Technical Note

Isolation of *cis*-Cinnamoylcocaine from Crude Illicit Cocaine via Alumina Column Chromatography

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ABSTRACT: The isolation procedure of gram quantities of *cis*-cinnamoylcocaine from crude cocaine base is provided. Isolation was achieved through classical alumina column chromatography and recrystallization. The procedure will enable forensic scientists to obtain a standard of *cis*-cinnamoylcocaine for cocaine signature analyses and related research.

KEYWORDS: *cis*-Cinnamoylcocaine, Column Chromatography, Isolation, Cocaine Signature Analyses, Forensic Chemistry

Introduction

Cocaine signature analyses have become routine in many forensic laboratories. These analyses are intended for both sample-to-sample comparison work (tactical intelligence) and geographic origin classification (strategic intelligence). Several chromatographic methods have been published over the past 15 years which utilize *cis*-cinnamoylcocaine (Figure 1), a naturally occurring product in coca, as one of the target compounds (1-6). Since *cis*-cinnamoylcocaine is not commercially available, standard material must be either synthesized or isolated from illicit cocaine. However, the synthesis procedure with followup purification by preparative high performance liquid chromatographic (HPLC), as reported by By, Lodge, and Sy (7), is problematic for forensic laboratories not staffed for synthetic work or equipped with a preparative HPLC. Similarly, the isolation from

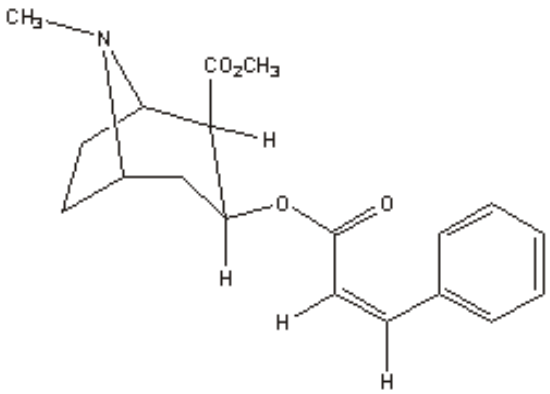

Figure 1. *cis*-Cinnamoylcocaine.

illicit cocaine utilizing ion-pair chromatography, as reported by Moore (8), yields only milligram quantities and cannot be scaled up. Herein, we provide a simple chromatographic procedure for the isolation of gram quantities of *cis*-cinnamoylcocaine from crude cocaine base.

Experimental

Materials: A crude cocaine base exhibit containing approximately 13 percent *cis*-cinnamoylcocaine was acquired from the research collection of this laboratory. All solvents were distilled-in-glass products of Burdick and Jackson Laboratories (Muskegon, MI). All other chemicals were of reagent-grade quality and were products of Aldrich Chemical (Milwaukee, WI). Alumina (basic) was deactivated slightly by adjusting the water content to 4 percent (w/w).

Gas Chromatography/Mass Spectrometry (GC/MS): Analyses were performed using an Agilent (Palo Alto, CA) Model 5973 quadrupole mass-selective detector (MSD) interfaced with an Agilent (Palo Alto, CA) Model 6890 gas chromatograph. The MSD was operated in the electron ionization (EI) mode with an ionization potential of 70 eV, a scan range of 34 - 700 mass units, and at 1.34 scans/second. The GC was fitted with a 30 m x 0.25 mm ID fused-silica capillary column coated with 0.25 µm DB-1 (J & W Scientific, Rancho Cordova, CA). The oven temperature was programmed as follows: Initial temperature, 100 ^{O}C; no hold, program rate, 6 ^{O}C/min; final temperature, 300 ^{O}C; final hold, 5.67 min. The injector was operated in the split mode (21.5:1) and at a temperature of 280 ^{O}C. The auxiliary transfer line to the MSD was operated at 280 ^{O}C.

Fourier Transform Infrared Spectroscopy - Attenuated Total Reflectance (FTIR-ATR): Spectra were obtained on a Nexus 670 FTIR equipped with a single bounce attenuated total reflectance (ATR) accessory. Spectra were collected using 32 scans between 4000 cm^{-1} and 400 cm^{-1} at a resolution of 4 cm^{-1}.

Proton Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR): Spectra were obtained on a Varian Mercury 400 MHz NMR using a 5 mm Varian Nalorac indirect detection, variable temperature, pulse field gradient probe with PulseTune® (Varian, Palo Alto, CA). The compound was dissolved in deuterochloroform ($CDCl_3$) containing 0.03 percent v/v tetramethylsilane (TMS) as the 0 ppm reference. The temperature of the sample was maintained at 25 ^{O}C. Standard Varian pulse sequences were used to acquire the proton spectra. Processing of data was performed using software from Applied Chemistry Development (ACD/Labs, Toronto, Canada).

Isolation of cis-Cinnamoylcocaine: Crude cocaine base (170 grams containing approximately 13 percent *cis*-cinnamoylcocaine) was dissolved into one liter of warm diethyl ether/hexane (1:1) and eluted on a glass chromatographic column (100 cm x 5.5 cm ID) containing 1.0 kilogram of basic alumina (150 mesh). The column was then eluted with 1.0 liter of diethyl ether, followed by 1.0 liter of diethyl ether/chloroform (1:1). The bulk of the *cis*-cinnamoylcocaine was contained in the diethyl ether fractions. The combined diethyl ether fractions were evaporated *in vacuo* to an oil (34 grams of 55 percent *cis*-cinnamoylcocaine), which was chromatographed again on 1.0 kilogram of basic alumina (same size column) using the following series of solvents: 500 mL diethyl ether/hexane (1:2), 500 mL diethyl ether/hexane (1:1), 500 mL diethyl ether/hexane (2:1), 500 mL diethyl ether/hexane (5:1), and 1500 mL diethyl ether. The diethyl ether/hexane (5:1) and 1500 mL diethyl ether fractions were then combined and evaporated *in vacuo* to a light yellow oil (9.9 grams of 88 percent *cis*-cinnamoylcocaine). The resulting oil was chromatographed again on 1.0 kilogram of basic alumina (same size column) using 500 mL diethyl ether/hexane (1:2), 500 mL diethyl ether/hexane (1:1), 500 mL diethyl ether/hexane (2:1), 500 mL diethyl ether/hexane (5:1), and 2000 mL diethyl ether. The first 750 mL of the diethyl ether fractions were combined and evaporated *in vacuo* to a clear oil (7.0 grams of 96 percent *cis*-cinnamoylcocaine) which crystallized slowly upon standing. The product was recrystallized from diethyl ether/petroleum ether (20 - 40 ^{O}C) to give 6.17 grams of 99 percent pure *cis*-cinnamoylcocaine as a white solid (28 percent recovery).

Results and Discussion

Crude cocaine base contains (mostly) cocaine, lesser amounts of both *cis*- and *trans*- cinnamoylcocaine, numerous other tropane alkaloids, and various processing impurities and byproducts. Under the described chromatographic procedures, cocaine and *trans*-cinnamoylcocaine predominate in the hexane/diethyl ether fractions and elute prior to *cis*-cinnamoylcocaine. Although cocaine and *trans*-cinnamoylcocaine have some carryover, *cis*-cinnamoylcocaine is enriched significantly in the diethyl ether fractions. More polar cocaine impurities such as norcocaine, ecgonine, and benzoylecgonine are retained by the alumina column. Two additional alumina column passes of the enriched *cis*-cinnamoylcocaine, followed by recrystallization, were sufficient to give an analytically pure (99 percent or better) sample. The FTIR-ATR, ^{1}H-NMR, and GC/MS spectra are illustrated in Figures 2 - 4, respectively. The reported procedure can be utilized to isolate *cis*-cinnamoylcocaine even from refined illicit cocaine exhibits containing as little as 3 percent *cis*-cinnamoylcocaine. Samples of *cis*-cinnamoylcocaine should be stored in amber glass bottles or in a dark location, as observations suggest that isomerization to *trans*-cinnamoylcocaine occurs over extended periods of time.

Acknowledgments

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[Figures 2 - 4 Follow.]

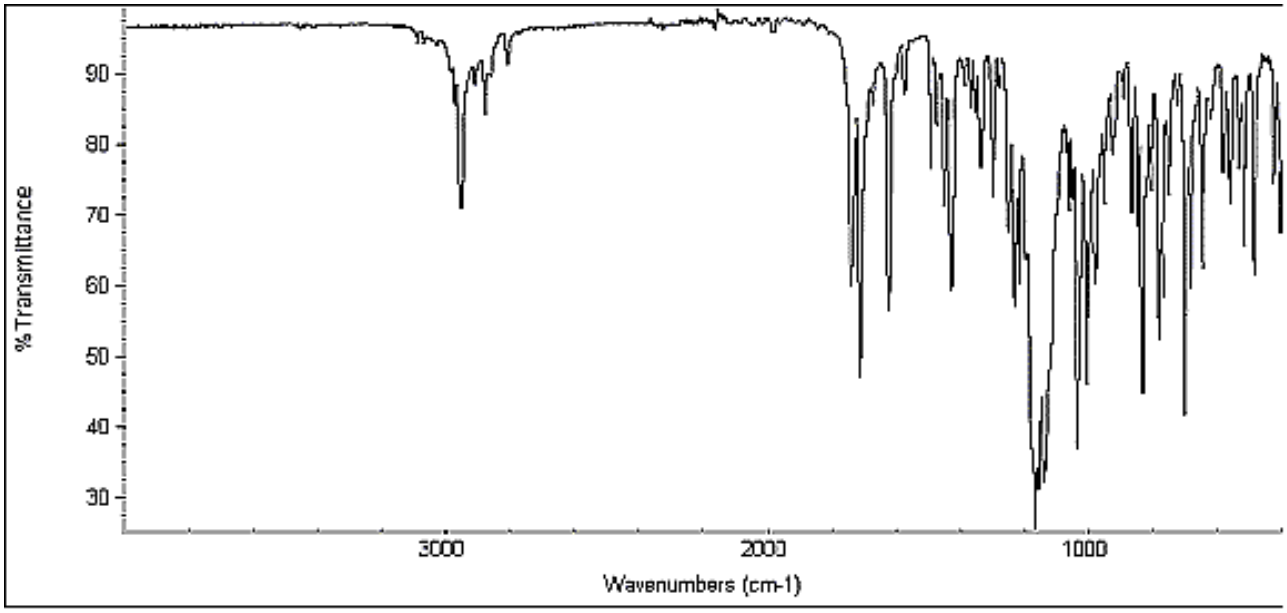

Figure 2. Infrared Spectrum (FTIR-ATR) of *cis*-Cinnamoylcocaine.

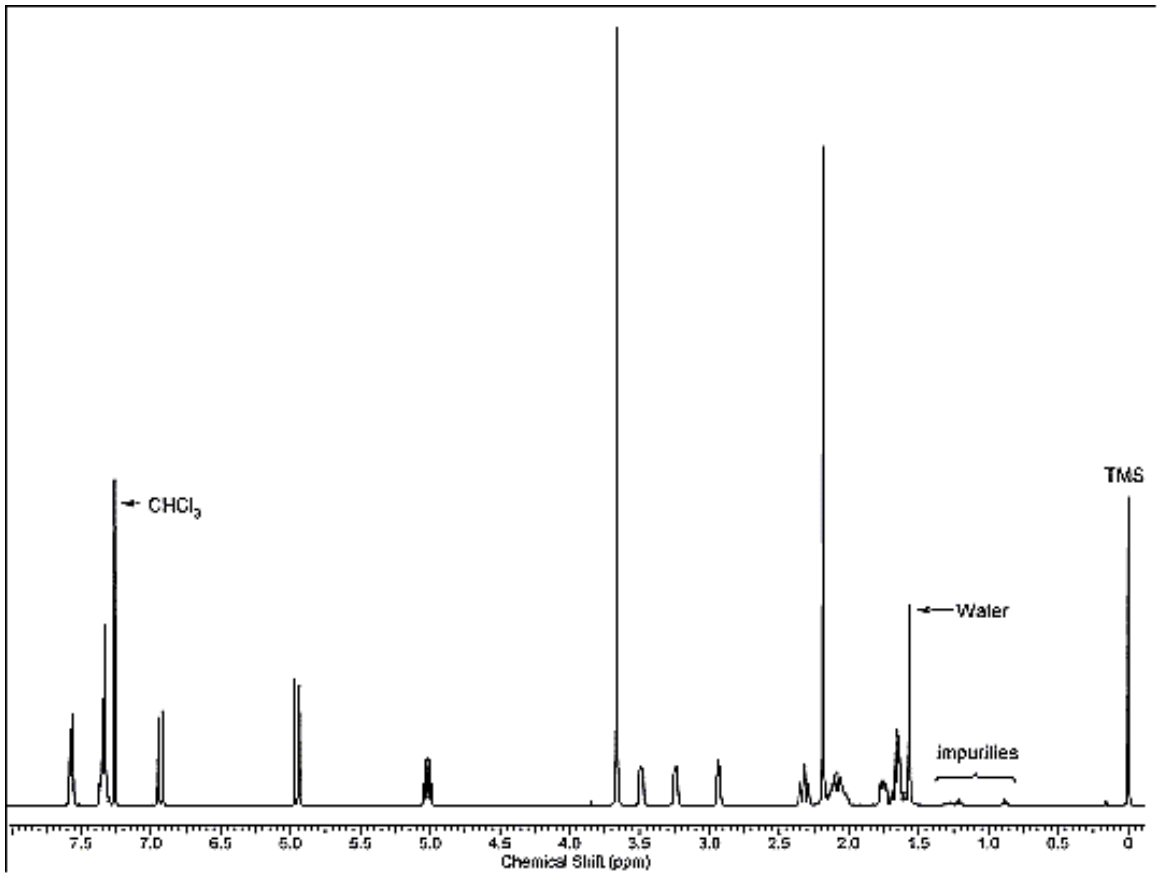

Figure 3. Proton NMR Spectrum of *cis*-Cinnamoylcocaine.

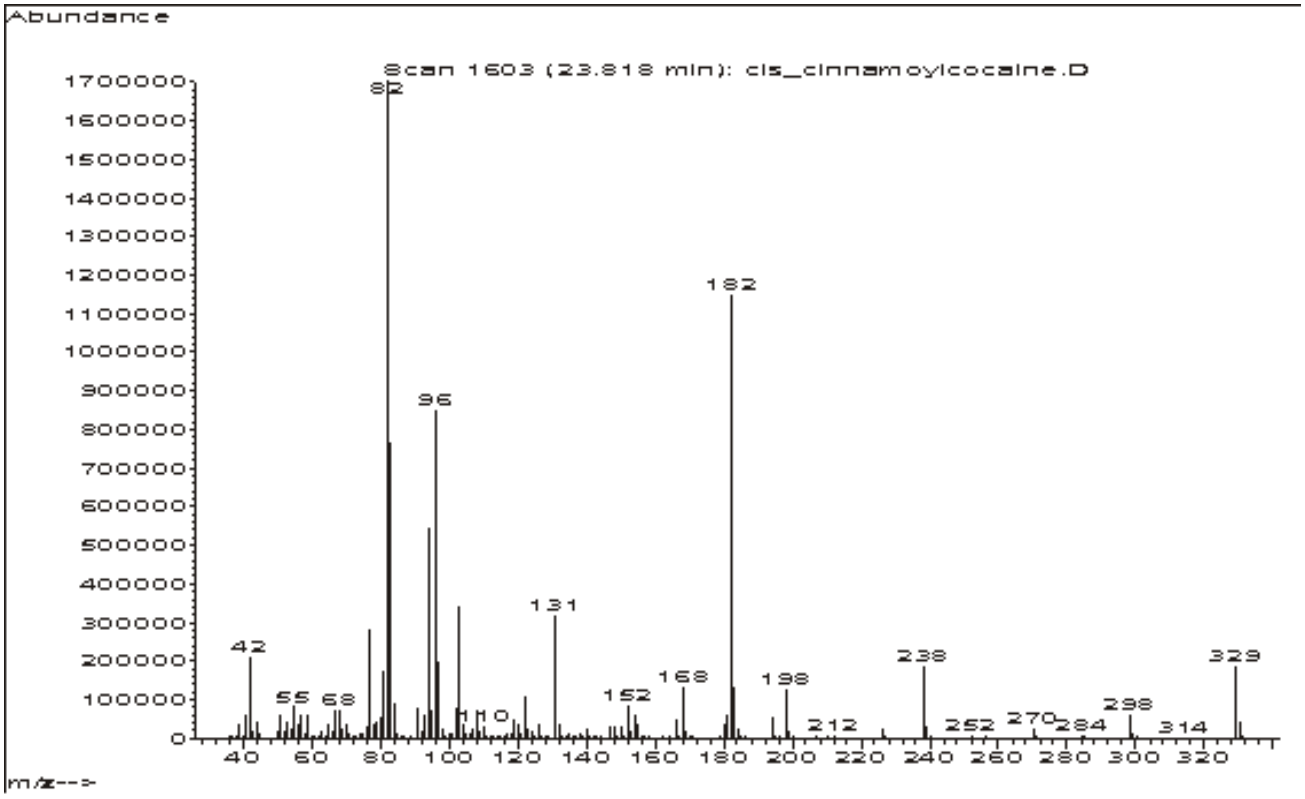

Figure 4. Gas Chromatography/Mass Spectra (70 eV EI) of *cis*-Cinnamoylcocaine.

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