

Structural Elucidation of Unusual Police Exhibits. II. Identification and Spectral Characterization of N-(2-Hydroxyethyl)amphetamine Hydrochloride

REFERENCE: Cyr, T. D., Dawson, B. A., By, A. W., and Neville, G. A., "Structural Elucidation of Unusual Police Exhibits. II. Identification and Spectral Characterization of N-(2-Hydroxyethyl)amphetamine Hydrochloride," *Journal of Forensic Sciences*, JFSCA, Vol. 41, No. 4, July 1996, pp. 608-611.

ABSTRACT: An unusual police exhibit having the physical appearance, color, and odor of methamphetamine hydrochloride was identified unequivocally on the basis of combined evidence from ¹H- and ¹³C-NMR, mass, and infrared spectroscopic examination as N-(2-hydroxyethyl)amphetamine hydrochloride (HEA•HCl). A minor contaminant of the exhibit was similarly identified as ethanolamine hydrochloride (HE•HCl), suggesting synthesis via reductive amination of phenylacetone. Relevant spectroscopic data (¹H-, ¹³C-NMR, mass, and FT-IR) and spectra are presented.

KEYWORDS: forensic science, structural elucidation, spectral characterization

Introduction

In mid-October 1994, a police street drug exhibit was received in these laboratories for identification. The pale buff-colored, finely crystalline substance, seized from a Montreal-based "biker," possessed all the visible characteristics, including odor, of methamphetamine hydrochloride ("speed"); therefore, it initially appeared to be a straight-forward identification. When, however, the substance was subjected to a routine ion-trap GC-MS screening analysis, a chromatogram was obtained showing a single main component whose mass spectrum displayed a base peak of 88 Daltons (Da) with an apparent molecular ion of 179 Da. This substance had never previously been encountered as an exhibit by the Bureau of Drug Research analysis unit, and MS spectral searches of the library afforded no useful clues. The exhibit was therefore passed on to the Spectroscopy Section for structural elucidation. Comprehensive spectroscopic analysis verified the identity of the unknown as N-(2-hydroxyethyl)amphetamine hydrochloride (HEA•HCl). A subsequent literature search confirmed that this is only the second

reported identification of this unusual analog drug (1). Herein, we present a detailed spectroscopic examination of HEA•HCl as Part II of a series on *Structural Elucidation of Unusual Police Exhibits*. Part I of this series reported on Dimethylpramide ("Dimetcarb") (2).

Experimental

All NMR spectra were acquired on a Bruker AM 400 spectrometer operating at 297°K. The proton spectra (400.13 MHz) and carbon spectra (100.61 MHz) were obtained using either CDCl₃ or DMSO-*d*₆ as the solvent. Chemical shifts were referenced to solvent peaks—i.e., 7.26 ppm (¹H) and 77.00 ppm (¹³C) for CDCl₃ and 2.49 ppm (¹H) and 39.50 ppm (¹³C) for DMSO-*d*₆. All experiments were performed using standard Bruker software (version DISRVK01).

The mass spectral experiments were performed on a VG AutoSpec Q (VG Analytical Ltd., Manchester, UK) equipped with a DEC 3000 Model 300 computer operating Open VMS-Alpha (Digital Equipment Corp., Maynard, MA) and Opus Motif Version 3.1X mass spectral software. The MS was interfaced to a Hewlett Packard 5890 Series II Gas Chromatograph (Waldbronn Division, Germany). The GC capillary column was a Hewlett Packard HP-5MS (crosslinked 5% phenyl methylsilicone, length 30 m, film thickness 0.25 μm, column ID 0.25 mm). The GC oven temperature program was: 70°C for 1 minute, then 25°/min to 140°, then 8°/min to 260°C. The retention times of methamphetamine and ephedrine relative to HEA (RT = 4.72 min.) were 0.575 and 0.814, respectively. The injection and transfer line temperatures were 250°C. The chemical ionization reagent gas was 2-methylpropane, with a source pressure of 5 × 10⁻⁵ mbar.

Infrared spectra were recorded from KBr disks using a Bomem MB100 FT-IR spectrometer (BOMEM Inc., Quebec, P.Q., Canada). Twenty scans were collected at a resolution of 4 cm⁻¹.

Results and Discussion

MS Investigation

The substance was examined by conventional GC-MS to obtain an EI mass spectrum. The base peak at 88 Da was the only prominent feature and no apparent molecular ion was found (Fig. 1). The sample was then subjected to GC/chemical ionization analysis; a spectrum (Fig. 2) was obtained showing an M + 1 peak at m/z 180 (and the associated M + 43 peak at m/z 222) indicative of MW 179. Other significant fragment ions in this CI spectrum were seen at m/z 162 (i.e., -18, water), 119 (-61, H₂NCH₂CH₂OH),

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Received for publication 31 May 1995; revised manuscript received 6 Sept., 30 Oct., and 14 Dec. 1995; accepted for publication 18 Dec. 1995.

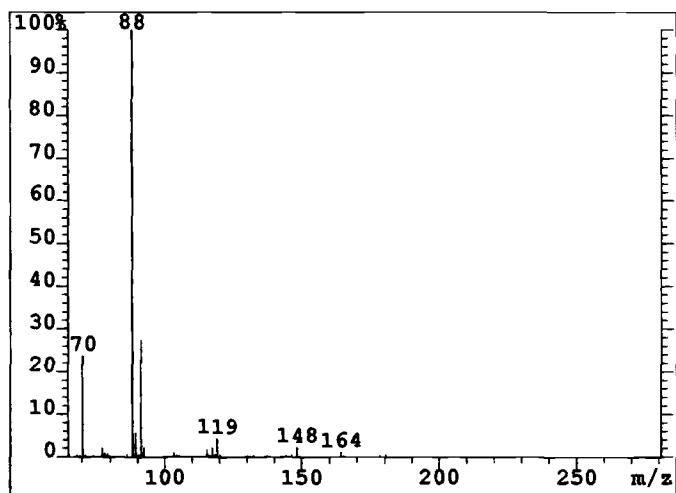


FIG. 1—GC/CI mass spectrum of the major component in the exhibit as received, HEA•HCl.

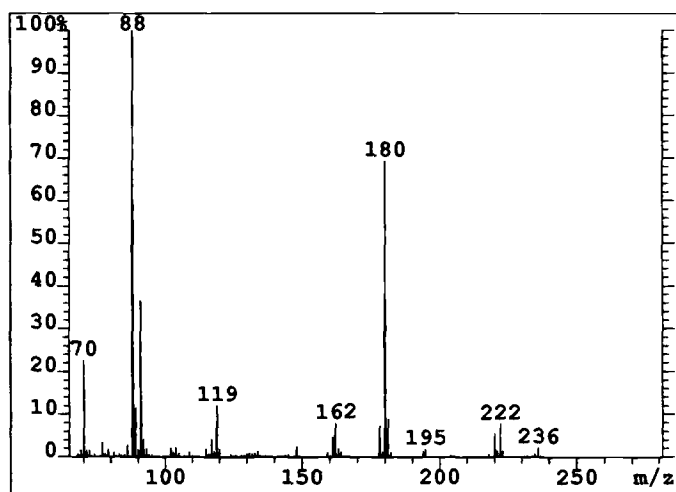


FIG. 2—GC/CI mass spectrum of the major component in the exhibit as received, HEA•HCl.

and 88 ($\text{CH}_3\text{CH}=\text{NHCH}_2\text{CH}_2\text{OH}$), and 91 (C_7H_7^+). The material was then subjected to GC/CI-high resolution analysis scanning from 200 to 160 Da at a rate of 5 seconds per decade. The spectrum showed the protonated molecular ion to be 180.143728 Da, which is only 27.1 ppm greater than the calculated mass of 180.138839 Da for $\text{C}_{11}\text{H}_{18}\text{NO}$ (Table 1) with 3.5 double bond equivalents (the half resulting from the charge). This is a very good match between determined and calculated mass for a magnet scan.

TABLE 1—Elemental compositions that agree to within 100 ppm with the experimentally determined mass, 180.143728 Da.

Limits:		3	0	0	0	0		
Mass	mDa	ppm	Calc. Mass	DBE	C	H	N	O
180.1437	-4.9	-27.1	180.1388	3.5	11	18	1	1
	-6.2	-34.6	180.1375	4.0	9	16	4	0
	6.3	35.2	180.1501	3.5	10	18	3	0
	7.7	42.7	180.1514	3.0	12	20	0	1
	-17.5	-96.9	180.1263	4.0	10	16	2	1

NMR Investigation

A proton NMR spectrum was obtained on the material as a CDCl_3 solution (Fig. 3). The spectrum showed aromatic resonances at 7.26 and 7.22 ppm (integrating as 2:3 protons, respectively), four multiplets centered at 4.05, 3.49, 3.22 and 2.86 ppm (integrating as 2:2:2:1 protons, respectively) and a 3 proton doublet at 1.34 ppm. There were also two very broad signals at about 9.0 and 5.0 ppm. A COSY spectrum indicated correlations between the resonances at 3.49, 2.86 and 1.34 ppm, as well as between 4.05 and 3.22 ppm (Fig. 4). This suggested that there are two aliphatic chains. One contained a methylene, methine and methyl group, while the other contained two methylene groups. From these results, it was

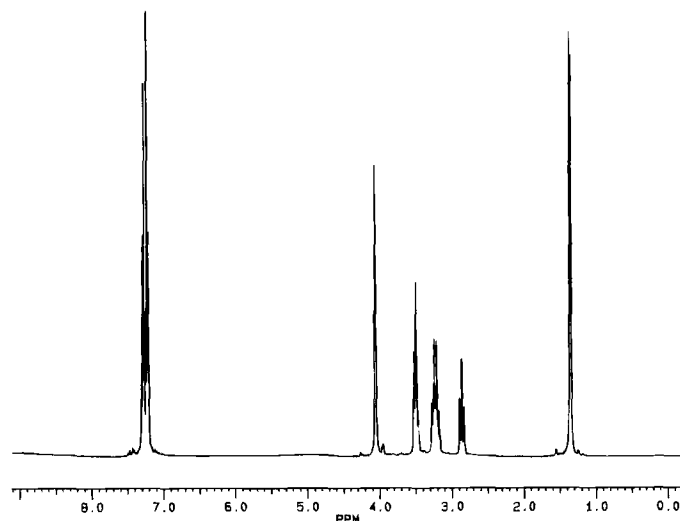


FIG. 3—A ^1H -NMR spectrum of the CDCl_3 soluble material of the exhibit, HEA•HCl.

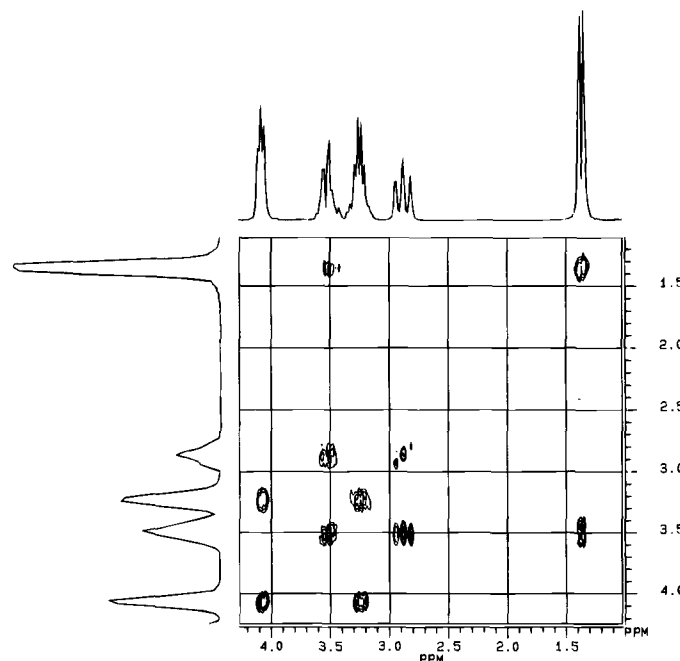


FIG. 4—An ^1H - ^1H correlation spectroscopy (COSY) diagram showing the aliphatic resonance region for the CDCl_3 soluble component of the exhibit, HEA•HCl.

deduced that the most probable structure for the unknown is protonated N-(2-hydroxyethyl)amphetamine.

After the spectrum had been obtained, it was noticed that there were crystals adhering to the sides of the tube. The solution was therefore poured off and the tube dried with a stream of nitrogen. Deuterated dimethylsulfoxide (DMSO- d_6) was then added to the tube and a proton spectrum was obtained (Fig. 5). The spectrum shows essentially two components, i.e., protonated HEA and an unknown, with a relatively greater percentage of the former due to the fact that the residual $CDCl_3$ solution (after decanting) was simply removed under a stream of nitrogen in order to conserve the insoluble entity. New multiplet resonances were observed at 3.56 and 2.84 ppm, and there were also new signals at 7.9 (a broad singlet) and 5.13 ppm (a triplet). The ratio of these four signals was 2:2:3:1 protons, respectively. It was concluded that the $CDCl_3$ -insoluble material was most likely a salt form of ethanolamine (a likely precursor of HEA). This was verified by spiking the DMSO- d_6 solution with some ethanolamine (HE). The only other resonances in Fig. 5 are from DMSO- d_5 and water, both of which are impurities in the DMSO- d_6 . Integration of the respective methylene group signals in a spectrum of the whole exhibit in DMSO- d_6 indicated that it contained about 15% HE on a molar basis.

In order to further verify the structure, carbon-13 spectra were obtained for the $CDCl_3$ soluble material. Distortionless enhancement by polarization transfer (DEPT) (3) was also carried out to determine the number of protons attached to each carbon. As expected, these spectra indicated the presence of four non-equivalent aromatic carbons (3 methines and 1 quaternary), and five aliphatic carbons (3 methylenes, 1 methine, and 1 methyl). All the ^{13}C -NMR evidence is consistent with HEA. In addition, the 1H -NMR evidence from the integrals of the NH and OH proton regions indicated that each substance (HEA and HE) is protonated by a strong acid, most probably hydrochloric.

IR Investigation

An FT-IR spectrum (Fig. 6) determined on the police exhibit as received, save for admixture with potassium bromide to form a disc, showed N^+H stretching salt bands in the 2400 cm^{-1} region characteristic of amine hydrochloride salts. When the substance

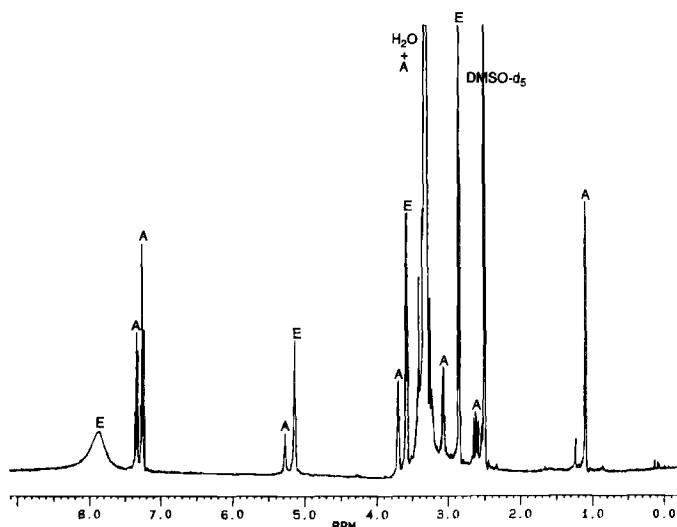


FIG. 5—A 1H -NMR spectrum in DMSO- d_6 of the $CDCl_3$ insoluble portion of the exhibit showing spectra of the two components, ethanolamine hydrochloride (E) and N-(2-hydroxyethyl)amphetamine (A) (see text).

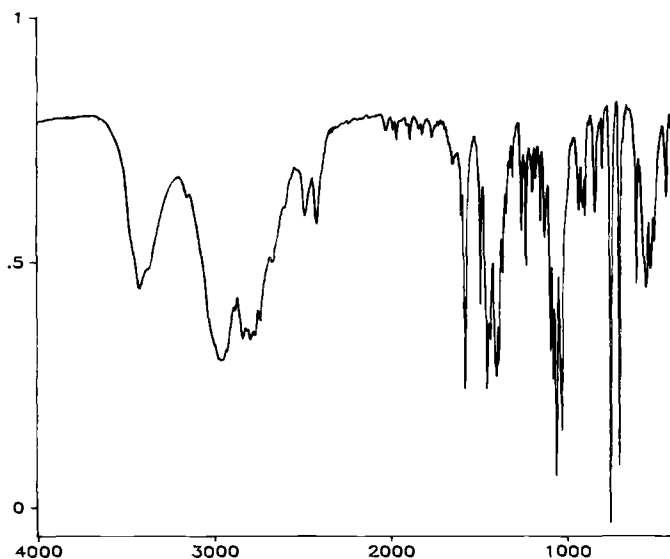


FIG. 6—Infrared spectrum ($4000\text{--}400\text{ cm}^{-1}$) determined on the police exhibit as received, HEA \cdot HCl plus EA \cdot HCl.

was extracted with chloroform, its filtrate evaporated to dryness, and the residue re-examined by FT-IR, a somewhat sharper spectrum was obtained which was more consistent with HEA without the minor contaminant HE \cdot HCl. A difference IR spectrum of these two spectra showed features consistent with HE \cdot HCl. IR spectroscopy, therefore, provided further evidence that both components were in the form of their hydrochloride salts. Later comparison of these spectra with published IR spectra of HEA \cdot HCl and HE \cdot HCl (1) confirmed the identities of the two substances.

Discussion

Once the identity of the police exhibit had been established unequivocally by molecular spectroscopic examination, then a thorough search of the chemical literature could be undertaken to determine if the substance was known. Interestingly, recent reference to the identification of a street incidence of N-(2-hydroxyethyl)amphetamine (HEA) had been previously reported by Carpenter et al. (1); however, this Southern Ontario exhibit was described as a light green odorous powder (significantly different from the exhibit received by the Bureau of Drug Research). In addition, the previous report did not indicate whether their material was found in a salt or base form, although its identity was given as the base form. While the IR spectra of the base and hydrochloride salt forms appear to have been determined by Carpenter et al. on synthesized materials, it was not stated whether their mass spectrum (reported for the base form) was determined on the exhibit or synthesized materials. Regardless, GC-MS determinations on amine hydrochloride salts would be detected only as the mass spectrum of the free base, since complete thermal decomposition of the halide salt form would have occurred upon injection to the GC column. The synthesis of HEA base and its HCl salt, together with their respective melting points, was also reported in earlier Russian literature (4) along with a series of other N-substituted amphetamines. However, apart from reference to HEA in various Patents in the 1950s obtained by Smith, Kline and French during the heydays of new amphetamine syntheses, the only other recent commercial or pharmaceutical linkage of HEA is for the synthesis of the stimulant fenethylamine from condensation of HEA with theophylline (5).

As mentioned above, the seized material possessed all the physical appearances of methamphetamine, including color and odor. On this basis, the substance could be easily marketed on the "street" as methamphetamine, again illustrating the risk associated with use of uncharacterized street drugs, and especially those with unknown pharmacological effects.

Our finding of ethanolamine hydrochloride as a minor contaminant in the seized exhibit clearly implicates it as a precursor in the preparation of HEA•HCl via the usual phenyl-2-propanone reductive amination route (e.g., as described for the preparation of 3,4-methylenedioxy-N-(2-hydroxyethyl)amphetamine (i.e., hydroxyethyl-MDA) (6)). Whether the illicit laboratory operator(s) confused ethanolamine with ethylamine in an attempt to produce ethylamphetamine, as suggested by our Scarborough HPB colleagues (1), or whether the reaction was undertaken with the intent of producing a new "street" drug cannot be determined from the available evidence.

Conclusion

Through the combined evidence obtained by ¹H- and ¹³C-NMR, mass, and infrared spectroscopy, the identity of a novel police exhibit was established as N-(2-hydroxyethyl)amphetamine hydrochloride (HEA•HCl) contaminated with 15% ethanolamine hydrochloride (HE•HCl).

Acknowledgment

The technical assistance of D. Bruce Black in determining NMR spectra, and Jean-Claude Ethier and Dr. Elly Kourany-Lefoll for mass spectrometric determinations is gratefully acknowledged.

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ERRATUM

An author's name was inadvertently omitted in the Table of Contents as well as in the Reference section for the paper entitled "Structural Elucidation of Unusual Police Exhibits. II. Identification and Spectral Characterization of N-(2-Hydroxyethyl)amphetamine Hydrochloride" published in the July 1996 issue.

The Table of Contents entry should read: Structural Elucidation of Unusual Police Exhibits. II. Identification and Spectral Characterization of N-(2-Hydroxyethyl)amphetamine Hydrochloride—TERRY D. CYR, BRIAN A. DAWSON, ARNOLD W. BY, GEORGE A. NEVILLE AND HERBERT F. SHURVELL

The Reference (in new format) should read: Cyr TD, Dawson BA, By AW, Neville GA, Shurvell HF. Structural elucidation of unusual police exhibits. II. Identification and spectral characterization of N-(2-hydroxyethyl)amphetamine hydrochloride. *J Forensic Sci* 1996 Jul;41(4):608–11.