γ_D are the magnetogyric ratios of the proton and deuteron, respectively, a value of $\pm 14·5 \pm 0·4$ c./sec. for the proton–proton spin-coupling constant in the methyl group of γ-picoline is computed.

[8] Tiers, *J. Chem. Phys.*, 1958, **29**, 963; Gutowsky, *ibid.*, 1959, **31**, 1683.

The theoretical calculations of Gutowsky, Karplus, and Grant [9] predict that the coupling constant decreases from $+32$ c./sec. for a bond angle of $100°$ to -2.5 c./sec. at $130°$. The measured value thus corresponds to an HCH bond angle of $108.2°$, if it is assumed that the coupling constant is positive. More recent calculations [10] give a similar value, and in view of the agreement between the theoretical relation and experimental values of the coupling constant for bond angles less than $112°$ it seems unlikely that the value of $108.2°$ is in error by more than $1°$.

The ease with which deuterium may be substituted in each position of the molecule can be determined from the intensities of the proton lines in the spectrum. If deuteration were entirely random, then, of the molecules with one hydrogen atom, 28.5% would have their single hydrogen atom in the α-position, 28.5% in the β-position, and 43% in the methyl group. The spectrum would consist, therefore, of three absorption peaks with intensities in the ratio $2:2:3$ corresponding to the hydrogen atoms in the α-, β-, and methyl position, respectively.

The actual intensities of the lines (Fig. 2) do not show this simple relationship. The intensity ratio was obtained from the areas of the absorption peaks, which were measured by cutting out and weighing six spectra recorded on a 10-in. recorder. Since saturation effects can produce considerable errors in such measurements, care was taken to have the radio-frequency level such that, if it were increased slightly, the intensity ratio did not alter.

The measured intensities indicate that 16% of the residual hydrogen atoms are in the α-position, 31% in the β-position, and 53% in the methyl group. These values were averaged from the six spectra and were reproducible within 3%. It is therefore evident that deuterium substitution proceeds more easily in the α- than in the β-position, and more easily in the ring than in the methyl group.

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[9] Gutowsky, Karplus, and Grant, *J. Chem. Phys.*, 1959, **31**, 1278.
[10] Gutowsky, Mochel, and Somers, *J. Chem. Phys.*, 1962, **36**, 1153.