



Matrix effects in the infrared examination of methamphetamine salts

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Abstract

The infrared transmission spectra of some hydrogen halide salts of methamphetamine are observed to display significant variations dependent upon the alkali halide matrix in which the salt is dispersed for examination. These effects appear to arise from a chemical exchange of halide ions between the methamphetamine salt and the matrix material, which can complicate the interpretation of the spectra. A strong absorption in the hydrogen-stretching region of the infrared spectrum is found to be particularly sensitive to the anion present in the salt, and changes in the appearance of this absorption band can be revealing of any chemistry between the salt and the alkali halide matrix. The analyst should be aware of this phenomenon in the forensic identification of methamphetamine salts, as well as its possible occurrence with other amine drug substances.

Keywords: Infrared spectroscopy; Methamphetamine; Alkali halide; Matrix effects

1. Introduction

A common method of solid sample preparation for infrared examination is the dispersion of the sample in an alkali halide salt, popularly potassium bromide, which may then be pressed into a window for infrared transmission measurements. On occasion, though, the infrared properties of some solid materials may be altered when dispersed in an alkali halide matrix under pressure [1,2]. This concern has, in fact, been raised with regard to the hydrochloride salts of some drugs [3], like

phencyclidine (PCP) (J.A. Heagy, DEA, pers. comm.). Observations made on the hydrogen halide salts of methamphetamine have revealed significant differences in the infrared spectra that are dependent upon the halide ion of the matrix material. The identification of the halide salt-form for methamphetamine may be complicated by these effects, and the prudent forensic chemist should be aware of the differences present in the infrared spectra. The matrix effects may be particularly relevant to clandestine laboratory investigations, where the determination of the salt-form for methamphetamine (or its ephedrine precursor) can be revealing as to the method or means of methamphetamine manufacture [4].

2. Experimental

Infrared studies were conducted with a Fourier-transform infrared spectrometer (Nicolet, model 205), operated at 32 scans per measurement with 4 cm^{-1} resolution. Samples were generally prepared by grinding the methamphetamine salt with an agate mortar and pestle for particle size reduction, followed by grinding an appropriate amount of potassium halide matrix material in with the salt. Comparative preparations were made by mixing ground samples of the salt and matrix material without additional grinding of the mixed preparation. The samples were then pressed without the application of a vacuum at approximately 18 000 psi pressure (with a Carver press) into rectangular transmission windows within cut-out blotter cards. The pressed windows were examined promptly after preparation (within 3 min of mixing the sample and matrix material). The matrix materials employed were reagent grade potassium chloride (KCl) and potassium iodide (KI), and spectroscopic grade potassium bromide (KBr). The moisture content of the matrix materials was minimized by drying the potassium halide salts in an oven at 120°C for 20 h and subsequently storing in a desiccator under vacuum. Mulls of the salts were also prepared with a fluorolube oil for comparison purposes.

The *d*-methamphetamine hydrochloride salt (HCl) employed in this study was equivalent to pharmaceutical grade with a high purity assay ($>99\%$), and exhibited a sharp melting point ($171\text{--}172^{\circ}\text{C}$) consistent with literature values [5]. The hydrobromide (HBr) and hydroiodide (HI) salts of methamphetamine were prepared by the complexation of methamphetamine base with hydrobromic and hydriodic acids, respectively, in concentrated aqueous solutions. The base was prepared by the neutralization of the HCl salt in aqueous solution with concentrated ammonium hydroxide, followed by extraction of the aqueous solution with petroleum ether and evaporation of the solvent to obtain the base oil. The methamphetamine base was then dissolved into the HBr or HI solutions, and the ion-pair extracted with chloroform. The chloroform extract was passed over a column of anhydrous sodium sulfate to remove any residual moisture from the sample, and the HBr and HI salts were recovered by solvent evaporation of the chloroform solution on a steam bath. All three salt-forms were recrystallized as fine, white crystals with a needle-like habit from acetone upon the addition of ethyl ether. The crystals were washed well with ethyl ether to remove any remaining impurities and then stored in a desiccator under vacuum. Sharp melting points were

measured for methamphetamine HBr (132–133°C) and methamphetamine HI (98–99°C), consistent with relatively pure salts. All solvents and chemical reagents used were reagent grade.

3. Results and discussion

Spectra of methamphetamine HCl dispersed in KCl and KBr are shown in Fig. 1. The spectra are generally similar with common peak positions and shapes

Transmission (arbitrary units)

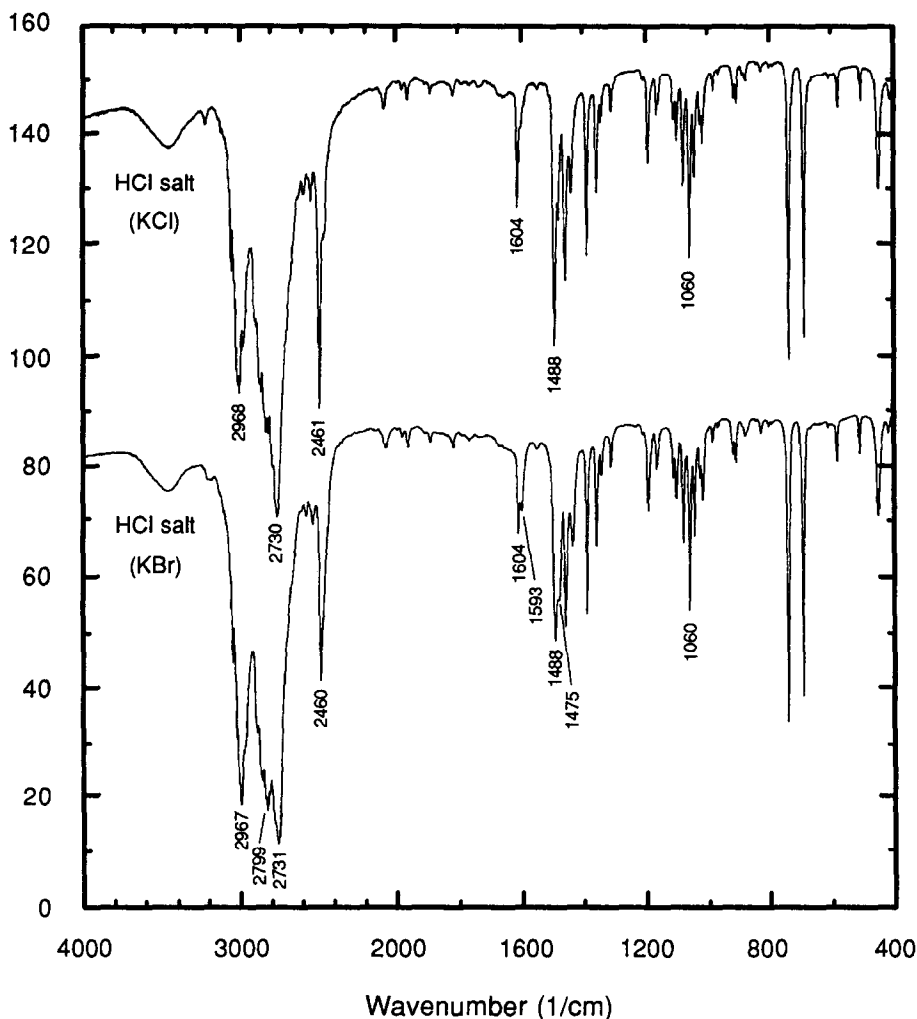


Fig. 1. Comparison of the infrared transmission spectra for methamphetamine HCl (HCl salt) prepared in a KCl and a KBr matrix.

throughout the mid-infrared region. However, the strong absorption envelope in the hydrogen-stretching region between 3000 and 2700 cm^{-1} displays a significantly different shape between the two spectra. Most notable, the relative intensity of the two prominent peaks near 2970 cm^{-1} and 2730 cm^{-1} varies appreciably for the two spectra, where the 2970 cm^{-1} peak is markedly stronger for the salt in KBr. The absorption envelope in this spectral region presents the same shape for the HCl salt when prepared as a fluorolube mull as in a KCl matrix, indicating some alteration in the infrared properties for the HCl salt when dispersed in KBr.

The change in the spectrum of methamphetamine HCl when dispersed in a KBr matrix may be attributed to the addition of spectral features of methamphetamine HBr. This effect is illustrated in Fig. 2, where a calculated difference in the spectra of Fig. 1 is compared to the spectrum of methamphetamine HBr dispersed in KBr. The shape of the absorption envelope between 3000 and 2700 cm^{-1} for methamphetamine HBr is strikingly similar to the analogous feature in the difference spectrum, and is distinctly different in appearance from the absorption band observed for the HCl salt in KCl. This absorption envelope for methamphetamine HBr lacks the single prominent peak at 2730 cm^{-1} , but displays a pair of peaks near 2800 cm^{-1} and 2750 cm^{-1} with a cleft in the absorbance at 2770 cm^{-1} . This feature is absent in the spectrum of methamphetamine HCl in KCl, but a distinct cleft is present at 2770 cm^{-1} in the spectrum of methamphetamine HCl when dispersed in KBr. The difference spectrum also reveals the presence of a sharp peak near 2440 cm^{-1} and a smaller shoulder peak at 2416 cm^{-1} when the HCl salt is prepared in a KBr matrix. These features agree in position and appearance with the corresponding peaks present in the spectrum of methamphetamine HBr. The shape of these peaks and the absorption envelope observed for the HBr salt dispersed in KBr appears characteristic to the HBr salt-form and is the same for the salt when prepared as a fluorolube mull.

The spectra of the HCl salt in KCl and KBr reveal some other significant differences in the mid-infrared region, which upon close examination show a correspondence to spectral features of methamphetamine HBr. Specifically, a single sharp peak is observed at 1604 cm^{-1} for methamphetamine HCl in KCl, but a distinct second peak or shoulder at 1593 cm^{-1} is observed for the salt when dispersed in KBr. This feature derives from a single peak near 1590 cm^{-1} illustrated in the difference spectrum, which correlates with the sharp peak at 1589 cm^{-1} in the spectrum of methamphetamine HBr. The two small shoulder peaks present on this peak in the spectrum of the HBr salt are apparently unresolved in the difference spectrum, likely due to their relative weakness. Similarly, the series of peaks between 1500 and 1400 cm^{-1} appear different for the two salt-forms, where the most prominent peak in this area shifts from 1488 cm^{-1} for the HCl salt to near 1470 cm^{-1} for the HBr salt. This change is detected in the spectrum of the HCl salt when dispersed in KBr as the difference spectrum presents a prominent peak at 1472 cm^{-1} as well as a sharp but weaker feature at 1493 cm^{-1} . These peaks match the relative appearance of the same series of peaks in the spectrum of methamphetamine HBr. Other features present in the mid-infrared region appear largely equivalent for the two salt-forms, or are too weak to distinguish between methamphetamine HCl and methamphetamine HBr.

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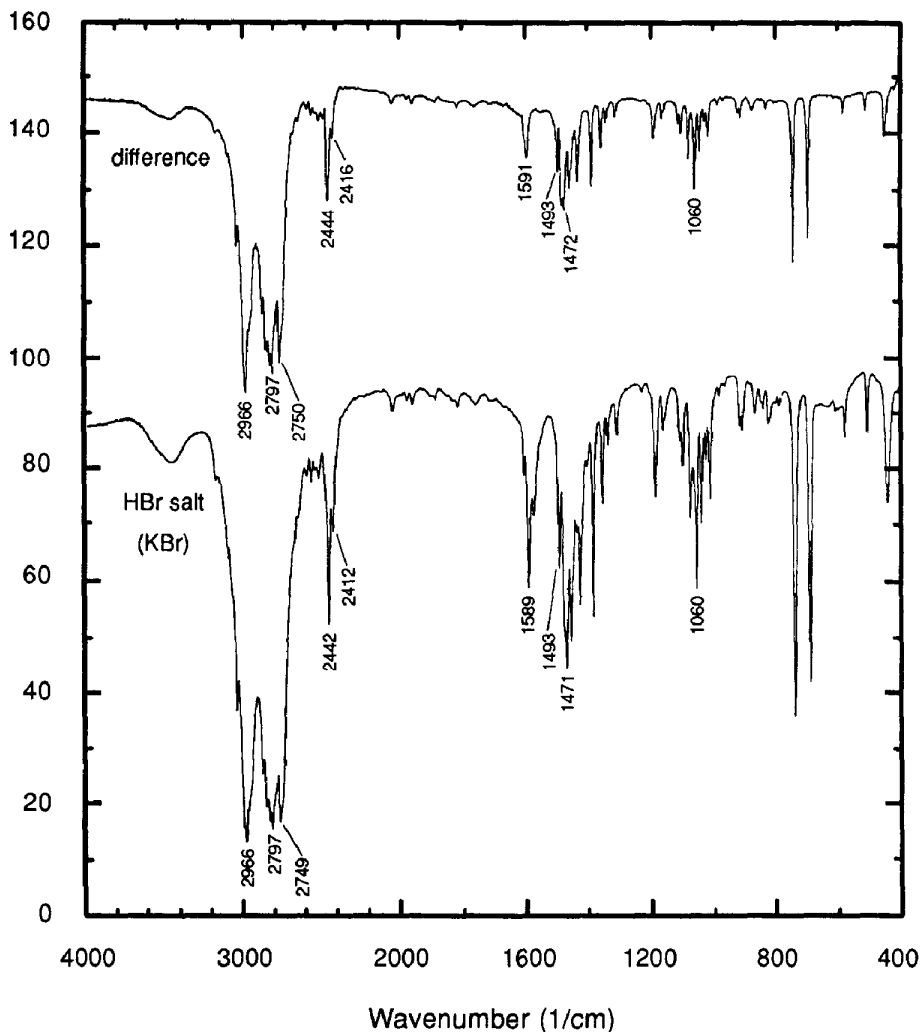


Fig. 2. Comparison of the infrared transmission spectrum for methamphetamine HBr (HBr salt) prepared in KBr with a difference spectrum calculate from the infrared transmission spectra of methamphetamine HCl in Fig. 1. The difference spectrum was generated by a point-by-point subtraction of the corresponding absorption spectra of the HCl salt prepared in KCl and KBr with the resultant spectrum converted back to a transmission form for comparison purposes. The calculation weighted the spectrum of the HCl salt in KCl by a factor (0.65) that gave the best comparison to the spectrum of the HBr salt.

This phenomenon also occurs with methamphetamine HCl when dispersed in KI, as demonstrated in Fig. 3, where transmission spectra of the HCl salt dispersed in KCl and KI are compared to that of the HI salt in a KI matrix. Considerable

Transmission (arbitrary units)

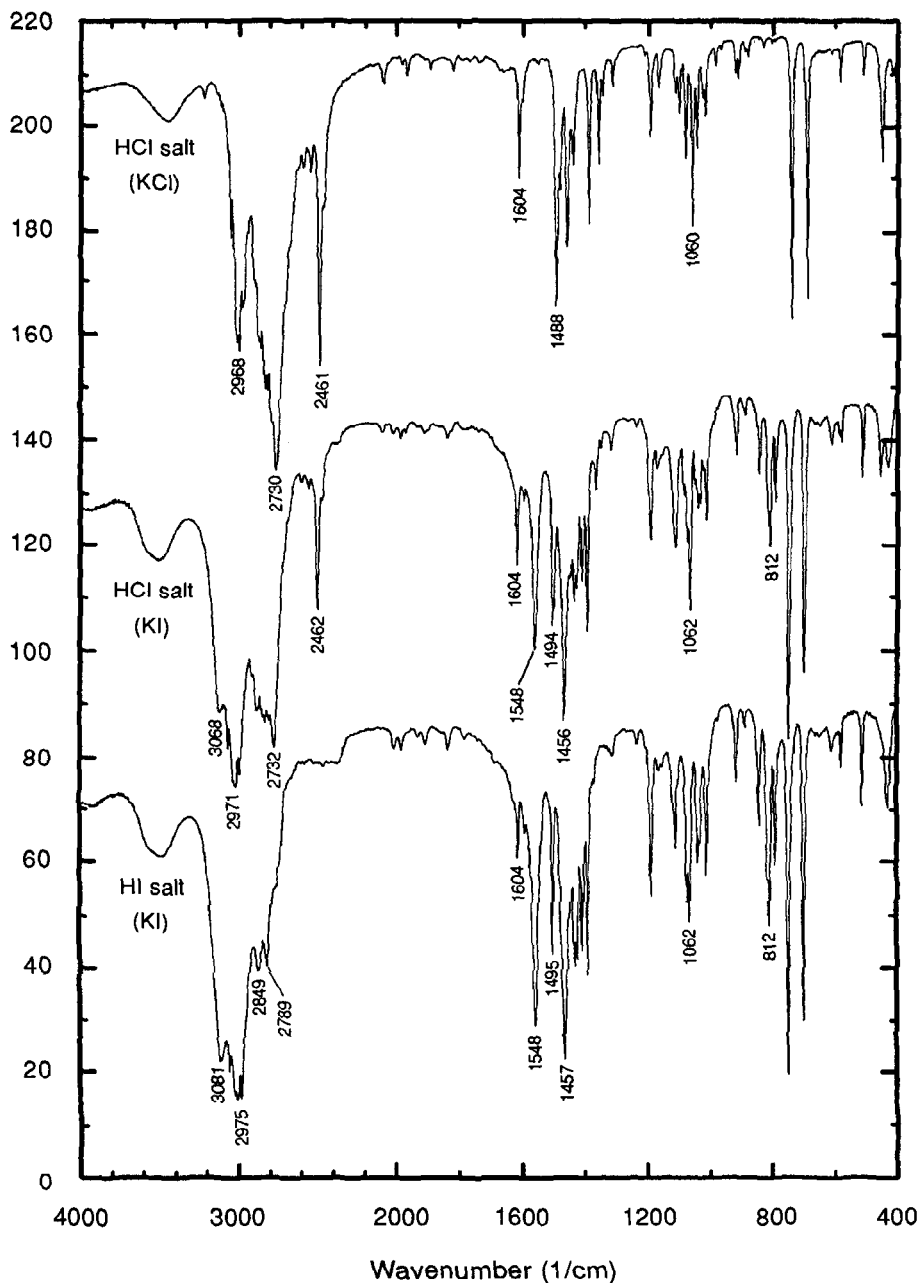


Fig. 3. Comparison of the infrared transmission spectra for methamphetamine HCl (HCl salt) prepared in KCl and KI with the spectrum of methamphetamine HI (HI salt) prepared in a KI matrix.

differences are observed between the spectra for the HCl salt, where many spectral features of methamphetamine HCl (as observed in KCl) are reduced in intensity or modified for the salt when dispersed in KI. These features correlate to the spectrum of methamphetamine HI [4], which appears quite different from the spectrum of the HCl salt in KCl (as well as that of the HBr salt in KBr). Specifically, several new strong peaks have appeared in the mid-infrared region, like that at 1548 cm^{-1} and those between 900 and 800 cm^{-1} . The sharp peak near 2460 cm^{-1} is also absent for the HI salt dispersed in KI, and the strong absorption envelope between 3100 and 2700 cm^{-1} for the HI salt displays a shape that sharply contrasts the appearance of the envelope for the HCl and HBr salt-forms. The absorption envelope for the HCl salt when dispersed in KI displays features near 3000 cm^{-1} quite similar to that of the HI salt, but with the addition of a second peak near 2730 cm^{-1} that coincides with the predominant peak of the spectrum of methamphetamine HCl in KCl. As with the HCl and HBr salts of methamphetamine, the HI salt possesses a distinctive shape for this absorption envelope, which appears the same as the envelope observed for the HI salt when prepared as a fluorolube mull.

These effects by the potassium halide matrix appear to arise from chemical interactions between the dispersed microcrystalline particles of the salt and the matrix material within the pressed transmission window. The physical environment created by the alkali halide matrix may in principle alter the crystalline structure of the salt-form (polymorphism) [2] and, thereby, modify the infrared properties observed for the salt without any change in the chemical composition of the sample. This description, however, does not apply to the observations for the methamphetamine salts since the spectrum from a sample dispersed in a potassium halide matrix with the same halide ion as the salt appears equivalent to the spectrum of the salt when prepared as a mull.

Alternatively, a chemical reaction in which there is an actual exchange of different halide ions between the particles of the salt and the matrix would produce a distinctly different chemical phase with potentially altered crystalline structure and infrared properties [1,2]. The appearance of distinctive spectral features of the HBr or HI salts of methamphetamine within the spectrum of methamphetamine HCl (when the HCl salt is dispersed in KBr and KI, respectively), strongly indicates a chemical reaction and the apparent formation in situ of a methamphetamine salt containing the halide ion of the matrix in which the HCl salt is dispersed. An exchange of halide ions can complex the methamphetamine ammonium ion with the halide ion of the matrix to precipitate crystallites of a new salt phase, which then contribute to a composite infrared spectrum. This precipitate phase can either be composed solely of the halide ion of the matrix, or may be of mixed character and contain halide ions of both the original methamphetamine salt as well as the ion of the matrix. (A crystal phase containing both halide ions may entail the regular placement of chloride and bromide ions within the structure, or alternatively, the random placement of both ions in a regular position within the crystal, as in an alloy). A composite spectrum of the HCl salt and the HBr or HI salt derived from the matrix material appears to account for the changes observed in the spectra.

Halide ion exchange with the matrix is also supported by melting point measurements made on the methamphetamine salts recovered from pressed transmission windows. The methamphetamine salts present within some matrix preparations were extracted by grinding the pressed window and washing this powder with methylene chloride. The precise identity of the crystal form of these phases is lost when the methamphetamine salts dissolve into the extract solution, but the melting point of the solids recovered from the solution can still reveal a change in composition. Extracts of methamphetamine HCl preparations in KCl yield a solid that melts near 170°C, consistent with a relatively pure HCl salt. Samples of the HCl salt prepared in KBr and KI, however, give solids that melt much lower (< 150°C), and typically melt near the melting point of the methamphetamine salt-form with the same halide ion as the matrix employed in the preparation. (The precise form of the melting behavior reflects the nature of the crystalline form as precipitated from the extract solution, i.e. mechanical mixtures or alloys may possibly form). This melting behavior is complementary evidence of halide ion exchange between the methamphetamine salt and the potassium halide matrix.

Some variability in the transmission spectra is observed among sample preparations for the HCl salt, which appears attributable to variations in the relative amounts of the salt phase precipitated from the matrix and the original HCl salt. The rate of halide ion exchange between the original salt-form and the matrix material determines the composition of the transmission window at the time of the measurement, and is indicated to be influenced by several factors. Mixing the powder of both the salt and matrix material without any additional grinding of the preparation initially results in less modification of the spectrum. The mechanical action of grinding the powders together apparently promotes the reaction responsible for the phase change, possibly through frictional heating or improved mixing and contact of the solids. However, the pressed sample is observed to transform with time (while stored under vacuum), and the spectral features of the methamphetamine salt derived from the halide ion of the matrix strengthen considerably within 1 h of preparation. Older samples can show additional changes to their spectra and appear to reach an equilibrium state that predominantly displays the features of the methamphetamine salt precipitated from the matrix.

Atmospheric humidity and the moisture content of the sample also play a role in the rate at which the reaction progresses and spectral changes develop within the sample. Both the methamphetamine salts and the alkali halide salts are recognized for their hygroscopic properties, whereby atmospheric water adsorbs to the surfaces of the solids to varying degrees. In this study, an effort was made to minimize moisture in the preparations, although some trace moisture is likely present or is quickly adsorbed from the atmosphere. Samples of illicit methamphetamine salts are particularly susceptible to the adsorption of water due to the highly hygroscopic nature of some common trace contaminants, i.e. methylamine. Adsorbed water can significantly alter the surface state of a solid, which apparently facilitates the reaction between the particles of these substances within the matrix [2]. In theory, water may also become bound within the crystalline structure of the salt to produce a hydrated phase with modified infrared properties. This latter effect, however, is

not indicated since the hydration reaction may occur when the methamphetamine salt is dispersed in any potassium halide matrix, although spectral changes (relative to the mull preparations) are not observed for a matrix with the same halide ion as the methamphetamine salt.

Analogous matrix effects are also observed for the HBr salt when dispersed in KCl or KI, where spectral features of the HCl and HI salts respectively, are introduced into the spectrum of methamphetamine HBr. Interestingly, similar matrix effects have not appeared in the infrared examination of methamphetamine HI when this salt is dispersed in either KCl or KBr, even for extended periods of time (several weeks). Apparently, the HI salt is unreactive with the potassium halide matrix, probably due to an enhanced stability for the crystalline phase of methamphetamine HI relative to the HCl and HBr salts. The distinctive spectrum observed for the HI salt suggests a different character to the cohesive interactions within the crystal structure of this salt, in which the association between the methamphetamine ammonium cation and iodide anion is likely more covalent in nature than that present within the HCl and HBr salts. This binding difference for the ion-pair can also increase the activation barrier for halide ion exchange and, thereby, inhibit the reaction between the HI salt and the matrix.

These observations also provide some insight into the interpretation of the infrared spectra of the methamphetamine salts. Several features within the infrared spectrum are notably sensitive to the halide ion present in the salt, although particularly strong effects are observed on the shape of the strong absorption envelope in the hydrogen-stretching region ($3100\text{--}2700\text{ cm}^{-1}$) beyond that found in the 'fingerprint' region ($2000\text{--}500\text{ cm}^{-1}$). The strength of this absorption appears to derive from the vibrations of the ammonium protons within the strong dipole field of the ammonium-halide ion-pair, while the breadth of the envelope results from the long-range interactions between these vibrations within the crystalline state of the salt. The fine structure observed in the envelope is apparently further shaped by interactions between the ammonium proton vibrations and some hydrogen-stretching modes of the methamphetamine molecule [6]. Importantly, the appearance of this absorption is sensitive to the anion present, since the anion largely defines the character of the ion-pair and, thereby, directly influences the interactions responsible for the absorption. In principle, this phenomenon applies to any ammonium salt-form and, therefore, should describe a general infrared property of amine drug substances. A broad absorption envelope in the hydrogen-stretching region ($3200\text{--}2400\text{ cm}^{-1}$) is observed for most amine salt-forms, although the intensity of this absorption is reduced in some cases. Highly polarizable constituents (like unsaturated groups) common to alkaloid molecules can electrostatically screen the dipole of the ion-pair, which effectively lessens the strength of this absorption.

The chemical exchange of halide ions between the methamphetamine salts and the alkali halide matrix is principally determined by the relative stability of the different salt-forms for methamphetamine and, specifically, whether there exists a stable methamphetamine salt phase containing the halide ion of the matrix. This chemistry is quite possible with other amine salts, as has been indicated for the salts

of phencyclidine, as well as 3,4-methylenedioxy-methamphetamine (in which the degree of hydration is also suggested to change with the halide ion of the matrix material). Matrix effects may be detected by subtle, yet significant, spectral changes between preparations of a sample, especially when different alkali halide matrices are employed. Unfortunately, spectral variation among preparations of amine salts may be mistakenly confused with a polymorphism that does not involve hydration or anion exchange with the matrix. Attention should be drawn to effects on the shape of the absorption envelope within the hydrogen-stretching region, which can be particularly revealing of any chemistry between an amine drug substance and the alkali halide in which it is dispersed.

4. Conclusion

In summary, the infrared spectrum of methamphetamine HCl is observed to be significantly altered when the salt is dispersed in a KBr matrix for infrared examination. The observations suggest a chemical reaction between the particles of methamphetamine HCl and KBr, which leads to some exchange of the halide ions and the subsequent formation of a bromide containing methamphetamine salt phase. This phenomenon may complicate the identification of the salt-form, but can be avoided with samples of methamphetamine HCl when KCl or NaCl is employed as the matrix material. Similar behavior is observed for the HCl salt when dispersed in KI, and analogous effects occur for the HBr salt of methamphetamine when prepared in KCl and KI. In contrast, no effects are detected for the HI salt when dispersed in either KCl or KBr. This chemistry should be of note in forensic drug analysis since these effects may not only influence the interpretation of the infrared spectra for the methamphetamine salts, but can also apply to other amine drug compounds.

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References

- [1] J.E. Stewart, *Infrared Spectroscopy — Experimental Methods and Techniques*, Marcel Dekker, New York, 1970, pp. 515–524.
- [2] N.L. Alpert, W.E. Keiser and H.A. Szymanski, *Theory and Practice of Infrared Spectroscopy*, Second Edition, Plenum Press, New York, 1973, pp. 329–339.
- [3] D.I. Chapman, Infra-red absorption spectrophotometry. In E.G.C. Clarke (ed.), *Isolation and Identification of Drugs*, The Pharmaceutical Press, London, 1969, p. 111.
- [4] H.F. Skinner, Methamphetamine synthesis via hydriodic acid/red phosphorus reduction of ephedrine. *Forensic Sci. Int.*, 48 (1990) 123–134.
- [5] *The Merck Index*, 11th edition, Merck and Company, Inc., Rahway, NJ, 1989, p. 937.
- [6] J.S. Chappell, *Some Infrared Properties of Organic Charge Transfer Salts*, Ph.D. Thesis, The Johns Hopkins University, Baltimore, MD, 1983.