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TECHNICAL NOTE

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Analysis of Impurities in Illicit Methamphetamine Exhibits. III: Determination of Methamphetamine and Methylamine Adulterant by Nuclear Magnetic Resonance Spectroscopy

For this third paper in a series reporting the results of analyses of illicit methamphetamine preparations [*1,2*], exhibits of dl-methamphetamine hydrochloride (I) appearing as off-white blocks or hygroscopic powder were examined and found to contain substantial quantities of methylamine hydrochloride (II). Some of the powder exhibits contained, as diluents, mannitol (III), dextrose (IV), or a combination of one of these with magnesium sulfate. Examination for other impurities indicated only traces, at most, of unidentifiable compounds.

Identification and simultaneous determination of I, II, and either III or IV have been conveniently accomplished via nuclear magnetic resonance (NMR) spectroscopy. Interference from other impurities has been negligible because of the extremely low concentrations at which they have occurred.

The suitability of NMR spectroscopy for the analysis of mixtures is well documented; pharmaceutical applications include aspirin-phenacetin-caffeine tablets [*3*], barbiturates [*4,5*], methylxanthines with benzoates and salicylates [*6*], hypoglycemics [*7*], hypnotics [*8*], and pyrazolones [*9*]. 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 employed for the determination of many compounds once they have been identified. This feature is of great significance to forensic chemistry laboratories in that expensive, difficult-to-get standard materials need not be used.

Experimental Procedure

Screen exhibits spectroscopically and microscopically, as discussed previously [*2*]. For quantitative analysis, dissolve accurately weighed portions of the exhibit and maleic acid in deuterated water to produce a concentration of approximately 60 mg each per millilitre. Transfer about 0.5 ml of this solution to an analytical tube and place in an NMR spectrometer (60 MHz minimum). Scan the spectrum, adjusting the spin rate to eliminate spinning sidebands from regions of interest. Integrate the analytical regions a sufficient number of times to attain desired precision.

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Discussion

The 60-MHz spectrum of I is shown in Fig. 1*a*. Absorption assignments are as follows: phenyl (5H), about 7.3 ppm;[2] methine (1H), 3.64 ppm; methylene (2H), about 3.0 ppm; N-methyl (3H), 2.69 ppm; and C-methyl (3H), 1.26 ppm. A suggested means for the determination of I has been based on comparative measurement of the phenyl signal with that resulting from the CH (6.4 ppm) of maleic acid (V), chosen as internal standard [*10*].

Compound II, detectable by its N-methyl contribution at 2.65 ppm (Fig. 1*b*), may be

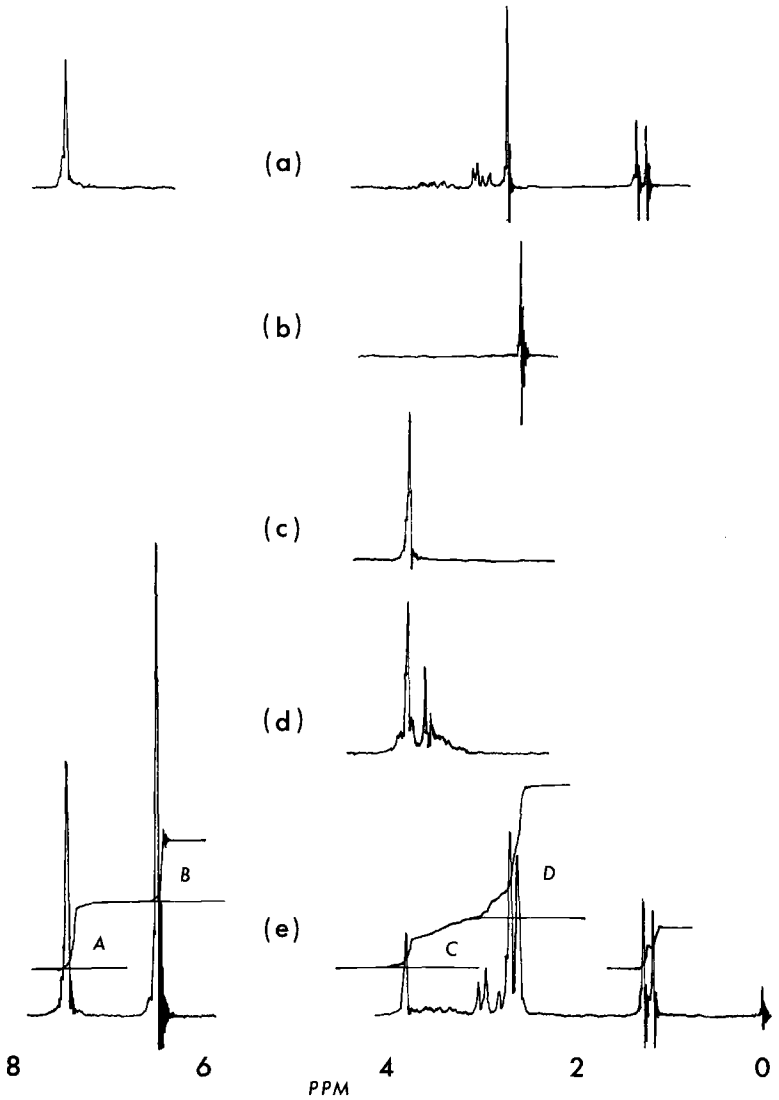

FIG. 1—*Sixty-megahertz NMR spectra (D_2O) of* (a) *dl-methamphetamine hydrochloride* (*I*), (b) *methylamine hydrochloride* (*II*), (c) *mannitol* (*III*), (d) *dextrose* (*IV*), *and* (e) *mixture of I, II, and III with maleic acid* (*V*).

[2] From TSP (sodium 3-trimethylsilylpropionate-2,2,3,3-d4).

confirmed by its unique spectral response to pH modification [2] or by infrared spectroscopy [11]. As may be seen in Fig. 1*e*, the N-methyl signal of II is not sufficiently resolved from that of I to permit its direct measurement. However, since absorption regions A and D (Fig. 1*e*) each reflect a contribution from five hydrogen atoms of I, the net absorption caused by II may be determined by subtraction of the measurement of A from that of D. Similarly, the contribution of III or IV to region C[3] (Figs. 1*c*, *d*, *e*) may be obtained by subtraction of A/5, to correct for the methinyl contribution of I. Thus, the weight of each component may be calculated as follows:

$$W_{\mathrm{I}} = (A \times E_{\mathrm{I}} \times W_{\mathrm{V}})/(B \times E_{\mathrm{V}})$$

$$W_{\mathrm{II}} = [(D - A) \times E_{\mathrm{II}} \times W_{\mathrm{V}}]/(B \times E_{\mathrm{V}})$$

$$W_{\mathrm{III}} = \{[C - (A/5)] \times E_{\mathrm{III}} \times W_{\mathrm{V}}\}/(B \times E_{\mathrm{V}})$$

$$W_{\mathrm{IV}} = \{[C - (A/5)] \times E_{\mathrm{IV}} \times W_{\mathrm{V}}\}/(B \times E_{\mathrm{V}})$$

where *A*, *B*, *C*, and *D* are the measured integrals of the regions so labeled in Fig. 1*e*, *E* is the NMR equivalent weight (molecular weight divided by the number of protons producing absorption signal to be measured [12]; see Table 1), and *W* reflects component weight.

Synthetic mixtures were examined by the foregoing procedure, each spectrum being integrated ten times. Results are shown in Tables 2 and 3.

TABLE 1—*Analytical information for NMR determinations.*

Abbreviation	Compound	Molecular Weight	Equivalent Weight	Analytical Region
I	methamphetamine hydrochloride	185.69	37.14	A
II	methylamine hydrochloride	67.53	22.51	D
III	mannitol	182.17	22.77	C
IV	dextrose	180.16	30.03	C
V	maleic acid	116.07	58.04	B

As may be seen, determinations of I were generally accurate to within 2%. Not unexpectedly, the precision and accuracy of analysis for the other components reflected the extent to which I absorbed in their analytical regions. Thus, as the ratio of such components to I diminished, a concomitant increase in variation of *net* measurement ratio and relative error occurred. Nevertheless, deviations for these compounds usually did not exceed 2 mg/100 mg I, an important consideration in view of the large proportions generally encountered in actual exhibits. If greater precision and accuracy are desired, however, the sample solution may be rendered alkaline and the free base of I removed with deuterochloroform; extractability of the other components is insignificant. Substance II and either III or IV may then be determined from direct measurements made on the residual aqueous solution.

Table 4 lists findings for a number of exhibits of I in which II was also found. They were screened by NMR and gas chromatography/mass spectroscopy as described pre-

[3] Representing eight and six hydrogen atoms per molecule, respectively [10].

TABLE 2—*Determination of synthetic mixtures.*

Synthetic Sample[a]	I				II				III				IV			
	Added, mg	Found, mg	Deviation		Added, mg	Found, mg	Deviation		Added, mg	Found, mg	Deviation		Added, mg	Found, mg	Deviation	
			mg	%			mg	%			mg	%			mg	%
1	...	...	...	...	50.7	50.3	0.4	0.8	...	...	...	...	...	...	...	...
2	78.3	79.7	1.4	1.8	19.1	18.2	0.9	4.7	...	...	...	...	...	...	...	...
3	61.7	62.4	0.7	1.1	40.9	41.0	0.1	0.2	...	...	...	...	...	...	...	...
4	54.4	53.3	1.1	2.0	48.4	46.9	1.5	3.1	...	...	...	...	...	...	...	...
5	82.8	84.1	1.3	1.6	46.6	45.3	1.3	2.8	22.9	23.6	0.7	3.0	...	...	...	...
6	90.1	90.0	0.1	0.1	10.4	9.8	0.6	6	10.3	11.8	1.5	15	...	...	...	...
7	82.0	81.1	0.9	1.1	22.4	21.5	0.9	4.0	...	...	...	...	40.6	41.2	0.6	1.5
8	92.7	92.8	0.1	0.1	10.8	7.4	3.4	32	...	...	...	...	12.1	14.3	2.2	18

[a] Dissolved in 1 ml of solution (D_20) containing 117.82 mg of V, the internal standard.

TABLE 3—*Measurement precision in analysis of synthetic mixtures.*

Synthetic Sample	*A/B*		*D/B*		*(D − A)/B*		*C/B*		*[C − (A/5)]/B*	
	Mean	RSD[a]	Mean	RSD	Mean	RSD	Mean	RSD	Mean	RSD
1	...	...	1.101	1.97	1.101	1.97	...	...	...	...
2	1.057	3.05	1.456	2.03	0.399	2.59	...	...	...	...
3	0.828	2.30	1.725	1.79	0.897	2.52	...	...	...	...
4	0.708	2.15	1.735	1.75	1.027	2.63	...	...	...	...
5	1.115	1.39	2.107	1.79	0.992	3.45	0.734	2.30	0.511	3.28
6	1.194	3.98	1.409	1.78	0.215	18.5	0.493	2.91	0.255	3.39
7	1.076	2.43	1.547	2.15	0.472	5.15	0.891	2.00	0.676	2.22
8	1.231	2.32	1.394	1.46	0.163	13.9	0.482	2.92	0.235	5.11

[a]Relative standard deviation.

TABLE 4—*Analysis of exhibits.*[a]

No.	Physical Appearance	Methamphetamine HCl, %	Methylamine HCl, %	Other Substances Detected
1	off-white blocks of compressed powder	84.3	12.1	...
2	off-white blocks of compressed powder	79.8	14.3	...
3	off-white blocks of compressed powder	87.6	13.7	...
4	off-white blocks of compressed powder	64.6	30.5	...
5	off-white blocks of compressed powder	57.5	33.0	...
6	off-white blocks of compressed powder	62.8	31.3	...
7	brown, coarse granules and lumps	68.7	29.0	...
8	brown, coarse granules and lumps	67.8	33.4	...
9	brown, coarse granules and lumps	66.3	23.6	...
10	fluffy, off-white powder	74.9	21.8	...
11	moist, slightly off-white powder	69.1	31.3	...
12	off-white blocks of compressed powder	76.9	21.0	...
13	moist, light yellow mass unsuitable for microscopic examination	20.2	7.7	magnesium sulfate (small to moderate amount); dextrose, 10.9%
14	moist white clumps, unsuitable for microscopic examination	24.8	9.2	mannitol, 8.7%
15	fluffy white powder	28.7	14.0	mannitol, 20.3%; magnesium sulfate
16	viscous brown liquid with suspended particulate matter	large amount	small to moderate amount	1-phenyl-2-propanol (large amount); amphetamine HCl (small to moderate amount); methylbenzyl ketone (small to moderate amount); unidentified trace impurity, probable molecular weight 98–112
17	off-white chunks of compressed powder	82.3	19.8	trace impurity identical to that observed in Exhibit 16

[a]Exhibits have been grouped on the basis of similarities observed during screening that suggest a common source of manufacture.

viously [2], and, when possible, were also examined microscopically. Comparisons were made to indicate possible common sources of manufacture.

A common element to all these exhibits is the large proportion of II to I coupled with the absence of other impurities above trace levels. This contrasts markedly with findings in other impure exhibits which do not contain II although known to be manufactured by a process in which it is employed as a major reactant.

Exhibit 16, sold as "liquid methamphetamine," may represent a penultimate stage of a synthesis common to all these exhibits. This aspect is being further investigated.

Summary

Nuclear magnetic resonance spectroscopy, employed for the identification of methamphetamine with methylamine impurity, has also provided a rapid means for the determination of both substances. In addition, diluents representative of sugars and sugar alcohols have been determined without need for prior separation.

Although the contribution of either methylamine or diluent to its measured absorption region has a direct bearing on the precision of its determination, the levels at which these compounds have appeared in actual exhibits have been deemed sufficiently high to permit determinations of reasonable accuracy.

Acknowledgments

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