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Analysis of Illicit Drug Exhibits by Hydrogen-1 Nuclear Magnetic Resonance Spectroscopy

Positive identification of most illicit laboratory exhibits routed to the Special Testing and Research Laboratory of the Drug Enforcement Administration (DEA) for the identification of unknown constituents has been rapidly achieved with the aid of a nuclear magnetic resonance (NMR) spectrometer. This technique often provides valuable quantitative data as well. Magnetic resonance spectroscopy of the hydrogen atom provides information on the chemical nature of a single hydrogen atom (or group of atoms) within a molecule, the number of hydrogen atoms in a particular group, and the number and relative position of hydrogen atoms in neighboring groups.

To produce the magnetic resonance necessary to effect the energy change that results in a recorder response, a sample is placed within a strong magnetic field and subjected to high frequency radiation. Either field or frequency is altered over a very narrow range, usually within 8 ppm, to obtain resonance for hydrogen at all locations of the compound under investigation. Most instruments operate with a radiation frequency of 60 MHz. The required magnetic field strength is 1409.2 mT (14 092 gauss). An instrument operating at 90 MHz would require a concomitant increase in field strength of 50%.

The absorption frequency or "chemical shift" for a hydrogen nucleus depends on its electronic environment. As electronic shielding about this nucleus is intensified the radiation frequency or field strength must be increased for resonance to occur. Except for when electronic fields are themselves altered by the influence of the magnetic field, one may generally observe a relationship between the chemical shift of a hydrogen nucleus and predictable electron inductive or withdrawal effects of adjacent elements. An example of this principle and several others germane to the applicability to NMR is found in the spectrum of ethanol (Fig. 1).

Three groups of signals are evident. Their relative intensities, as measured by peak areas, are 3 to 2 to 1. The 3-unit group has three peaks; the 2-unit group has four peaks; and the 1-unit group is a singlet. The splitting phenomenon has been explained by an "$n + 1$" rule, whereby a group of protons "coupled" to an adjacent group will produce an absorption band that is split by 1 plus the number of protons in the second group. Where protons are very labile, like hydroxyl or sulfhydryl protons in acid media, they will not couple and will therefore produce a single peak like the 1-unit singlet (an added droplet of hydrochloric acid was effective in this case). The quartet is produced by a hydrogen group adjacent to a methyl group (3 + 1); the area of 2 units confirms that the quartet results from the absorption of the methylene protons. The electronegative effect of the adjacent oxygen lowers the absorption frequency of this group. The methyl protons absorb at the highest frequency; coupling with the methylene protons results in the signal splitting into a triplet, with the integrated intensity indicating that there are three protons.

In summary, the principal features of an NMR spectrum relevant to determining chemical structure are the chemical shift, splitting pattern, and integrated intensity.

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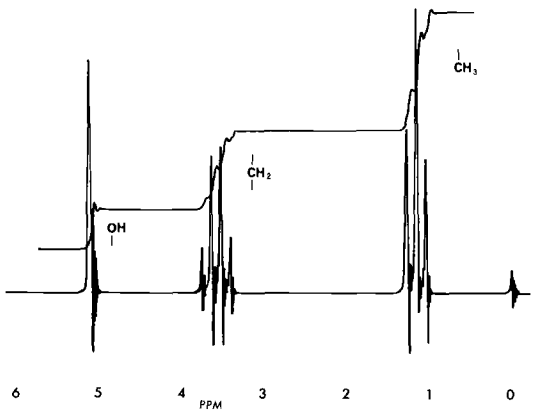

FIG. 1—*NMR spectrum of ethyl alcohol (droplet of hydrochloric acid added).*

Overlap of patterns because of molecular complexity or the presence of more than one compound may render spectrum interpretation more difficult and sometimes seemingly impossible. Several procedures mitigate many such problems and allow the technique to be applied to the analysis of a broad range of substances, as the examples discussed here will demonstrate.

Solvents and Liquid Reagents

The simple NMR spectra generally produced by solvents and liquid reagents [*1,2*] frequently permit their identification and quantitation in a fraction of the time required for classical procedures. Among such compounds identified in this laboratory have been 2-propanol, phenylacetic acid, chloroform, ethyl ether, formic acid, methanol, and 1-phenyl-2-propanol.

Ethanol has been found in opium extracts and in seized laboratory exhibits of morphine. One exhibit contained a mixture of ethanol and water with a calculated weight ratio of approximately 20:1, indicating that the solvent was probably commercial 95% ethanol. Comparative integration of hydroxyl to either methylene or methyl absorption indicated an area increase of about 25% above the calculated value predicated for pure ethanol. Water, with a molecular weight of 18, contributes absorption equivalent to two hydrogen atoms per molecule, whereas ethanol, with a molecular weight of 46, contributes only one. Thus the contribution of absorption per unit weight of water is five times that of ethanol, and hence a 25% increase in hydroxyl absorption because of the presence of water reflects a weight contribution of only 5%.

Three structurally related compounds often encountered under a variety of circumstances are acetone, acetic acid, and acetic anhydride. They may be distinguished in various ways with NMR spectroscopic techniques. All three compounds produce a singlet for the acetyl hydrogen atoms at about 2 ppm [from tetramethylsilane (TMS)] in carbon tetrachloride (Fig. 2). The peak assignments were 2.08 for acetone, 2.16 for acetic anhydride, and 2.00 for acetic acid. Not shown is the carboxylic acid peak for acetic acid, which generally appears in the region of 11 to 12 ppm, the exact location depending on factors of concentration and the influence of other compounds.

The effects of partitioning these compounds between equal volumes of water and carbon tetrachloride in the sample tube are also shown in Fig. 2. A single extraction with water removes virtually all of the acetic acid, approximately two thirds of the acetone, and about one third of the acetic anhydride.

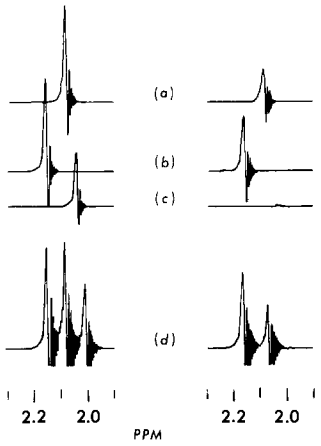

FIG. 2—*NMR spectra (carbon tetrachloride) of* (a) *acetone,* (b) *acetic anhydride,* (c) *the acetyl group of acetic acid, and* (d) *a mixture of* (a), (b), *and* (c) *before and after extraction with an equal volume of water.*

The gradual hydrolysis of acetic anhydride to acetic acid in aqueous solution provides a convenient test for its identification. Figure 3 shows how NMR may be used to monitor this process.

A liquid seized in the raid of a laboratory alleged to be manufacturing amphetamines was examined neat, then diluted with carbon tetrachloride. No significant differences were noted. The spectrum of the carbon tetrachloride solution (Fig. 4*a*) showed two or more sharp, intense peaks in the acetyl region (about 2 ppm), a peak in the phenyl region (about 7 ppm), a sharp peak at 11.4 ppm (suggesting -COOH), and a peak at about 3.5 ppm, which, at first glance, might be attributed to methoxy by virtue of its chemical shift and lack of splitting; however, the sharpness usually observed for absorption by such a group was lacking. A strong possibility was that it was produced by a methylene group attached to phenyl, which is subjected to poorly resolved splitting as a result of long-range coupling with protons in the ortho position to the substitution site.

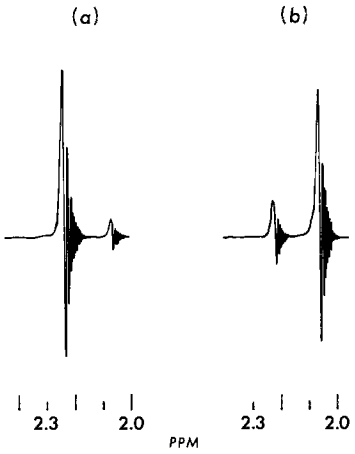

FIG. 3—*NMR spectrum of acetic anhydride (water),* (a) *5 min and* (b) *30 min after solution.*

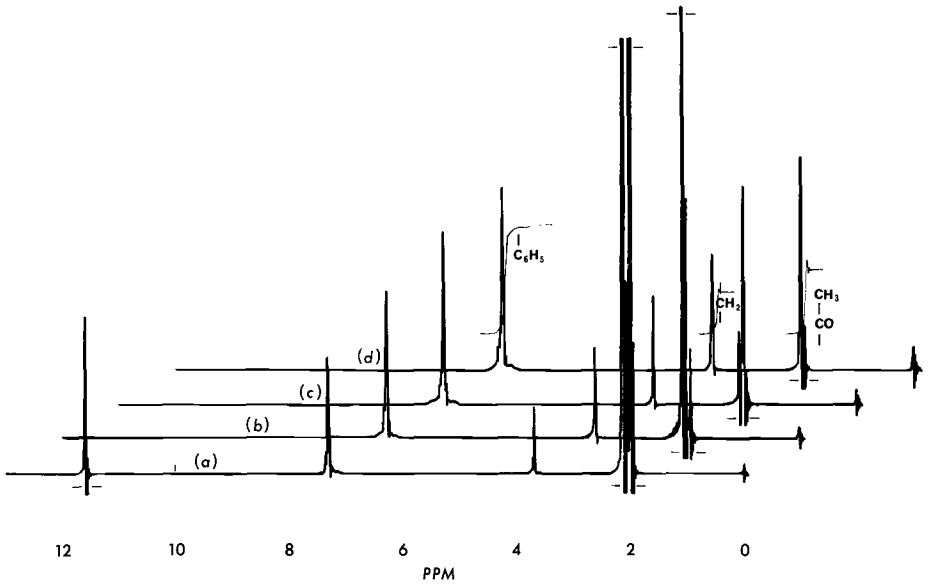

FIG. 4—*NMR spectra of* (a) *unknown in carbon tetrachloride solution,* (b) *after extraction with equal volume of water,* (c) *after several extractions with water, and* (d) *methyl benzyl ketone reference (carbon tetrachloride).*

After a single extraction with water, the following changes were observed (Fig. 4*b*): the peak attributed to -COOH had disappeared, indicating that the compound producing it had been extracted, and one of the peaks in the acetyl region (2.00 ppm) had almost disappeared. Concurrently, a peak at 2.03 ppm, previously obscured, was now evident.

The aqueous extract produced a large peak at 2.07 ppm [from sodium 3-trimethylsilylpropionate-2,2,3,3-*d*4 (TSP)] and a smaller one at 0.15 ppm further downfield. There was no absorption in the region of 11 to 12 ppm but the solvent (water) peak was shifted downfield of its neutral position, and hence this fraction was presumed to contain acetic acid.

Additional washings of the carbon tetrachloride solution gradually produced a diminution of the peak at around 2.1 ppm without affecting the intensity of the peaks at 2.03, 3.5, and 7.2 ppm. Comparative integration of the unaffected peaks revealed a proton ratio of 3 to 2 to 5, respectively. With absorption at 2.03 ppm attributed to an acetyl group, the structure of methyl benzyl ketone was hypothesized. This was confirmed by comparison with standard material (Fig. 4*d*) and by standard addition.

The presence of acetic anhydride, suspected of producing the peak at 2.1 ppm in carbon tetrachloride and at 2.23 ppm in water, was confirmed by procedures discussed earlier.

Amphetamines

Nuclear magnetic resonance spectroscopy has been particularly effective in the identification of amphetamine derivatives and analogs. The literature includes studies of 3,4-methylenedioxyamphetamine (MDA), mescaline, and their reaction precursors [*3*]; dimethoxyamphetamines [*4-6*]; *N*-methylated analogs of amphetamines and isomers [*7*]; and an extensive report covering 18 phenylpropylamines [*8*]. The identification of 3,4-methylenedioxymethamphetamine (MDMA) in this laboratory [*9*] provides a vivid example of this approach.

Figure 5*a* depicts a spectrum of amphetamine hydrochloride in deuterated water. The following spectral-structural correlations may be noted: the methyl doublet at 1.3 ppm, the methylene doublet at 2.9 ppm, and the methine multiplet centering at about 3.6 ppm. The phenyl hydrogens are nearly all equivalent as the substitution of a methylene group has little effect. Consequently, there is a near singlet in the region of 7.3 ppm, the same location as the absorption for the protons of benzene.

Commonly occurring spectral modifications may be the introduction of a sharp singlet at 2.7 ppm resulting from a methyl substituent on the nitrogen atom (methamphetamine, Fig. 5*b*) and a sharp singlet at about 6 ppm produced by a methylenedioxy group (MDA, Fig. 5*c*). In the latter case, there is a dramatic change in the phenyl pattern resulting from influence of the oxygen atoms and diminution of overall intensity as the number of hydrogen atoms is reduced from five to three. Interestingly, the effect of oxygen on the chemical shift of ring protons is opposite that on alkyl protons in that it effects an upfield shift for those protons ortho and meta to the substituent.

A sample analyzed several years ago had initially been suspected of being MDA hydrochloride. However, preliminary examination by infrared spectroscopy indicated that this was some other compound, very likely related to MDA. The NMR spectrum (Fig. 5*d*) differed from that of MDA only by the addition of a singlet at 2.7 ppm. Producing an intensity equivalent to three hydrogens, it was attributed to *N*-methyl. With proton counts, chemical shifts, and splitting patterns of all the other groups accounted for, the compound was identified as an MDMA salt. The anion was identified as chloride by other means. This compound has been observed a number of times since then, in other laboratories]*7*] as well as this one.

In another instance of a compound suspected of being an MDA salt, it was thought that the anion was organic and that NMR analysis would be suitable for its identification.

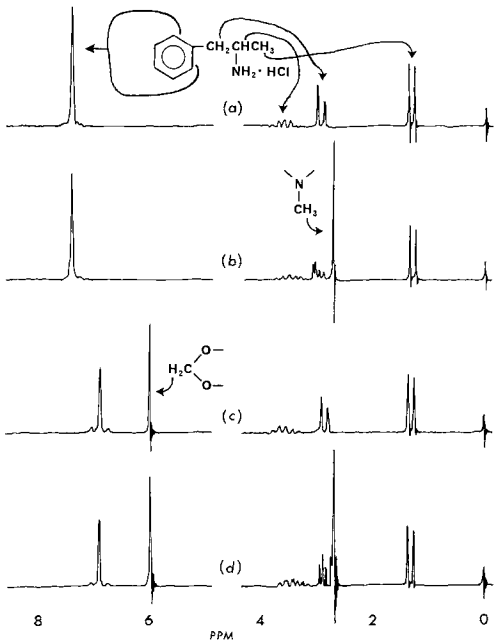

FIG. 5—*NMR spectra (deuterium oxide) of hydrochlorides of* (a) *amphetamine,* (b) *methamphetamine,* (c) *MDA, and* (d) *unknown, subsequently identified as MDMA.*

The NMR spectrum appeared identical to that of MDA hydrochloride (Fig. 5*c*) except for the addition of a sharp singlet at about 2 ppm. With an intensity reflecting three protons, the peak suggested acetate. The solution was made alkaline and then extracted with chloroform to remove MDA. Spectral examination indicated that the constituent producing the singlet remained in the aqueous layer. Acidification effected the evolution of acetic acid vapor, detectable by its characteristic odor.

Barbiturates

The analysis of barbiturates by techniques depending on the predictable crystallinity of a substance is often difficult because of the tendency of these compounds to form polymorphs or complexes with the solvents from which they are crystallized. Their examination by NMR bypasses this problem, since they are analyzed in solution. Comparative studies of a number of these compounds have been made by Lackner and Doring [*10*], Neville and Cook [*11*], von Philipsborn [*12*], and Rucker [*13*]. Avdovich and Neville [*14*] produced a compilation of spectra representing 30 of the most commonly encountered barbiturates. Accompanied by a thorough discussion and spectral data for some additional barbiturates, this compilation has proven to be a very useful reference work.

Exhibits alleged to be related consisted of white powders tentatively identified as the sodium salt of a barbiturate, the exact nature of which could not be determined either by microscopic or X-ray diffraction screening. This material was not extractable with deuterochloroform but did dissolve in deuterated dimethyl sulfoxide (DMSO). The spectrum (Fig. 6) was characterized by two ethyl groups of dissimilar proportion. One of these groups was believed to be attached to carbon on the basis of the chemical shift of its methylene absorption. Since the integrated intensity of this group was equal (within experimental error) to that of the absorption at 7.2 ppm (presumed to be monosubstituted phenyl), it was considered very likely that they were produced by the same molecule,

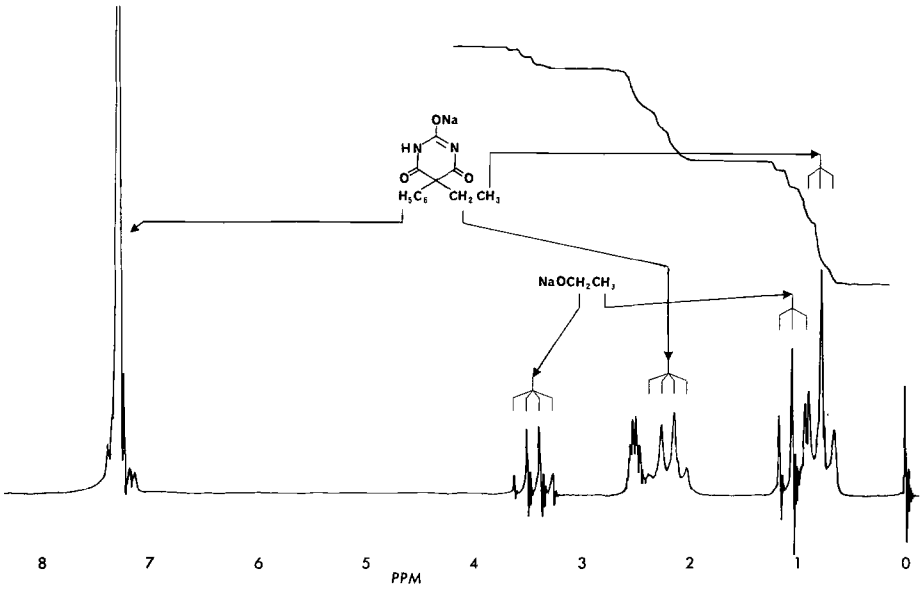

FIG. 6—*NMR spectrum (dimethyl sulfoxide-d_6) of mixture of two compounds identified as phenobarbital sodium and sodium ethoxide.*

probably some form of phenobarbital. Since the free barbituric acid is known to be soluble in chloroform, it was assumed that this compound was the sodium salt. This assumption was supported by successful comparison of spectral data [*14*] and by standard addition.

The other ethyl group, by virtue of the chemical shift of the quartet in particular, was believed to be attached to an oxygen. A likely source was ethyl ether or ethanol; however, since neither was detected by aroma or extractability with chloroform, a more likely possibility was the presence of ethanol as a sodium alkoxide, which, upon exposure to the moisture in DMSO, converts to the alcohol. This hypothesis is supported by the fact that sodium ethoxide is commonly employed in the synthesis of phenobarbital [*15*]. Confirmation was obtained by aqueous hydrolysis, which produced ethanol, characterized both by its aroma and by spectral response to standard addition. The molar proportion of the two components was determined by measuring relative intensities of the corresponding ethyl groups. Following multiplication by the appropriate molecular weight, approximate weight ratios of 7 parts sodium ethoxide to 93 of phenobarbital sodium were determined for each exhibit. The unusual circumstance of the presence of sodium ethoxide in such large quantities and occurrence of similar proportions in the various exhibits was significant to the prosecution of an alleged conspiracy.

Characterization of *N*-Methyl

Over the years, procedures have been reported for the characterization of *N*-methyl groups by NMR spectroscopy. An extensive review by Casy has covered a number of them [*16*]. Generally, they are based on the following considerations:

1. Protonation of the nitrogen atom confers a marked downfield shift on the methyl group.
2. Acidification of the solvent (pH less than 1) will generally slow the intermolecular exchange of amino protons to the extent that, at probe temperatures of less than 38°C (100°F), coupling with the methyl hydrogen atoms may be observed. For aromatic amines, however, the use of concentrated sulfuric acid is generally required to produce such interaction [*17*]. The resultant splitting pattern of the methyl absorption, and to some extent its effected shift, will reflect the extent of substitution on the nitrogen atom.
3. The shifts may be observed in aqueous and nonaqueous systems, the choice depending on considerations of solubility.

Day and Reilley [*18*] illustrated some of these principles in resolving a mixture of mono-, di-, and tri-methylamines in water. A change in pH from 13 to 7 induced downfield chemical shift changes of 0.78, 0.42, and 0.32 ppm for the tertiary, secondary, and primary amines, respectively. Further acidification to pH 1 did not affect the chemical shifts but did induce coupling between methyl and amino protons to produce the following splitting patterns for *N*-methyl:

(1) $(CH_3)_3NH^+$ ... doublet,
(2) $(CH_3)_2NH_2^+$ ... triplet, and
(3) $(CH_3)NH_3^+$ ... quartet.

Ma and Warnhoff [*19*], in an exhaustive study of *N*-methyl spectral characteristics, compared chemical shifts in deuterochloroform, perdeuteroacetic acid, and trifluoroacetic acid. Among other conclusions, they stated:

> The combination of a methyl peak at higher than 2.56 ppm in deuterochloroform, a downfield shift of ca 0.5-0.6 ppm in perdeuteroacetic acid, a ca 0.6-0.8 ppm shift in trichloroacetic acid, and splitting of the methyl peak into a doublet all taken together provide strong evidence for the *N*-methyl group of a tertiary amine.

Davis added excess trifluoroacetic acid to chloroform solutions of the free bases to observe induced shift changes and coupling [*20*].

This laboratory has reported the application of some of these techniques for the identification of methylamine in complex reaction mixtures [*21*] and as an adulterant in methamphetamine exhibits [*22*]. On many occasions, use of these procedures has assisted in the general spectral interpretation of unknown substances.

A suspected amine hydrochloride, upon examination by NMR, was shown to produce three singlets in aqueous solution (Fig. 7, *top*). The chemical shifts and proton ratios indicated a monosubstituted phenyl, a methylene, and a methyl group; very likely the latter two were separated by a nitrogen. The compound was extractable with chloroform from alkaline solution. The suspected methylene and methyl groups were both shifted upfield significantly. Treatment with excess trifluoroacetic acid now conferred a downfield shift on both groups and split them into doublets, thereby confirming their attachment to NH^+ and the identity of the compound as *N,N*-dimethylbenzylamine.

A spectral comparison with *N*-methylbenzylamine (Fig. 7, *bottom*), a secondary amine, highlights the structural difference between these two compounds via proton ratios, chemical shifts, and splitting patterns of the protonated amines. Interestingly, the same two compounds had been employed by Ma and Warnhoff [*19*] years earlier to illustrate both the contrast in chemical shifts and the splitting patterns obtained with their technique.

Use with Other Techniques

Information gleaned from an NMR spectrum may provide the structural "link" necessary to complete the identification of an unknown compound. For example, if the melting

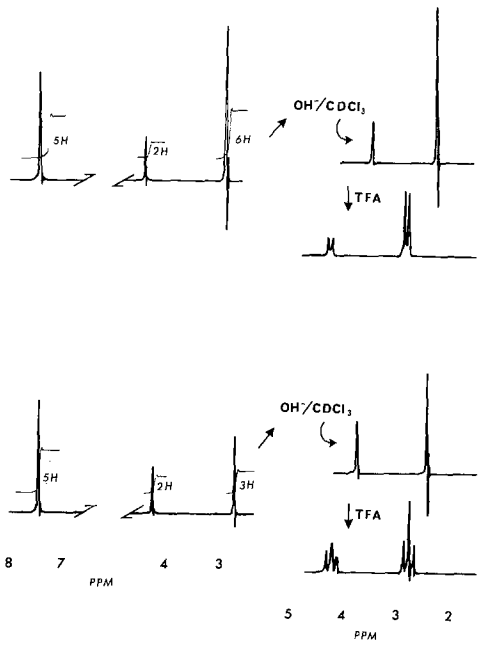

FIG. 7—*NMR spectra of* (top) *compound subsequently identified as* N,N-*dimethylbenzylamine and* (bottom) N-*methylbenzylamine.*

point or molecular weight of an unknown substance is supplemented with fragmentary structural data, such information may narrow the possible choice of compounds to one or two, thereby accelerating the process by which a positive identification may be made. The following examples illustrate this process.

In one exhibit, a compound sold as amphetamine was subsequently identified as a somewhat distant relative. In its NMR spectrum, the most dramatic indicator for the absence of amphetamine was the lack of phenyl absorption; indeed, there was no absorption beyond 4 ppm. However, there was indication of a CH_3CH, an *N*-methyl, and a cycloaliphatic group (Fig. 8).

A hydrochloride salt was prepared from a basic extract of this exhibit. Following recrystallization from chloroform-heptane (1 to 4), its melting point was determined (138°C or 280°F). A literature examination for compounds reported to melt within several degrees of this finding revealed only one with a structure consistent with the observed NMR spectrum: propylhexedrine (Fig. 9). This determination was supported by the mass spectrum, which indicated a base peak at *m/e* 58, a predictable result of β-cleavage [*23*], and an apparent molecular weight of 155. Confirmation was obtained by spectral comparison with a reference standard. Propylhexedrine is a sympathomimetic substance sold as an inhalant by the trade name Benzedrex®. The similarity to Benzedrine®, a commercial name for *dl*-amphetamine, was interesting in that the exhibit had been suspected to be amphetamine.[2]

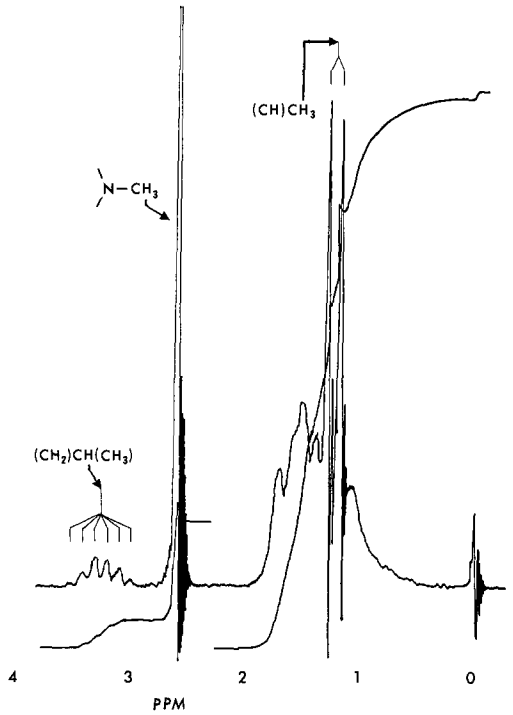

FIG. 8—*NMR spectrum (deuterium oxide) of compound subsequently identified as propylhexedrine. (No absorption was found beyond 4 ppm.)*

[2] Although propylhexedrine is sold over-the-counter, its abuse via intravenous injection has been increasing and has been implicated in a number of recent fatalities [*24,25*].

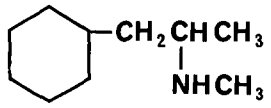

FIG. 9—*Structure of propylhexedrine.*

Another instance where combination of NMR with other techniques led to the identification of an unknown substance occurred recently. An injectable liquid was made basic and extracted with deuterochloroform (Fig. 10). Chemical shift, absorption pattern, and integration of the various groups in the spectrum suggested the following structural features: trisubstituted phenyl, three interacting methylene groups, and two methyl groups. The methylene groups were believed to be arranged in the order N-CH_2-CH_2-CH_2-X, X being either sulfur or oxygen. The methyl groups were believed to be attached to carbonyl or phenyl. The latter seemed more likely because of the pattern and location of the phenyl absorption.

Carbonyl substituents confer a marked downfield shift on ortho protons. Nitrogen, oxygen, and sulfur will effect an upfield shift. Methyl or methylene substituents, on the other hand, cause little change from the 7.2 to 7.3 ppm location of benzene protons, as mentioned earlier. Since the only aliphatic constituents available for attachment to the phenyl ring were the two methyl groups, it was postulated that these were present at the 1 — and 3 — positions, and another, unknown substituent was present at the 2 — position.

A hydrochloride salt was then prepared for melting point determination. The observed melting range of 165 to 167°C (329 to 333°F) was in good agreement with a literature finding for xylazine hydrochloride, reported to melt at 164 to 167°C (327 to 333°F) [*26*]. Furthermore, the structure of xylazine (Fig. 11) was consistent with the NMR spectral interpretation. Further support was obtained from the mass spectrum of the sample, which produced major fragments at *m/e* 220 and 205, corresponding, respectively, to the

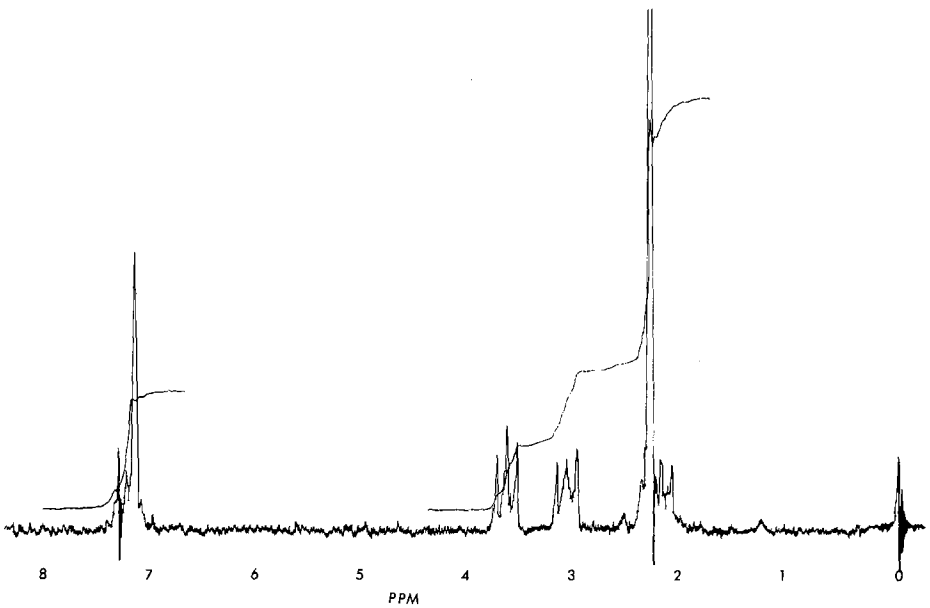

FIG. 10—*NMR spectrum (deuterochloroform) of compound subsequently identified as xylazine.*

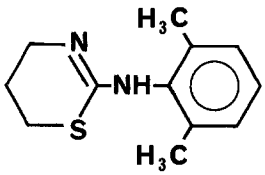

FIG. 11—*Structure of xylazine.*

molecular ion and expected loss of methyl. Finally, an infrared spectrum of xylazine obtained from the literature [*26*] was successfully compared with that obtained from a basic extract of the sample.

Xylazine hydrochloride is reportedly used as a veterinary analgesic. It has appeared in this laboratory on at least two occasions after seizures from clandestine laboratories.

The combined use of NMR and mass spectroscopy has been most effective in the analysis of illicit drugs. The unique features of each technique which allow them to complement one another have been examined by Bellman et al [*3*] in their examination of hallucinogenic derivatives of amphetamine, tryptamine, and benzylic acid. Extensive work in this area, reported since, demands a more comprehensive treatment than is possible here. A separate report on this subject is in process.

Quantitative Analysis

The proportions of components in a mixture may be ascertained from integration of their relative spectral contribution. However, to determine the absolute quantity of an ingredient, one may relate the absorption of a suitable region to one representing an internal standard of known quantity.

In the past decade, this procedure has found widespread use in pharmaceutical analysis, as may be noted in reviews by Parfitt [*27,28*], Rackham [*29,30*], and Kasler [*31*]. Applications of forensic interest include barbiturates [*13*], hypnotics [*32*], methylxanthines [*33*], and carbamate tranquilizers [*34*]. In this laboratory, it also has been used frequently for the quantitation of amphetamine derivatives and anesthetic compounds.

Basic requirements for rapid analysis of drugs by the internal standard procedure are these:

(1) compounds that produce a strong spectral feature (ideally, a singlet attributable to several equivalent protons);

(2) an internal standard, the analytical region of which does not overlap any peaks from the sample; and

(3) a solvent whose spectrum is transparent in the analytical regions and in which sample and standard are very soluble.

When these requirements are met, the sample preparation and analysis follow a common procedure that requires few modifications for different drugs [*35*]: sample and internal standard are weighed accurately into a common container, then shaken thoroughly with the chosen solvent. The resulting solution is then decanted into an NMR tube and scanned, and the analytical regions are integrated. The amount of active ingredient is calculated in the following manner:

$$W_u = (A_u E_u W_s)/(A_s E_s)$$

where

u = component being assayed,
s = internal standard,
W = weight in mg,
A = integral intensity of selected proton absorption signal, and
E = NMR equivalent weight (molecular weight divided by number of protons producing absorption signal to be measured).

An exhibit consisting of a white powder was found upon trituration with deuterochloroform to be completely soluble in it. The spectrum suggested the presence of cyclic aliphatics and one or more monosubstituted phenyl groups (Fig. 12*a*). Upon partitioning with an equal amount of deuterated water, the chloroform layer produced a clear spectrum of protonated phencyclidine (Fig. 12*c*). The aqueous layer produced a clear spectrum of piperidine, also as a salt (Fig. 12*b*). Both were subsequently identified as hydrochlorides. The concentration of phencyclidine in the sample was determined by NMR with deuterated water as solvent and maleic acid as the internal standard. The phenyl absorption of phencyclidine, representing five protons, was utilized. The olefinic absorption of maleic acid, at 6.4 ppm, representing two protons, served for the quantitative comparison.

Calculation of the amount of active ingredient proceeded as shown earlier. In the case of phencyclidine hydrochloride, the sample equivalent weight is equal to 279.85/5 or 55.97, and the standard equivalent weight is 116.08/2 or 58.04. The NMR analysis, in addition to providing an identification of constituents, demonstrated the ease with which halide salts of phencyclidine and piperidine may be partitioned between water and chloroform.

Use of this technique for the simultaneous determination of methamphetamine with methylamine adulterant and mannitol diluent was recently discussed [*22*]. The metham-

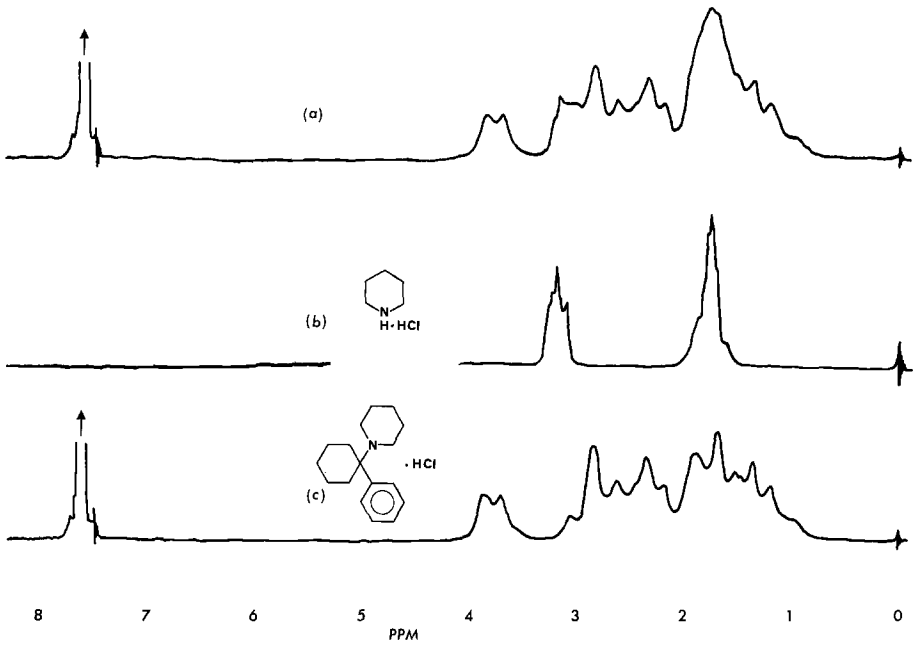

FIG. 12—*NMR spectra of* (a) *unknown mixture* (*deuterochloroform*), (b) *deuterium oxide extract* (*component identified as piperidine hydrochloride*), *and* (c) *solution depicted in* (a) *after extraction with deuterium oxide* (*component identified as phencyclidine hydrochloride*).

phetamine is determined directly from quantitative comparison of its five-proton phenyl contribution to the two-proton absorption of maleic acid, as in the preceding example. The quantities of methylamine and mannitol are similarly determined after the contribution of methamphetamine to their respective absorption regions has been subtracted. Since the contribution to the methylamine region, from methamphetamine's *N*-methyl and methylene absorption, represents five protons, the correction here is equal to the integral value of the phenyl absorption. Similarly, methamphetamine's methine contribution to the analytical absorption region of mannitol may be corrected for by subtracting one fifth of the phenyl absorption.

Besides considerations of speed and specificity, which are often mentioned in connection with the applicability of this technique to pharmaceutical analysis, of particular importance to forensic laboratories performing qualitative and quantitative analyses of a wide variety of chemicals is that since signal intensity is directly proportional to the number of hydrogen atoms producing it, regardless of their source, reference standards are not required. Thus, internal standards of predetermined purity may be readily used for the determination of many compounds once they have been identified. The need for standard materials that may be expensive or difficult to obtain is therefore obviated.

Conclusion

This discussion was intended to be illustrative rather than exhaustive. The examples cited comprise but a fraction of the interesting applications to which NMR spectroscopy may be put in a forensic drug laboratory. In the DEA laboratory, structural determinations, in the absence of available standard materials, have included a large number of drugs, reagents, intermediates, and by-products incidental to illicit syntheses.

By providing significant structural information complementary to that obtained by mass and infrared spectrometry, NMR spectrometry has also aided in the identification of many additional compounds.

Summary

Hydrogen-1 NMR spectroscopy has been used for identification and quantitation of drugs, reaction intermediates and by-products, and solvents. Sample handling techniques and principles of spectral interpretation have been illustrated by examples from exhibit analysis performed in this laboratory. The technique has the capability for providing qualitative and quantitative information quickly and uniquely, frequently in the absence of standard reference compounds.

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