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AN NMR STUDY OF ORIENTATION EFFECTS IN THE CATALYTIC DEUTERATION AND TRITIATION OF AROMATIC COMPOUNDS.[1] SIMPLIFICATION OF SPIN-COUPLED NMR SPECTRA BY THE METHOD OF MASSIVE DEUTERATION[2]

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A GENERAL procedure for the platinum-catalysed exchange of aromatic compounds with heavy water has already been reported.[3,4] The technique has been demonstrated to be a useful method for the synthesis of tritium labelled compounds when tritium oxide is used;[5] it possesses significant advantages over conventional techniques of recoil tritiation[6] and tritium gas irradiation.[7]

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[1] Part V of a series entitled "Deuterium Exchange Reactions, Reactions with Substituted Aromatics". (Part IV, see reference 4).

[2] Proton NMR Spectroscopy. XIII (Part XII, J.Phys.Chem. In press).

[3] W.G. Brown and J.L. Garnett, J.Amer.Chem.Soc. 80, 5272 (1958).

[4] J.L. Garnett and W.A. Sollich, Aust.J.Chem. In press.

[5] International Atomic Energy Agency Symposium, "The Detection and Use of Tritium in the Physical and Biological Sciences", Vienna, May 3-10, 1961.

[6] R. Wolfgang, F.S. Rowland and C.N. Turton, Science 121, 715 (1955).

[7] K.E. Wilzbach, J.Amer.Chem.Soc. 79, 1013 (1957).

The procedure involves a relatively simple one-step synthesis, the organic substrate need not be water soluble, no solvent is necessary, and a high level of tritium incorporation is achieved with most compounds when tritiated water of high specific activity is used. The labelled compound is obtained with a minimum of tritiated impurities, since by-product formation occurs only by catalytic means and not as a result of radiation-induced decompositions, etc., which often render difficult the radiochemical purification of the desired product.[8]

This catalytic method provides a source of labelled compounds which are difficult to obtain by other means. It also permits of simultaneous double-labelling when both deuterium and tritium are used in the exchange media; this is advantageous for isotopic distribution studies, since conventional tritiation procedures[6,7] yield only a tritiated product in which distribution must be evaluated by tedious chemical methods. When appreciable deuteration has occurred, a spectroscopic method may be used to determine isotopic distribution; for this purpose the proton NMR spectrum is particularly suitable at high deuterium contents, since the positions occupied by residual hydrogen are readily identifiable.

A typical example of the catalytic deuteration (or tritiation) procedure follows. Sodium benzoate (144 mg) was shaken in an evacuated sealed amoule with pre-reduced platinum oxide (12 mg) and 99.5% heavy water (500 mg) at 130°C for 10 hr. An 80 to 90% yield of benzoic acid containing 70 atom % D in the ring was obtained. A second sample, subjected to three consecutive treatments according to this procedure, contained over 90 atom % D in the ring.[9,10]

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[8] W.G. Brown and J.L. Garnett, Int.J.Appl.Rad.Isotopes **5**, 114 (1959).

[9] Deuterium analyses were performed on a Metropolitan Vickers Type MS-2-G mass spectrometer, by the procedure of Graff and Rittenberg, Analyt.Chem. **24**, 878 (1952).

[10] Tritiations have been conducted in an exactly similar manner. Tritium analyses were performed by the procedure of J.L. Garnett, W.K. Hannan and S.W. Law, Anal.Chim.Acta In press.

It is thus evident that highly deuterated compounds are readily produced by this technique. While many uses can be foreseen for such materials, it will suffice to introduce here a particular application to NMR spectroscopy, permitting the simplification and assignment of certain types of spectra which will later be used to determine the orientation effects in catalytic deuteration.

It is well-known that NMR is useful for the identification of positional isomers of aromatic compounds. However, in some cases (notably C_6H_5X and o-and m-C_6H_4XY) highly complex spectra are obtained, and the computations required for analysis are costly and time-consuming. The technique of "spin decoupling"[11] is generally inapplicable, owing to the small frequency difference between the interacting nuclei. We have therefore devised a new procedure for the simplification of spin-coupled NMR patterns which is based on random replacement of hydrogen atoms by deuterium to the level of ca. 75 to 95 atom % D. Under these conditions the residual hydrogen atoms will with high probability be spin-coupled only to deuterium atoms. The proton NMR spectrum thus will show only the much finer splittings characteristic of coupling to deuterium ($J_D/J_H = 0.1535$), with consequent minimization of second-order effects.

If it be necessary, the deuterium splittings may be wholly eliminated by means of H-D spin decoupling, thus providing perfectly sharp lines centered at the true shielding values.

This general method, termed "massive deuteration", is most satisfactory when all sites are equally deuterated (i.e. equilibrated) since then the areas of the separated NMR peaks will be proportional to the numbers of equivalent sites; for example, the peak due to para hydrogen in phenyl

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[11] W.A. Anderson, Phys.Rev. **102**, 151 (1956); J. Itoh and S. Sato, J.Phys. Soc.Japan **14**, 851 (1959); R. Kaiser, Rev.Sci.Instrum. **31**, 963 (1960).

derivatives is thus identified unambiguously. While any D-exchange method may be used, for example strong acid catalysis, the use of transition metal catalysts often permits of more facile equilibration and easier isolation of product.

The NMR spectrometer and techniques have been described.[12] However, owing to the relatively low hydrogen content of the samples, which is, of course, inherent in the method of massive deuteration, it is often desirable to use rather high sample concentrations, i.e. 6 to 10% (by volume or wt/vol) in CCl_4 or other solvent. Another difficulty stems from the electric quadrupole moment of deuterium, which causes the protons spin-coupled to it to give slightly broadened lines (ca. 2 c/s width at half-height); this effect too would be eliminated if H-D spin decoupling were employed. The τ-values[12] for several compounds which ordinarily exhibit rather complex spectra are listed in increasing order in Table 1. There is an evident correlation between shielding values and the electron-donating power of the substituent, and, as expected, the *meta* position is less sensitive than the *para*. However, no exact correspondence to Hammett's σ-values or to Taft's

Table 1

Shielding Values[12] for Phenyl Derivatives as Determined by the Method of Massive Deuteration

Compound (10% wt/vol in CCl_4)	τ 2-H	τ 3-H	τ 4-H
Benzoyl chloride	1.90	2.50	2.39
Benzoic acid	1.88	2.57	2.48
Methyl benzoate	2.01	2.63	2.53
Fluorobenzene	3.01d	2.75d	2.91
Phenol	3.27	2.90	3.19
Aniline	3.49	2.97	3.35

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[12] G.V.D. Tiers, J.Phys.Chem. 62, 1151 (1958); G.V.D. Tiers and F.A.Bovey, J.Phys.Chem. 63, 302 (1959).

inductive or resonance parameters is observed. This point will be dealt with in future publications.

For these measurements the 90% deuterated sample of benzoic acid, prepared above, was converted to the acyl chloride and the ester; the other compounds were deuterated to a similar level. In the case of fluorobenzene the o- and m-H absorptions were doublets because of spin coupling to the fluorine atom.

Once the assignment of NMR peaks to residual hydrogen at various positions has been made, it is a simple matter to determine the orientation by identifying the positions at which deuterium exchange is relatively slow. To do this it is only necessary to interrupt the exchange before complete equilibration has been achieved. Examples of orientation effects which have been observed for some of the compounds studied are listed in Table 2; further experiments are in progress. As contrasted with the reactivity at the ring, it is significant that the non-aromatic hydrogens in methyl benzoate, anisole, stilbene, and trans-cinnamic acid do not undergo appreciable exchange. However, the aliphatic hydrogens of bibenzyl are deuterated readily, and it had previously been found that the methyl hydrogens of toluene are very active toward exchange when treated with Raney nickel plus D_2O.[13]

Such observations are of importance in studies of the mechanism of transition-metal catalysis. The term "charge-transfer no-bond adsorption" has been used[14] to describe chemisorption[15] of aromatic compounds; to explain the relative reactivities of various aromatics, it has been postulated that chemisorption involves π-electron delocalization.[14] For example

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[13] G.V.D. Tiers, Ph.D. Dissertation, The University of Chicago, 1956, pp. 121-132.

[14] Presented at the May 1960 meeting of the University of New South Wales Chemical Society and subsequently published in Proc.Royal Aust.Chem.Inst. In press.

[15] F.A. Matsen, A.C. Makrides and N. Hackerman, J.Chem.Phys. 22, 1800 (1954).

Table 2

Orientation Effects in Catalytic Deuteration

Compound	Atom % D in ring[a]	Position[b]	Atom % D[c]
Sodium benzoate	90	ortho	90 ± 2
		m + p	90 ± 2
Sodium benzoate	70	ortho	57 ± 2
		m + p	79 ± 1
Sodium benzoate	61	ortho	26 ± 1
		m + p	84 ± 1
Phenol	52	meta	63 ± 1
		o + p	45 ± 1
Pyridine	35	α	53 ± 2
		β + γ	23 ± 1

[a] The extent of deuteration was carried to 65-85% of the limiting value in all cases except the first, in which near-equilibration was achieved by three successive treatments. Analyses for total ring D done according to reference 9.

[b] When two peaks are not adequately resolved for separate integration, the combined value is given.

[c] Amounts of deuterium were obtained by difference from the amount of residual hydrogen determined by means of an electronic integrator built according to plans furnished by Varian Associates.

pyridine may be chemisorbed by its lone-pair or by the π-electrons; while the results of Table 2 indicate a definitely greater reactivity at the α-position, this is by no means as large as might have been expected if lone-pair adsorption were dominant.[16]

The results of Table 2 are indicative of orientation, but to deduce true relative rates from such measurements would require additional data, e.g. exact values for equilibrium deuterium content, etc.[13] Work of this nature is in progress.

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[16] W.M. Lauer and L.A. Errede, J.Amer.Chem.Soc. 76, 5162 (1954).

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