No. 09-1533

In The
# Supreme Court of the United States

FRANTZ DEPIERRE,

*Petitioner,*

v.

UNITED STATES OF AMERICA,

*Respondent.*

**On Writ Of Certiorari To The United States Court Of Appeals For The First Circuit**

## BRIEF OF INDIVIDUAL PHYSICIANS AND SCIENTISTS ROBERT BOOTH, PhD, ET AL. AS *AMICI CURIAE* IN SUPPORT OF PETITIONER

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

## INTEREST OF *AMICI CURIAE*[1]

*Amici curiae* are scientists and physicians who have written, taught and consulted about medical and public health issues relating to controlled substances.[2] All but one are university professors. *Amici* have spent their careers studying, writing about, and promoting a better understanding of, controlled substances including cocaine. They are in a unique position to assist the Court in understanding the chemical definitions of the substances covered by 21 U.S.C. §841.



[1] Respondent and Petitioner have consented to the appearance of *amici curiae* in this matter; their letters of consent are submitted with this brief. Pursuant to Supreme Court Rule 37.6, counsel for *amici* states that counsel and *amici* are the sole authors of this brief, and that no person or entity other than counsel and *amici* contributed monetary support to this brief's preparation and submission.

[2] *Amici curiae* are, in alphabetical order: Robert Booth, PhD, Professor, Department of Psychiatry, University of Colorado School of Medicine; R. Douglas Bruce, MD, MSc, MA, Assistant Professor of Medicine (AIDS) and of Epidemiology (Microbial Diseases), Yale School of Medicine; Robert Heimer, MSc, PhD, Professor of Epidemiology and Associate Professor of Pharmacology, Yale University School of Public Health; Richard Schottenfeld, MD, Professor of Psychiatry, Yale School of Medicine and Yale School of Public Health; Jay Siegel, MSc, PhD, Professor and Chair of the Department of Chemistry and Chemical Biology, Indiana University-Purdue University Indianapolis; and Sharon Stancliff, MD, Medical Director of the Harm Reduction Coalition.

## SUMMARY OF THE ARGUMENT

This brief is offered to make a few (hopefully simple) points about the chemical definitions of the substances covered by 21 U.S.C. §841.

Cocaine is an alkaloid found in the coca plant, primarily in the variety *Erythroxylon coca*. Richard Ashley, *Cocaine, Its History, Uses and Effects* 13 (St. Martin's Press, 1975); Dominic Streatfield, *Cocaine, An Unauthorized Biography* 2 (Virgin Publ. Ltd., 2001); Roger D. Weiss, MD, Steven M. Mirin, MD and Roxanne L. Bartel, MD, *Cocaine* 5 (American Psychiatric Press, 2d ed. 1994). Alkaloids are commonly defined as basic chemical compounds that contain nitrogen and occur naturally in a large variety of organisms, including plants. Ashley, *supra,* at 18; G. Marc Loudon, *Organic Chemistry* 1108 (Oxford Univ. Press, 2002); T.W. Graham Solomons and Craig B. Fryhle, *Organic Chemistry* 994 (John Wiley & Sons, Inc., 8th ed. 2004); *see, United States v. Brisbane*, 367 F.3d 910, 911 (D.C. Cir. 2004) ("Cocaine is a naturally occurring alkaloid – that is, a base."). Most alkaloids have pronounced physiological effects when administered to animal organisms; and many have psychotropic effects as well. Ashley, *supra,* at 18; Solomons and Fryhle, *supra,* at 994.

Basic compounds (bases), such as alkaloids, are defined by the established and widely used Lewis Acid and Base Theory as: substances comprised of molecules each of which can *donate* an electron pair to another molecule. Solomons and Fryhle, *supra,* at

99. The chemical formula for cocaine is $C_{17}H_{21}NO_4$; the nitrogen atom (N) has an electron pair that it can donate. Loudon, *supra,* at 1108. The ability to donate an electron pair to another molecule is what makes cocaine a base. Solomon and Fryhle, *supra,* at 99.

Cocaine can be converted into a salt, which has a distinct molecular structure, by combining it with a third chemically distinct substance, an acid (such as hydrochloric acid, HCl). Weiss, Mirin and Bartel, *supra,* at 10. The Lewis Acid and Base Theory defines acids as: substances comprised of molecules each of which can *accept* an electron pair from another molecule. Solomon and Fryhle, *supra,* at 99. The chemical reaction between the base (electron pair donator) and acid (electron pair acceptor) changes the molecular structure of the base to form a distinct compound, a salt. *Ibid.,* at 102, 108.

In the case of cocaine, when cocaine (base) is combined with hydrochloride (acid), it becomes cocaine hydrochloride (salt). Philip Bean, *Cocaine and Crack* 3 (St. Martin's Press, Inc., 1993). The chemical formula for cocaine hydrochloride is $C_{17}H_{22}NO_4^+Cl^-$, a distinct molecule from cocaine. The distinction between these chemical compounds does not translate into differences in the pharmacological effects on the human body: "The active part of the drug remains unchanged whichever form is used, and the effects on the human body are the same whether the base [cocaine] or salt [cocaine hydrochloride] form is ingested." Bean, *supra,* at 3. That said, cocaine ($C_{17}H_{21}NO_4$) and cocaine

hydrochloride ($C_{17}H_{22}NO_4^+Cl^-$), have distinct chemical definitions.

Cocaine hydrochloride can be reconverted into cocaine by combining the salt with water and another base, for example sodium bicarbonate ($NaHCO_3$). Weiss, Mirin and Bartel, *supra,* at 11. The chemical reaction between the cocaine hydrochloride and sodium bicarbonate reconverts the cocaine hydrochloride ($C_{17}H_{22}NO_4^+Cl^-$) into cocaine ($C_{17}H_{21}NO_4$). Bean, *supra,* at 3. Cocaine made by crushing and dissolving coca leaves will have more impurities, and will be far less pharmacologically potent, than cocaine made by reconverting cocaine hydrochloride. Bean, *supra,* at 3. But as a matter of chemical definition, they are the same: $C_{17}H_{21}NO_4$. *Id.* ("crack is cocaine").

The foregoing describes chemical reactions that cause one compound to become another, distinct compound: cocaine becomes cocaine hydrochloride, which in turn can be reconverted into cocaine. These conversions affect how the substances are ingested. For example, cocaine can be vaporized and inhaled into the lungs ("smoked") while cocaine hydrochloride is unsuitable for "smoking" because it decomposes at relatively low temperatures. Bean, *supra,* at 3. On the other hand, cocaine is relatively insoluble, whereas cocaine hydrochloride dissolves readily in water and can be made into an injectable solution. Weiss, Mirin and Bartel, *supra,* at 23.

The way in which cocaine or cocaine hydrochloride is ingested is affected not only by chemical

reactions that can convert it from one compound into the other, but also by other changes – to the purity and physical form of the mixture that contains the compound – that occur during processing. Coca leaves can be chewed, or they can be crushed and mixed with solvents to dissolve the leaves and form a paste which can be "smoked." *Id.* at 10, 19-20. Processing paste from coca leaves does not involve a chemical reaction and does not change the chemistry of the compound: coca leaves and cocaine paste are both cocaine ($C_{17}H_{21}NO_4$). Only when cocaine is combined with hydrochloric acid (HCl) is there a chemical reaction that converts it into a different compound, *i.e.* cocaine hydrochloride ($C_{17}H_{22}NO_4^+Cl^-$).

Similarly, cocaine hydrochloride can be insufflated (breathed in through the mucous membranes in the nose); or it can be mixed with water and injected into a vein. *Id.* at 15-16, 23. Dissolving cocaine hydrochloride in water does not involve a chemical reaction; the injectable mixture is still $C_{17}H_{22}NO_4^+Cl^-$. It is when cocaine hydrochloride is combined with a base, for example sodium bicarbonate dissolved in water ($NaHCO_3$), that there is a chemical reaction which reconverts the cocaine hydrochloride into cocaine. Bean, *supra,* at 3. The pasty mixture containing cocaine can be heated to draw off the water, and cooled to form crystals ("crack") which can be "smoked." Weiss, Mirin and Bartel, *supra,* at 11. This last part of the process does not effect a change in the cocaine mixture's chemical makeup: the chemical definition of crack is $C_{17}H_{21}NO_4$. Bean, *supra,* at 3.

As varied as the physical forms, ways of ingesting, and potency of these mixtures may be, as a matter of chemistry, they are either cocaine or cocaine hydrochloride. A mixture containing cocaine hydrochloride, whether it is in powder or liquid form, is $C_{17}H_{22}NO_4^+Cl^-$. A mixture containing cocaine, whether it is coca paste or crack, is $C_{17}H_{21}NO_4$. A paste made from crushed coca leaves has more impurities and is pharmacologically less potent than crack, but the substances have the same chemical definition: $C_{17}H_{21}NO_4$. Bean, *supra,* at 3.

As they stated at the beginning of this summary, *amici* devote this brief to making a few points about the chemistry of cocaine. They do not address the pharmacological effects of the drug; nor do they construe 21 U.S.C. §841(b). That said, to the extent that the statute is read to distinguish mixtures containing "cocaine," *see* 21 U.S.C. §841(b)(1)(A)(ii), from mixtures containing "cocaine base," 21 U.S.C. §841(b)(1)(A)(iii), *amici* hope to make it clear that there is no such distinction in chemistry. To a scientist, cocaine *is* a base, and a mixture containing cocaine has one chemical definition: $C_{17}H_{21}NO_4$.

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## ARGUMENT

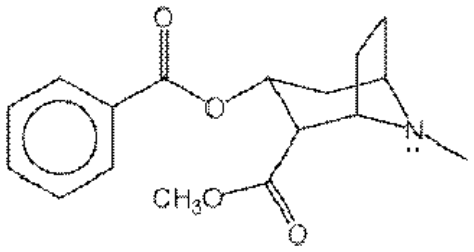
### I. THE STRUCTURE AND REACTIONS OF COCAINE AND COCAINE HYDROCHLORIDE

#### A. Cocaine.

Cocaine is an alkaloid named after the *Erythroxylon coca*, a leafy plant which grows principally in the northern South American Andes, and to a lesser extent in India, Africa, Sri Lanka and the West Indies. Ashley, *supra,* at 13. Alkaloids are commonly defined as basic chemical compounds that contain carbon, hydrogen, oxygen and nitrogen atoms and occur naturally in a large variety of organisms, including plants. Ashley, *supra,* at 18; Loudon, *supra,* at 1108; Solomons and Fryhle, *supra,* at 994. Alkaloids are noted for their pronounced physiological, and often psychotropic, effects on animal organisms. Ashley, *supra,* at 18; Solomons and Fryhle, *supra,* at 994. Alkaloids often, but not always, are named after the plant in which they were first discovered: *cocaine* is named for the *coca* plant. Solomons and Fryhle, *supra,* at 994. Some other well known examples of alkaloids are nicotine (named for Nicot, a French ambassador who sent tobacco seeds to France) and morphine (named for Morpheus, the Greek god of sleep and dreams.) *Id.* at 995, 997. While alkaloids occur naturally, most can now be reproduced synthetically in a laboratory. *See id.* at 994 (independent synthesis has confirmed structure of alkaloids).

Alkaloids are nitrogen-containing bases. Loudon, *supra,* at 1108; *see Brisbane*, 367 F.3d at 911 ("Cocaine is a naturally occurring alkaloid – that is, a base."). There are a number of ways to define a "base," but for purposes of this fundamental discussion, an appropriate definition is provided by the well accepted and widely applicable Lewis Acid and Base Theory: a base is a substance comprised of molecules each of which can *donate* an electron pair to another molecule. Solomons and Fryhle, *supra,* at 99.

The chemical formula for cocaine is $C_{17}H_{21}NO_4$. This molecule has an electron pair on the nitrogen atom (N) that it can donate:



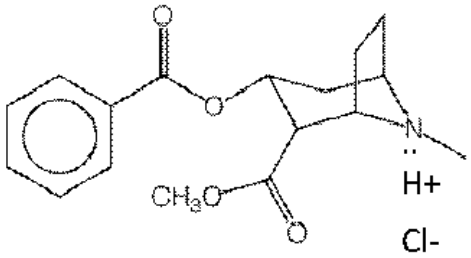

In cocaine as shown in Diagram A, the nitrogen has a free pair of electrons (··). This is what makes cocaine a base. Solomons and Fryhle, *supra,* at 99.

### B. Cocaine Hydrochloride.

Cocaine can be converted from a base into a salt (which has a distinct molecular structure) by combining it with a third chemically distinct substance, an acid (such as hydrochloric acid, HCl). Weiss, Mirin and Bartel, *supra,* at 10. The Lewis Acid and Base

Theory defines an acid as a substance comprised of molecules each of which can *accept* an electron pair from another molecule. Solomon and Fryhle, *supra,* at 99. When hydrochloric acid (HCl) is dissolved in water, it disassociates into $H^+$ and $Cl^-$. The $H^+$ is the acid part. It seeks out a pair of electrons. When the cocaine base is dissolved in the HCl solution, the $H^+$ combines with the free electrons on the cocaine's nitrogen, forming cocaine $^+Cl^-$, the salt form of cocaine (cocaine hydrochloride).

The formula for cocaine hydrochloride is $C_{17}H_{22}NO_4{}^+Cl^-$. This distinct molecule is depicted in Diagram B:




The differences between the molecular structures of cocaine and cocaine hydrochloride do not translate into differences in the pharmacological effects on the human body: "The active part of the drug remains unchanged whichever form is used, and the effects on the human body are the same whether the base [cocaine] or salt [cocaine hydrochloride] form is ingested." Bean, *supra,* at 3. That said, the chemical definitions of the compounds are distinct: cocaine hydrochloride is $C_{17}H_{22}NO_4{}^+Cl^-$; cocaine is $C_{17}H_{21}NO_4$.

Once cocaine hydrochloride has been formed, it can be converted back into cocaine by reaction with a basic (alkaline) substance. Bean, *supra,* at 3. This base can be ammonia ($NH_3$), sodium hydroxide (NaOH), sodium bicarbonate ($NaHCO_3$) or sodium carbonate ($NaCO_3$). All are bases; they all have a part (the $OH^-$ or the $HCO_3^-$ or the $CO_3^=$) with a free pair of electrons. When cocaine hydrochloride is dissolved in water that contains one of these bases, the extra $H^+$ that is attached to the nitrogen on the cocaine is removed and attaches to the alkaline substance in the solution. The cocaine hydrochloride ($C_{17}H_{22}NO_4^+Cl^-$) is thus reconverted into cocaine ($C_{17}H_{21}NO_4$). This reconverted "base form, usually called crack" "is cocaine." *Id*.

### C. Distinct Properties Of Cocaine And Cocaine Hydrochloride.

The conversions and reconversions – from cocaine ($C_{17}H_{21}NO_4$) to cocaine hydrochloride ($C_{17}H_{22}NO_4^+Cl^-$) and back again – affect the substances' potency and means of ingestion. Cocaine can be put in a pipe and heated until the cocaine vaporizes and can be inhaled into the lungs ("smoked"). *Id.* Cocaine hydrochloride is unsuitable for "smoking" because it decomposes at relatively low temperatures, and so is destroyed by the time the substance is hot enough to vaporize. *Id.* But unlike cocaine, cocaine hydrochloride dissolves easily in water, so it can be made into a solution and injected. Weiss, Mirin and Bartel, *supra,* at 23;

*see* Solomons and Fryhle, *supra,* at 108, 994 ("water insoluble amines," including alkaloids like cocaine, can be converted through "acid-base reactions" "into soluble salts").

The means of ingesting these drugs are affected not only by chemical reactions that can convert and reconvert the chemical compounds, but also by other changes – to the purity and physical form of the mixture that contains the cocaine or cocaine hydrochloride – that occur during processing. These changes are addressed below.

## II. PROCESSING AND INGESTING COCAINE AND COCAINE HYDROCHLORIDE

The following discussion is by no means comprehensive; it describes just a few of the means of processing and ingesting cocaine and cocaine hydrochloride, respectively. The discussion is included for the limited purpose of distinguishing processing that effects changes in the purity and certain physical attributes of the substances from the chemical reactions that convert one compound into the other and back again.

### A. Cocaine.

Coca leaves can be chewed, but they are bulky and contain a lot of organic matter in addition to cocaine. Bean, *supra,* at 2; Weiss, Mirin and Bartel, *supra,* at 10. Coca leaves can be crushed and mixed

with solvents to dissolve the leaves and form a paste that is less bulky and can be "smoked" (or, more accurately, vaporized and inhaled). Weiss, Mirin and Bartel, *supra,* at 10, 19-20. This process does not involve a chemical reaction and does not change the nature of the compound: just like coca leaves, cocaine paste contains $C_{17}H_{21}NO_4$. Only when cocaine is combined with hydrochloride (HCl) is there a chemical reaction that forms a different compound, cocaine hydrochloride ($C_{17}H_{22}NO_4^+Cl^-$).

### B. Cocaine Hydrochloride.

Cocaine hydrochloride can be insufflated (breathed in through the nose); or it can be mixed with water and injected into a vein. Weiss, Mirin and Bartel, *supra,* at 15-16, 23. Mixing cocaine hydrochloride with water does not cause a chemical reaction; the injectable mixture contains $C_{17}H_{22}NO_4^+Cl^-$. Only when cocaine hydrochloride is combined with a base, for example water containing sodium bicarbonate ($NaH^+CO_3^-$) is there a chemical reaction that converts it into a different compound, *i.e.* back into cocaine.

### C. Cocaine (Again.)

When cocaine hydrochloride is reconverted into cocaine, the result is a pasty mixture containing cocaine which can be heated to draw off the water, and cooled to form crystals (crack) which can be "smoked" (or more accurately, vaporized and inhaled).

Weiss, Mirin and Bartel, *supra,* at 11. The heating and cooling part of the process makes the cocaine mixture easier to smoke, but it does not effect a change in the mixture's chemical makeup: crack is $C_{17}H_{21}NO_4$. Bean, *supra,* at 3.

## CONCLUSION

Cocaine and cocaine hydrochloride have similar pharmacological effects on the body, but they have different chemical definitions. A mixture containing cocaine hydrochloride, however it is ingested and whatever its pharmacological potency, is $C_{17}H_{22}NO_4^+Cl^-$. A mixture containing cocaine, however it is ingested and whatever its pharmacological potency, is $C_{17}H_{21}NO_4$.

To put this very fundamental chemistry "lesson" in the context of 21 U.S.C. §841(b), while mixtures containing cocaine hydrochloride are chemically distinct from mixtures containing cocaine, there is no such distinction between mixtures containing "cocaine," *see* 21 U.S.C. §841(b)(1)(A)(ii) and mixtures containing "cocaine base," 21 U.S.C. §841(b)(1)(A)(iii). To a scientist, cocaine *is* a base, and a mixture

containing cocaine has only one chemical definition: $C_{17}H_{21}NO_4$.

Respectfully submitted,

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