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Thermal Decomposition of Cocaine and Methamphetamine Investigated by Infrared Spectroscopy and Quantum Chemical Simulations

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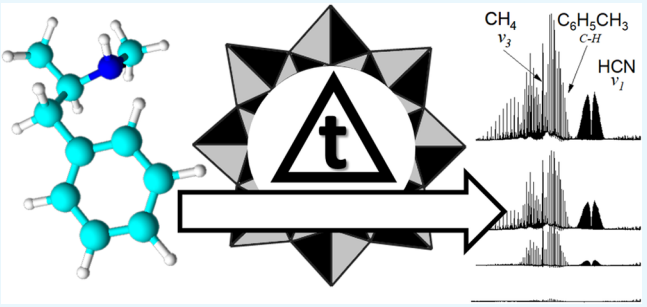
ABSTRACT: Examination of thermal decomposition of street samples of cocaine and methamphetamine shows that typical products detected in previous studies are accompanied by a wide palette of simple volatile compounds easily detectable by spectral techniques. These molecules increase smoke toxicity and their spectral detection can be potentially used for identification of drug samples by well-controlled laboratory thermolysis in temperature progression. In our study, street samples of cocaine and methamphetamine have been thermolyzed under vacuum over the temperature range of 350−650 °C. The volatile products (CO, HCN, CH_4, C_2H_4, etc.) have been monitored by high-resolution Fourier-transform infrared (FTIR) spectrometry in this temperature range. The decomposition mechanism has been additionally examined theoretically by quantum-chemical calculations for the highest temperature achieved experimentally in our study and beyond. Prior to analysis, the street samples have also been characterized by FTIR, Raman spectroscopy, energy-dispersive X-ray spectroscopy, and melting point determination.



1. INTRODUCTION

Contemporary drug detection, identification, and deep analysis include many analytical chemistry techniques, most of which are chromatographic.[1,2] The main advantages of chromatography are its high sensitivity and the discrimination of individual components of drug mixtures. High-performance liquid chromatography (HPLC),[3,4] gas chromatography (GC),[5,6] and supercritical fluid chromatography are frequently applied techniques.[7−11] Samples of blood can be analyzed using HPLC/diode array detection[12] or by mass spectrometry (MS).[13] Alternatively, LC using a hydrolytic interaction,[14] or the ionizing spray method (FAPA) with mass detection has the potential to replace GC.[15] In this case, the sample requires almost no preparation and the analysis provides quantitative data. These techniques have already practically replaced older techniques, for example, cocaine hydrochloride analysis by titration using perchloric acid in the environment of a nonaqueous 1,4-dioxane (weighed down by the interference of other organic bases in the sample), UV spectroscopy, piezoelectric sensors, ion-selective membrane electrodes,[16] or thin-layer chromatography.[17]

Apart from chromatographic techniques, nondestructive fast-screening methods such as Raman spectroscopy are being increasingly used.[18,19] Any sample can be analyzed repeatedly and the analysis is fast, affordable, reproducible with different spectrometers (within their method requirements and measurement limitations), and useable for forensic purposes. Fast-screening provided by Raman does not require prior preparation of the sample, such as purification, cleaning, or dissolution, and is not affected by the presence of water. A number of different techniques are used: dispersive Raman spectroscopy, Fourier-transform Raman spectroscopy, micro-Raman spectroscopy, or spectroscopy with excitation in the near-infrared region. Each technique serves a different purpose and is suitable for a different type of analysis, for example, dispersive techniques with the excitation radiation at 830 nm are more effective than Fourier-transform techniques at 1064 nm. This makes it possible to distinguish individual drugs in the mixture, including samples that contain various admixtures,

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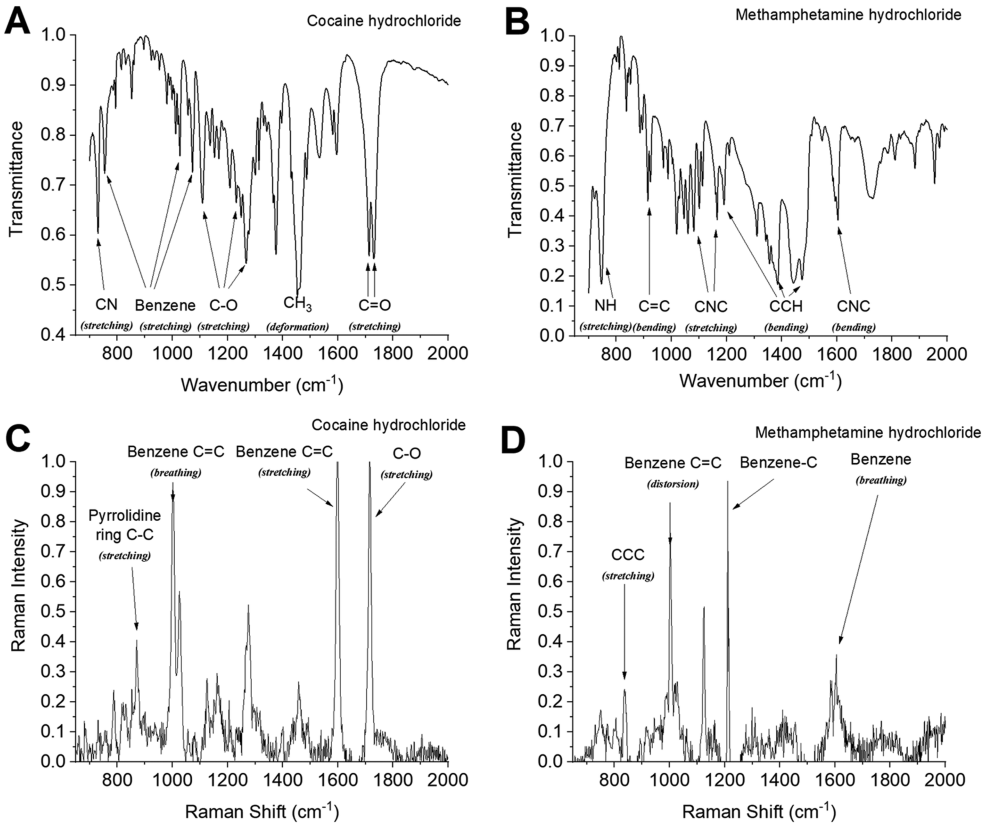

Figure 1. Spectral survey of cocaine and methamphetamine street samples. A,B) FTIR Nujol spectra of cocaine hydrochloride and methamphetamine hydrochloride, respectively. C,D Raman spectra of the same samples. The IR spectra are assigned using the data from refs[33−35] and references therein. The Raman spectra are assigned based on the data from ref 36.

or to distinguish between individual forms of the drugs (e.g., the salt of an alkaline form of cocaine with hydrochloride[20]). Disadvantages of Raman spectroscopy are its unsuitability for quantitative analysis, for the detection of extra added agents, the necessity to use multiple lasers at varying wavelengths in the case of a complex analysis, and the inability to analyze dark-colored samples.[20]

Pocket-sized Raman spectrometers, which can identify the dominant drug or the most represented substances for the preliminary analysis of a sample, have recently appeared on the market. However, these are characterized by low sensitivity and are unsuitable for complex samples that fluoresce strongly, interfering with the measurement,[20] and for dark-colored samples that can be decomposed by absorbing laser energy.

In this work, we have examined the thermolysis of street samples of cocaine and methamphetamine. Pure cocaine is a white crystalline alkaloid first isolated in 1860 by A. Niemann. Its name is derived from the coca bush (*Erythroxylon coca*), which contains cocaine in its leaves. It is a strong stimulant and partial anesthetic. For a short time after application, it brings on a strong euphoria, the feeling of self-confidence and concentration. Negative effects include loss of self-control, ischemia and tachycardia, and loss of the nasal septum in the case of sniffing. Chronic use leads to significant psychological addiction. Cocaine typically appears in two forms: the freebase typically obtained by isolation from leaves and a hydrochloride salt. Cocaine was classified as a drug in 1961, and since then, all manipulation with it is subject to strict restrictions. Illegally sold drug mixtures tend to contain admixtures such as talc, lactose, glucose, mannitol, caffeine, strychnine, amphetamine, or heroin.

The second drug examined in this study is methamphetamine.[21] It is a white crystalline substance derived from amphetamine. Synthetic in origin, it was first prepared in 1893 by N. Nagayoshi. Its effects include exhaustion suppression, increase of euphoria, and self-trust caused by a release of serotonin and dopamine. Long-term use leads to loss of teeth, damage to the central nervous system, and the onset of paranoid schizophrenia. For these effects, it was used during WWII as a stimulant for soldiers under the brand name Pervitin. Today, one of the enantiomers of methamphetamine is sporadically used to treat narcolepsy under the trademark Desoxyn. Synthesis of this substance is illegal, but frequent and common, because it may be prepared in simple reaction steps from pseudoephedrine, a substance contained in some anti-influenza drugs. Methamphetamine also appears in the form of a hydrochloride salt. It was first prepared in 1913 through a reaction of ephedrine with red phosphorus and iodine.

Understanding the thermolysis of drugs at a mechanistic level as well as detecting the compounds released by drug decomposition at different temperatures is highly important. First, smoking a cigarette mixed both with methamphetamine and cocaine is an abuse pattern among the younger generation. Smoking the free base form of cocaine, also known as crack, has been associated with various medical problems, including lung damage and neurological disorders. The pathophysiology is associated with the major organic molecule produced by "crack" smoking: anhydroecgonine methyl ester (AEME). The results of viability assays showed that AEME is an agent with

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greater neurotoxic potential than cocaine.[22] Among other molecules, amphetamine and dimethylamphetamine have been identified as major pyrolysis products of methamphetamine at relatively modest temperatures. The methamphetamine molecule is structurally similar to amphetamine and to the neurotransmitter dopamine but has longer lasting and more toxic effects than amphetamine.[23] The neurotoxic potential of dimethylamphetamine is lower than for methamphetamine.[24] A systematic analysis of the thermal decomposition products of methamphetamine (called pervitin) as well as cocaine (called crack) will help us understand the complex toxicity and danger for their smokers due to a possible synergy among thermolysis products.

A second reason for exploring thermal drug decomposition is for analytical purposes. Especially, the detection and the identification of volatile thermolysis products using infrared spectroscopy, or GC−MS, can overcome several problems with the analysis of street samples exhibiting variable purity, color, structure, and form. Thermal analysis under controlled conditions is a simple and robust method, which cannot be influenced by these factors and can provide valuable data for drug identification and multicomponent analysis when conducted in over a progression of temperatures.

In this study, we have employed ab initio molecular dynamics (AIMD) quantum chemical simulations of single cocaine and methamphetamine molecules; and for the experiments, we have thermally decomposed and inspected the volatile products of cocaine and methamphetamine with high-resolution Fourier-transform infrared spectroscopy (FTIR). The thermolysis of drugs is described mechanistically and the potential contribution of controlled thermolysis to the analysis and detection of drug mixtures is discussed.

2. RESULTS AND DISCUSSION

2.1. Sample Characterization. In our study, we have selected two street samples: "Pervitin 1213," further identified as methamphetamine hydrochloride, and "Cocaine 1281," further identified as cocaine hydrochloride. The melting point of the methamphetamine hydrochloride street samples was determined to be 172.4 °C (in the Pubchem database, 172.5 °C). The melting point of the street sample of cocaine hydrochloride examined in this study was measured to be 173.7 °C (in the literature,[32] 186−188 °C for a racemic mixture of (±)-cocaine HCl). Elemental analysis using the energy-dispersive X-ray spectroscopy (EDS) microprobe identified carbon (90.9%) and chlorine (8.6%) in the street sample of methamphetamine hydrochloride. The sample did not contain a detectable amount of metals or other inorganic materials and elements. The street sample of cocaine hydrochloride contained carbon (80%), chlorine (4.9%), oxygen (11.8%), and sulfur (3.1%).

We have also recorded the FTIR and Raman spectra of both samples. The combination of bond resonances detected in the Raman and condensed-phase FTIR spectra is sufficiently characteristic of methamphetamine hydrochloride and cocaine hydrochloride. The spectra are shown in Figure 1A−D.

2.2. Spectroscopic Survey of the Gas-Phase Products. Examples of the experimental FTIR spectra are shown in Figure 2. During vacuum thermolysis, the cocaine hydrochloride street sample released increasing amounts of methylchloride (CH_3Cl), ethylene (C_2H_4), methane (CH_4), hydrogen cyanide (HCN), carbonylsulfide (OCS), carbon disulfide (CS_2), carbon dioxide (CO_2), and carbon monoxide

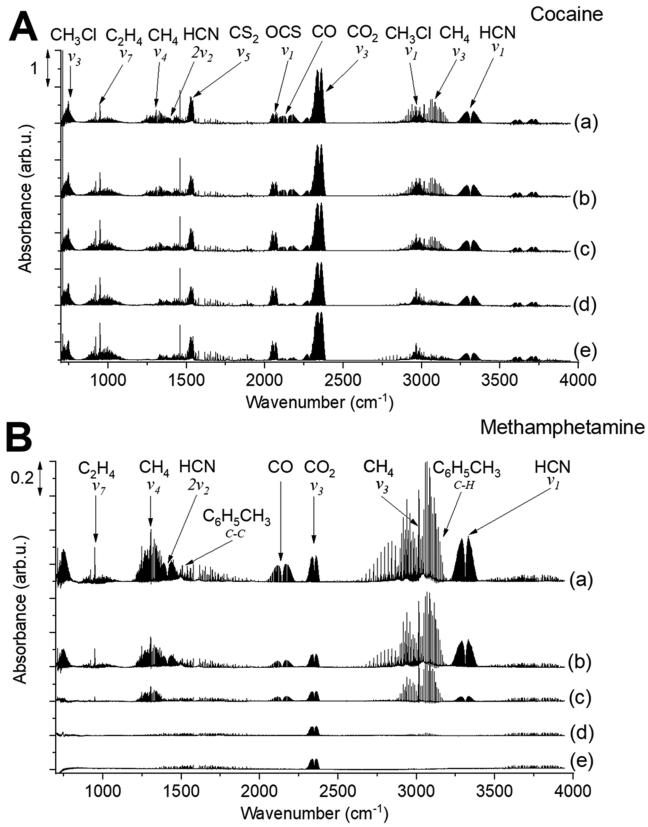

Figure 2. (A) Spectra recorded after thermal decomposition of cocaine. The spectra recorded after thermal decomposition of methamphetamine are shown in panel (B). The spectra correspond to temperatures equal to (a) 750, (b) 650, (c) 550, (d) 450, and (e) 350 °C.

(CO). It is very likely that CH_3Cl results from the hydrochloride form of this drug and sulfur-bearing species probably result from traces of solvents such as dimethyl sulfoxide used in illegal manufacturing laboratories or traces of extra ingredients added to cocaine (called "cutting agents") such as *N*-acetylcysteine. Figure 3A shows the measured column densities of species in centimeter of the absorption signal detected from thermolyzed cocaine hydrochloride for increasing temperatures. Over the 350−750 °C temperature range, there is an increased density of CH_4 and CO, and a slight increase for HCN. The concentration of other species remained roughly constant. Decomposition products of methamphetamine hydrochloride are released at temperatures over 550 °C with an increasing column density with temperature recorded for all detected species: methylchloride (CH_3Cl), ethylene (C_2H_4), methane (CH_4), hydrogen cyanide (HCN), toluene ($C_6H_5CH_3$), carbon dioxide (CO_2), and carbon monoxide (CO).

2.3. AIMD Computational Models. The thermal decomposition of cocaine and methamphetamine above 750 °C has been simulated by means of AIMD computations. These calculations can be applied for reactions at temperatures exceeding 1000 K. The thermal-decomposition channels of stable cocaine and methamphetamine molecules are observed when simulated at these high temperatures. According to these calculations, theoretical single-molecule decomposition is not initiated below 1000 K, suggesting that mechanisms explicitly involving intermolecular interactions could drive thermal

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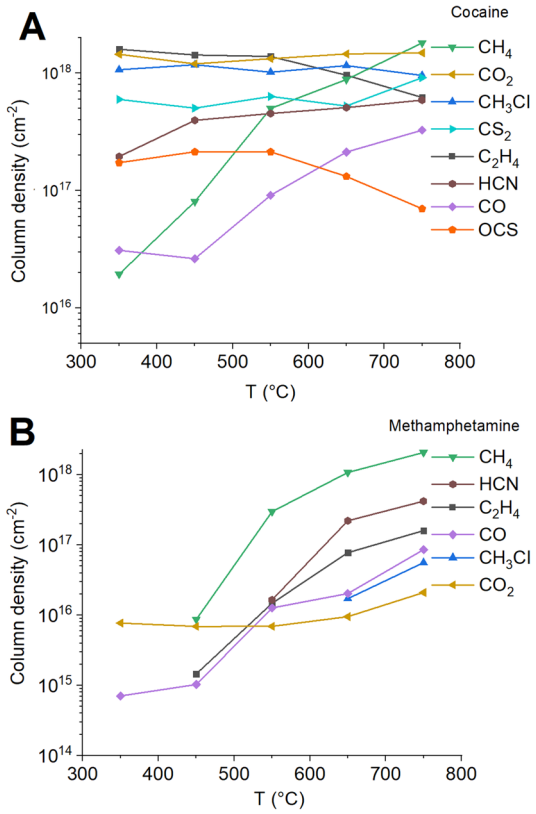

Figure 3. Column densities (proportional to their relative abundances) of products as a function of thermolysis temperature for cocaine (A) and methamphetamine (B). In the case of cocaine, qualitative features are constant for all temperatures. For methamphetamine, major changes occur at 550 °C, where more products other than CO_2 become detectable.

dissociation at these lower temperatures. As laid out in the Results and Discussion section, such a simplified model may lead to different products depending on the simulated temperature.

The simulation demonstrates that the thermal decomposition of single cocaine and methamphetamine molecule is strongly temperature dependent. Absolute temperatures inferred from these single-molecule simulations are not fully reliable but the reaction products and predicted dissociation mechanisms are robustly suggested within a rigorous Kohn–Sham density functional theory (DFT) framework. Simulations are based on simplified numerical systems compared to the real samples. They involve single-molecule systems and they are limited in the richness and complexity of the chemical products they produce, and the mutual reactions and subsequent decomposition of these products. Drug molecules can—and indeed do—interact/collide with each other and with the local chemical environment, and also impurities and unknown reactants may be present. This limitation is the main cause of differences between the decomposition products of drugs predicted by our single-molecule AIMD simulations. Because of the computational demand needed for executing quantum-based molecular dynamics simulations, we were forced in simulating the behavior of single-molecule numerical samples for a relatively reduced amount of time (≈100 ps). Those circumstances render questionable any strictly quantitative comparison with the laboratory experiments, where pieces of matter are thermalized at a given temperature for timescales order of magnitudes longer than those afforded by DFT-based molecular dynamics methods. For these reasons, AIMD simulations cannot provide a precise one-to-one correspondence of the temperature for thermolysis recorded in the laboratory experiments. On the other hand, useful indications—based on rigorous quantum-mechanical laws—emerge from these simulations in that they show how the simplest thermalization steps may proceed. Computationally demanding condensed-phase systems will be included in future investigations.

Nevertheless, our investigation reveals that the thermal decomposition reaction network of cocaine and methamphetamine is ruled by a quite complex chemistry. In fact, the predicted formation channels represent only one possible initial chemical springboard for further enrichment of samples at high temperatures. Also, the initially formed molecules in our computer experiment may be intermediates different from the final stable chemical products that are detected during laboratory experiments. In addition, more complex chemistry could be revealed by computationally expensive condensed-phase AIMD simulations employing enhanced sampling techniques. This latter analysis is, however, out of the scope of the present work and represents a topic for future investigations.

However, AIMD simulations are essential in order to mechanistically understand the initial steps of thermal decomposition of complex molecules and provide information complementary to the experimental FTIR data, which is limited to the gas-phase detection of light molecules and vapors of volatile compounds.

2.4. AIMD Model of Cocaine Thermolysis. The thermal decomposition of cocaine and methamphetamine is schematically depicted in Figure 4A and B, respectively, where the greater arrow thickness indicates higher simulation temperature, red arrows indicate the expected correlation of secondary-products of AIMD-predicted primary products with the FTIR-detected gas-phase species marked with red borders.

Our quantum-based computational investigations show that the first compounds that are released by thermal decomposition of the cocaine molecule are carbon monoxide, CO (3), acetaldehyde, CH_3CHO (2), and benzene, C_6H_6 (5), see Figure 4A, indicated by a thin blue arrow. This represents the seminal reaction pathway cocaine undergoes during the initial steps of thermal decomposition at the lowest temperatures in the AIMD model. At higher temperatures, the chemical decomposition of cocaine leads also to the formation of carbon monoxide, CO (3), carbon dioxide, CO_2 (7), acetylene, C_2H_2 (6), formaldehyde, H_2CO (1), benzene, C_6H_6 (5), and tetrahydropyridine, $C_6H_{11}N$ (8), indicated in Figure 4A, with thicker violet arrows. At very high temperatures, the simulated thermolysis of cocaine results in benzene, C_6H_6 (5), carbon dioxide, CO_2 (7), formaldehyde, H_2CO (1), carbon monoxide, CO (3), acetylene, C_2H_2 (6), hydrogen cyanide, HCN (10), and methane, CH_4 (4).

2.5. Overall Cocaine Hydrochloride Thermolysis Mechanism. Previous studies (see ref 37 and references therein) have also identified the formation of compounds additional to those predicted theoretically or detected in the gas phase by means of FTIR spectrometry. These products are depicted in Figure 4B: benzoic acid (11), methyl benzoate (12), *N*-methyl benzamide (13), isomers of methyl cycloheptatriene carboxylate (14), methyl-4-(3-pyridyl)-butyrate

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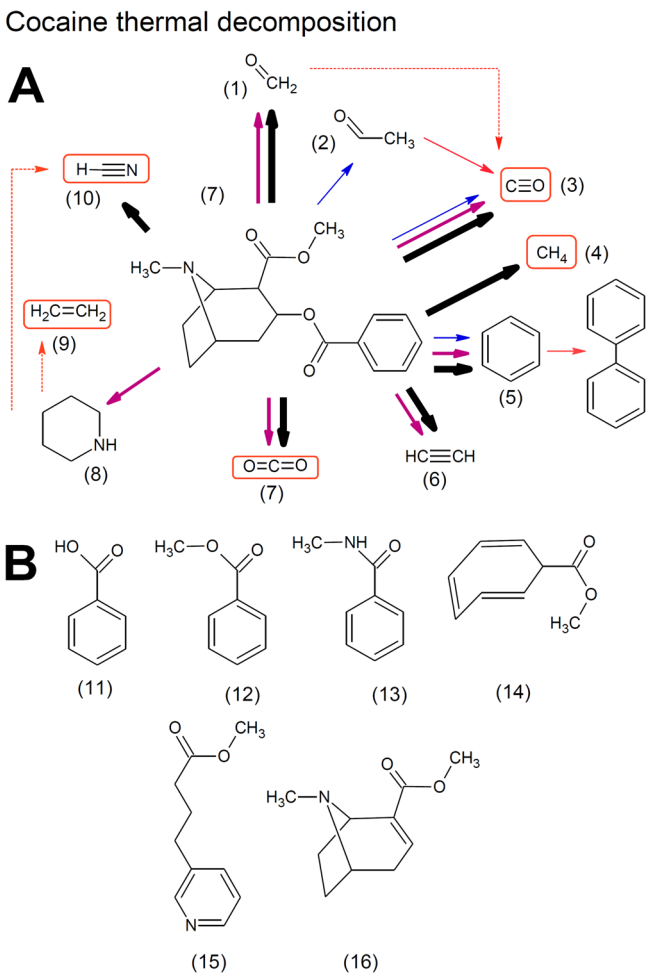

Figure 4. (A) Schematic of thermal decomposition products of cocaine calculated and detected for the street sample in the gas phase in this study. The thickness of arrows schematically corresponds to low (thin blue), moderate (thicker violet), and high (thick black) temperatures. Products detected in the gas phase by their FTIR spectrometry examination are marked by red rectangles. (B) Cocaine decomposition products concluded in ref 37. The product names are reported in Table 1.

(15), and AEME (16). The list of compounds detected in the gas phase after thermal decomposition of the street sample is compared with the list of molecules predicted by AIMD simulations and products detected in the study of Jacob et al.[37] in Table 1. This Table specifically provides a comparison between volatile substances detected in the gas phase of street sample cocaine hydrochloride following thermolysis between 350 and 750 °C (indicated in Table 1 by following numbers: 3, 4, 7, 9, 10, and 17−19), less-volatile organic compounds such as benzoic acid and AEME detected by GC−MS after cocaine hydrochloride thermolysis in temperature range 150−650 °C,[38] and other compounds concluded in,[37] nos. 11−16, products predicted by AIMD computations to be formed above 750 °C, nos. 1−8 and 10, and finally, thermolysis products attributed to the probable decomposition of impurities in the cocaine street sample, nos. 17 and 18. Compounds (11−16) are indicated to be important thermolysis products of cocaine hydrochloride according to refs 37 and 38. However, they cannot be detected in the gas phase in the temperatures used during our laboratory experiments. On the other hand, previous works[37,38] have not focused on volatile products detected in this study by FTIR and these results are, therefore, complementary and provide a complex picture of volatile molecules as well as heavier organic compounds formed by cocaine hydrochloride thermolysis upon temperatures up to 750 °C. It should also be noted that gas phase can be enriched by products formed from primary molecules released from cocaine hydrochloride. Such secondary decomposition can explain the experimental detection of methane, ethylene, and hydrogen cyanide. AIMD simulations also predict the release of several compounds, which should be detected by FTIR at least at the highest experimental temperature of 750 °C: acetaldehyde and benzene. However, neither of these two molecules has been detected. We suggest that these molecules are probably formed in low quantities and can be decomposed to simple molecules detected in the gas phase. Acetaldehyde is decomposed to methane and carbon monoxide,[39] and acetonitrile to methane and hydrogen cyanide.[40] Moreover, other compounds can also be decomposed to simple molecules at high temperatures: formaldehyde to carbon monoxide and hydrogen,[41] and pyridine to hydrogen cyanide and ethylene.[42] The only remaining issue is the negative detection of benzene and acetylene. It can be expected that benzene forms nonvolatile compounds such as polycyclic aromatic hydrocarbon or biphenile.[43] Formation of acetylene has been predicted by AIMD simulations for high temperatures and maybe, it does not represent a plausible decomposition channel at temperatures below 750 °C.

2.6. Overall Methamphetamine Hydrochloride Thermolysis Mechanism. Similar to cocaine, the organic compounds released by methamphetamine thermolysis have been also previously analyzed by the GC−MS.[37] These compounds are schematically depicted in Figure 5B. Using FTIR spectroscopy, we have been able to confirm the main decomposition of methamphetamine hydrochloride to toluene (20). Other detected gases such as methane (4), carbon dioxide (7), ethylene (9), hydrogen cyanide (10), and methylchloride (19) are not listed in previous studies, as concluded in Table 2. It is very likely that organic compounds (24)−(29) are present in concentrations below the detection limit of the FTIR method. Figure 6 shows a thermolysis experiment with two methamphetamine hydrochloride street samples at a temperature of 650 °C and a comparison with a toluene spectrum. Most broad bands across the spectrum can be attributed to toluene, except for two features at 915 cm^{-1}, which probably belong to the strongest band of traces of styrene (25), and a small peak at 2966 cm^{-1} mixed with a broad band of toluene, probably created by traces of ethylbenzene (26) identified among the products also in a previous study.[37] Spectra have been compared with the data from NIST Chemistry Webbook.

2.7. AIMD Model of Methamphetamine Thermolysis. In agreement with the experimental survey, AIMD simulations show that methamphetamine is more stable than cocaine with the first products detected above 550 °C. AIMD computations indicated that single methamphetamine molecules begin to decompose at high temperatures, as indicated in Figure 5A by violet thicker arrows, releasing methane, CH_4 (4), benzene, C_6H_6 (5), acetylene, C_2H_2 (6), propanyl, C_3H_4 (21), acetonitrile, C_2H_3N (22), and ethylimine, H_3C_2HN (23). High-temperature decomposition indicated by thick black arrows results mainly in propanyl, C_3H_4 (21), ethylimine, H_3C_2HN (23), and acetylene, C_2H_2 (6).

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Table 1. List of Products Detected in the Gas Phase After Thermal Decomposition of the Cocaine Street Sample, the List of Molecules Predicted by AIMD Simulations, and Products in Studies of Jacob et al.,[37] Martin et al.,[38] and References Therein[a]

ref number	detected 350−750 °C	calculated 1000−5000 K	note
1		formaldehyde	probable decomposition to carbon monoxide
2		acetaldehyde	methane and carbon monoxide are formed by its decomposition
3	carbon monoxide (*)		produced by direct decomposition as well as from acetaldehyde and formaldehyde
4	methane (*)		predicted for high temperatures theoretically, but probably also produced by subsequent decomposition
5		benzene	benzene can also form nonvolatile residua such as biphenyl at 700 °C
6		acetylene	acetylene has not been detected
7	carbon dioxide (*)		predicted for high temperatures theoretically
8		tetrahydropyridine	for 875−1050 °C, simple products of its decomposition are HCN, C_2H_4, and C_2H_2
9	ethylene		probable product of further decomposition (e.g., from pyridine)
10	hydrogen cyanide (*)		predicted for high temperatures theoretically, probable product of pyridine decomposition
11	benzoic acid		see Jacob et al., Martin et al.
12	methyl benzoate		see Jacob et al.
13	*N*-methyl benzamide		see Jacob et al.
14	methyl cycloheptatriene carboxylate		see Jacob et al.
15	methyl-4-(3-pyridyl)-butyrate		see Jacob et al.
16	AEME		see Jacob et al., Martin et al.
17	carbonyl sulfide		likely formed from sulfur-containing inpurities in the street sample
18	carbon disulfide		likely inpurity in the street sample
19	methylchloride		formed from the hydrochloride form of the compound

[a]Products marked (*) are both detected in gas phase and predicted by AIMD simulations. The products only detected, but not predicted by AIMD simulations for temperatures above 750 °C appear in the left column, products predicted by AIMD, but not detected in gas phase are listed in the right column.

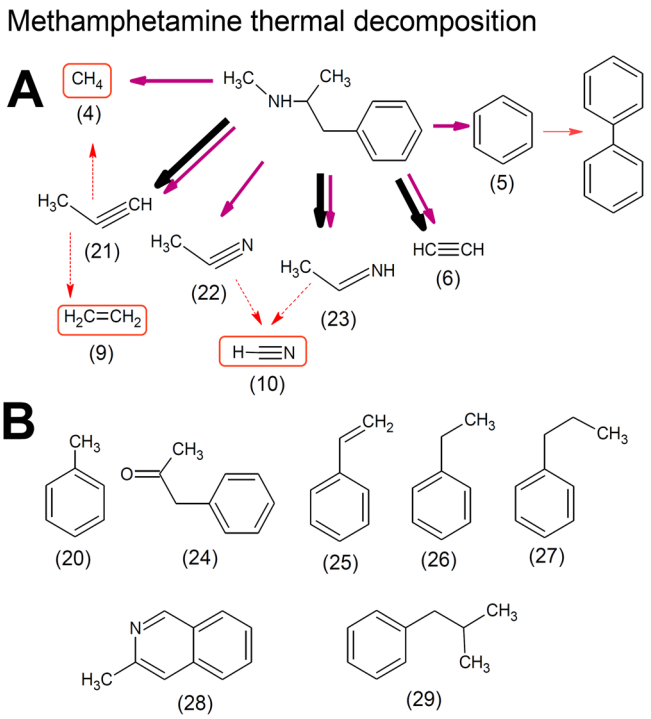

Figure 5. (A) Schematic of the thermal decomposition products of methamphetamine calculated and detected for the street sample in the gas phase in this study. The thickness of arrows schematically corresponds to low (thin blue), moderate (thicker violet), and high (thick black) temperatures. Products detected in the gas phase by its FTIR spectrometry examination are marked by red rectangles. (B) Cocaine decomposition products concluded in ref 37. The product names are listed in Table 2.

2.8. Importance of Thermolysis Products. Our experimental investigation as well as our theoretical calculations show that methamphetamine is a much more stable compound than cocaine. The volatile products ethylene, methane, carbon monoxide, hydrogen cyanide, and methylchloride are released at temperatures exceeding 550 °C. Previous studies[44,45] have shown that at temperatures under 350 °C, methylation and demethylation reactions take place and methamphetamine releases mainly amphetamine and dimethylamphetamine. Both compounds can be considered as less toxic than the original methamphetamine, although their pathophysiological behavior is comparable to the parent drug. At temperatures under 750 °C, another typical volatile product of methamphetamine decomposition is toluene, another compound causing neuropathological damage.[46] This finding shows that smokers of methamphetamine are exposed to a combination of thermolysis products exhibiting neurotoxicity (amphetamine, dimethylamphetamine, and toluene) as well as volatile poisons such as carbon monoxide and hydrogen cyanide, typical compounds in cigarette smoke. At higher temperatures in the range of 1000−5000 K, however unlikely to be achieved by cigarette smoking or by regular laboratory thermolysis, theoretical calculations predict release of propanyl, acetonitrile, benzene, acetylene, and ethylamine. These compounds, however, probably decompose to ethylene, methane, or hydrogen cyanide.

Cocaine is less stable and releases simple volatile molecules even at a temperature of 350 °C. These simple compounds, comparable to methylamphetamine, also involve ethylene, methane, carbon monoxide, hydrogen cyanide, and also methylchloride. The street samples examined in this study also produced carbonyl sulfide and carbon disulfide. Carbon monoxide, hydrogen cyanide, methyl chloride, and carbon disulfide are toxic compounds. Although acute poisoning is

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Table 2. List of Products Detected in the Gas Phase After Thermal Decomposition of the Methamphetamine Street Sample, the List of Molecules Predicted by AIMD Simulations, and Products Detected in the Study of Sato et al.[44a]

ref number	detected 350−750 °C	calculated 1000−5000 K	note
4	methane (*)		predicted for high temperatures theoretically, but probably also produced by subsequent decomposition
5		benzene	benzene probably forms nonvolatile residua such as biphenyl at 700 °C
6		acetylene	acetylene has not been detected
7	carbon dioxide (*)		formation not predicted theoretically, but also detected in lower quantities than for cocaine
9	ethylene		likely produced by further decomposition of products
10	hydrogen cyanide (*)		likely produced by further decomposition of products such as acetonitrile and ethanimine
19	methylchloride		formed from the hydrochloride form of the compound
20	toluene		thermolysis product, detected in this study and in Sato et al.
21		propanyl	predicted for high temperatures theoretically, possible decomposition to methane and other products
22		acetonitrile	predicted for high temperatures theoretically, possible decomposition to hydrogen cyanide and methane
23		ethylimine	predicted for high temperatures theoretically, unstable, likely undergoes decomposition to hydrogen cyanide and methane
24	phenylacetone		detected by Sato et al.
25	styrene (x)		detected by Sato et al.
26	ethylbenzene (x)		detected by Sato et al.
27	propylbenzene		detected by Sato et al.
28	3-methylisoquinoline		detected by Sato et al.
29	cumene		detected by Sato et al.

[a]Products marked (*) are both detected in the gas phase and predicted by AIMD simulations. The products only detected, but not predicted by AIMD simulations for temperatures above 750 °C appear in the left column, products predicted by AIMD, but not detected in the gas phase are listed in the right column. Products marked (x) have been tentatively identified based on detection of their strongest bands mixed with a series of toluene spectral features.

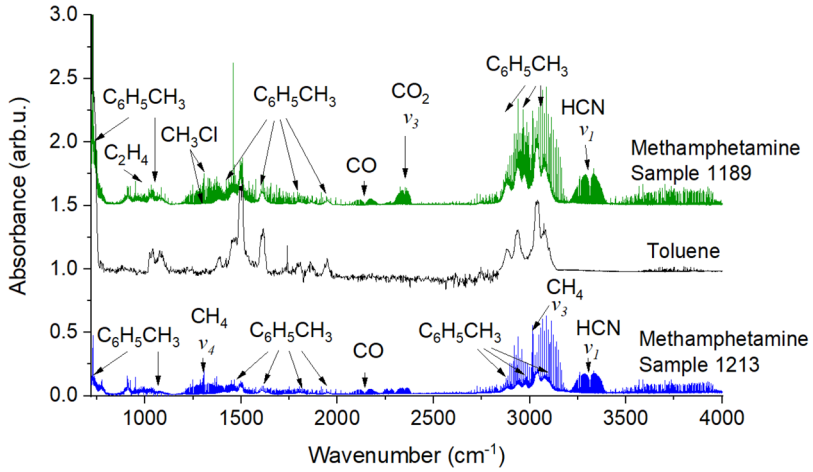

Figure 6. Two spectral surveys of methamphetamine hydrochloride thermolysis products by FTIR compared to the spectrum of toluene.

very unlikely to occur following regular smoking, carbon disulfide may exhibit embryotoxic and fetotoxic effects[47] and methylchloride is a suspected carcinogenic agent.[48] It should also be noted that AEME produced by thermal decomposition of cocaine[37,38] exhibits higher neurotoxical potential and smoking "crack", therefore, increases health risks over the original drug.[49] Our simulations show that at temperatures of 1000−5000 K, cocaine should release mainly simple molecules such as formaldehyde, acetaldehyde, benzene, acetylene, and tetrahydropyridine.

A spectroscopic survey of volatile cocaine and methamphetamine thermolysis products shows that both compounds release similar simple compounds, however, with large differences in their ratios with increasing experiment temperatures. The dominant product of methamphetamine thermolysis is methane (70−85% col. dens.) released by its demethylation. Another typical product is hydrogen cyanide (15% col. dens.). Both compounds can be found also among the products released by cocaine. However, neither methane nor hydrogen cyanide are the most abundant. The dominant volatile molecule among cocaine thermolysis products is ethylene (30% col. dens. at temperatures 350−550 °C) and methylchloride (20% col. dens.). It can be assumed that the ratio among simple volatile products can potentially indicate similar street samples and help with their association. In the future, the infrared spectroscopy of volatile products could become a complementary method to GC and other techniques in order to fully characterize and identify street samples of drugs, due to its high robustness, simplicity of the controlled thermolysis, weak influence from the sample's form and purity, and fingerprint identification of simple gas-phase molecules.

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3. CONCLUSIONS

Street samples of cocaine and methamphetamine investigated in this study have been identified as chloride salts following their examination with Raman spectroscopy, absorption spectroscopy in Nujol, and determining their melting point. The main products of cocaine experimental thermolysis are methylchloride and ethylene. Methamphetamine produces mainly methane and hydrogen cyanide. However, together with carbon monoxide, several volatile substances such as carbon dioxide, methane, hydrogen cyanide, and methyl chloride are released by both drugs following their thermal decomposition in the range 350−750 °C. Toluene is the only thermolysis product of methamphetamine, but carbon disulfide and carbonyl sulfide are identified as the thermolysis products of cocaine. We highlight that sulfur-bearing species very likely come from impurities in the street cocaine sample. Our study has shown that the ratio of simple molecules released by controlled thermolysis depends strongly on temperature. Absorption bands of all the molecules can be easily and robustly identified and fingerprinted by FTIR spectroscopy. We suggest that this method can be used, at least, as an auxiliary technique for the identification of drug samples. Considering the toxicity of the identified thermolysis products, we conclude that smoking street methamphetamine and cocaine risks exposure to a palette of dangerous volatile species (hydrogen cyanide, carbon monoxide, methylchloride, toluene, and carbon disulfide) as well as toxic organic compounds (amphetamine, dimethylamphetamine, and AEME).

4. EXPERIMENTAL SECTION

Street samples of cocaine and methamphetamine coming from criminal activities were supplied by the Institute of Criminalistics in Prague. In order to provide their characterization prior to thermolysis, the samples were analyzed by Raman spectroscopy, Fourier-transform spectroscopy of their powders in Nujol, EDS, and melting point determination. The street samples were then thermally decomposed at various temperatures. The evolution of gas-phase products was monitored by high-resolution FTIR, and their decomposition was theoretically modeled in order to (i) explore the initial steps of thermal decomposition, (ii) compare the results with those of experimental detection, and (iii) make a prediction of products expected for temperatures exceeding our experimental limits.

4.1. Thermal Decomposition and FTIR Detection. Five 100 mg street drug samples were inserted in evacuated silica tubes and independently heated for 10 min. Each sample was independently heated to a specific temperature; 350, 450, 550, 650, or 750 °C; then left to cool at room temperature and its gas-phase contents finally transferred to a 20 cm long spectroscopic cell equipped with ZnSe windows for measurement. The same sample was then evacuated and heated again to a higher temperature. For measurement, the cell was placed in the sample chamber of a fully evacuated Bruker IFS 125HR high-resolution Fourier-transform spectrometer (Bruker Optics, Germany). The composition of the gas phase in the cell was spectroscopically analyzed over the frequency range of 600−4500 cm^{-1} using a KBr beam splitter and nitrogen-cooled MCT detector. The spectra are measured with a resolution of 0.05 cm^{-1} and apodized by a Blackman−Harris 3-Term function. A total of 100 accumulated scans were needed to acquire a reasonable signal-to-noise ratio. The cell was evacuated, filled with air, and purged three times after each measurement. The collected rotational−vibrational spectra were evaluated by comparison with those of samples of neat standards or with current literature using the software Opus 6.0.

4.2. FTIR Spectroscopy of Solid Samples. A Bruker IFS 125 HR (Bruker Optics, Germany) FTIR spectrometer was also used to record infrared absorption spectra of solid drug samples. The samples were mixed with Nujol (99.99%, Sigma-Aldrich) and inserted between two KBr windows. The spectra were recorded over the 500−4000 cm^{-1} range using the MCT detector and a resolution of 0.1 cm^{-1}.

4.3. Raman Spectroscopy. A small amount of the sample (about 0.01 g) was inserted between two glass panes pressed together to produce an approximately constant sample thickness with no air cavities. Given the significant heterogeneity of the sample at the microscopic level, each sample was measured three times at various areas. Measurements were conducted with a 514 nm laser (green colored) using a HORIBA LabRAM instrument with a 18 mW source laser power and a laser power on the sample of 0.036 mW. The integration time was 30 s and a Peltier-cooled CCD detector was used. For cocaine samples, the power on the sample was increased to 0.36 mW by removing a neutral density filter and the integration time was reduced to 20 s. For methamphetamine, the power on the sample was increased to 1.10 mW with the same integration time. The measurement range was 50−4000 cm^{-1} using objectives 100× and 50× with the laser spot sizes of 0.8 and 1.5 μm, respectively. The spectra have been then examined and three the best representative Raman spectra showing the best signal were used for each sample characterization and subsequent evaluation.

4.4. Chemical Analysis. Chemical/elemental characterization was carried out with a Hitachi S-4800 field emission scanning electron microscope equipped with an energy-dispersive X-ray spectral analyzer. Acceleration voltage for EDS analysis was set to 25 kV with a working distance of 16 mm. For the EDS analysis, the powder sample is deposited onto the aluminum holder without the presence of commonly used carbon adhesive tape to avoid the false detection of the carbon element from the tape. An EDS detector (EDS Noran system 6) is equipped with a beryllium window to maintain vacuum of a semiconductor detector, so we are unable to detect light elements such as beryllium or boron. On the other hand, detection of carbon is possible as the emitted X-rays are not attenuated by the window. The standardless (semi-quantitative) automatic system is also frequently used for the analysis of carbon materials in general. The oxygen and nitrogen elements are detectable and are mentioned if those were detected in the amount higher than 0.1 wt %, therefore, were found as valid.

4.5. Molecular Simulations. To identify the simplest reaction pathways of decomposing cocaine and methamphetamine, and their single-molecule thermal dissociation channels, a series of state-of-the-art AIMD simulations were performed. The electrons constituting cocaine and methamphetamine molecules were treated via a rigorous density functional theory (DFT) framework within the Born−Oppenheimer approximation. The corresponding AIMD simulations were performed using the CP2K software suite for massively parallelized electronic-structure calculations.[25] In particular, samples of cocaine and methamphetamine are placed in cubic

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simulation boxes with 20 Å edges. The dynamical and chemical behavior of the investigated molecules is first equilibrated at room temperature over dozens of picoseconds and subsequently simulated at temperatures between 1000 and 5000 K for 100 ps. In particular, AIMD simulations were conducted, separately, at different fixed temperatures: 1000, 2000, 3000, 4000, and 5000 K. We have not simulated a progressive increase of the temperature.

The atomistic behavior of cocaine and methamphetamine was simulated by employing mixed atomic-based (Gaussian) basis sets (i.e., TZVP) and plane-wave basis sets. Goedecker–Teter–Hutter[26] pseudopotentials have been adopted, whereas exchange and correlation effects have been handled by means of the BLYP functional[27,28] along with Grimme's D3 dispersion corrections.[29,30] As usual for AIMD, a simulation time-step equal to 0.5 fs was set. The temperature was controlled by means of the canonical stochastic velocity rescaling method[31] employing a thermostat set at a time constant equal to 50 fs. The dynamics of the nuclei was simulated classically using the Verlet algorithm.

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Author Contributions

Contribution of M.F., G.C. and V.T. is the same. M.F. conducted the research and the experiments, and wrote the paper, G.C. conducted quantum chemical calculations and wrote the paper, V.T. conducted the research, A.H. analyzed the data, wrote, and revised the paper, L.P., A.K., and T.K. conducted the experiments and wrote the paper, M.B. characterized the samples by Raman spectroscopy and energy-dispersive X-ray spectroscopy, J.Š. and J.E.Š. supervised quantum calculations, P.K. evaluated the data, J.Š. and J.E.Š. conducted quantum chemical calculations, J.D. wrote the paper, and S.C. conducted the experiments, characterized the samples, and supervised experimental work.

Notes

The authors declare no competing financial interest.

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