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Formation of *O*-6-acetylmorphine in the 'homebake' preparation of heroin

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Abstract

When *O*-6-acetylmorphine is found in toxicological or in illicit drugs cases it is usually assumed to be the product of heroin degradation. It is, therefore, used as evidence for the prior existence of heroin. In this study, it was found that, when morphine is partly acetylated with acetyl chloride, *O*-6-acetylmorphine is produced. In some experiments, partial acetylation of morphine sulphate yielded mixtures which contained *O*-6-acetylmorphine, unreacted morphine and only traces of *O*-3-acetylmorphine and heroin. Therefore, in cases where *O*-6-acetylmorphine is found in the absence of heroin, it should not be used as evidence of heroin having been present.

Keywords: *O*-6-Acetylmorphine; Acetylation; Acetyl chloride; Clandestine laboratories; Heroin

1. Introduction

In toxicology and illicit drugs analysis, the presence of *O*-6-acetylmorphine (6AM) has become widely accepted as evidence of heroin having been present in a sample [1,2]. It has been accepted that 6AM is the result of the partial hydrolysis of heroin and that *O*-3-acetylmorphine (3AM) is the result of the incomplete acetylation of morphine during heroin manufacture (Fig. 1) [3]. In this paper, evidence is presented that the partial acetylation of morphine by acetyl chloride, can produce 6AM with the virtual absence of heroin.

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Most of the research done in the last 20 years on the acetylation of morphine has been done using acetic anhydride [3–5], but early workers were of the opinion that heroin was more easily prepared using acetyl chloride [6]. Perhaps because of its volatility and relatively unpleasant and dangerous properties, acetyl chloride does not appear to have been used for research into the production of 3AM and 6AM during heroin formation.

Some workers reported that incomplete acetylation of morphine resulted in the formation of both 3AM and 6AM [5,7]. After experiments with acetic anhydride, Moore and Klein disagreed [3]. They concluded that most of the 6AM resulted from the hydrolysis of heroin, whereas most of the 3AM resulted from the incomplete acetylation of morphine (Fig. 1) [3]. Huizer also found that, using acetic anhydride, the incomplete acetylation of morphine resulted in the formation of 3AM with no detectable 6AM [4].

A dramatic decline in the availability of imported heroin occurred in New Zealand in 1980. Since then many drug users make their own heroin in what has become known as the 'homebake' procedure [8]. This procedure involves the extraction of codeine base from commercially available pharmaceutical products, the demethylation of the codeine to morphine using pyridine hydrochloride, the

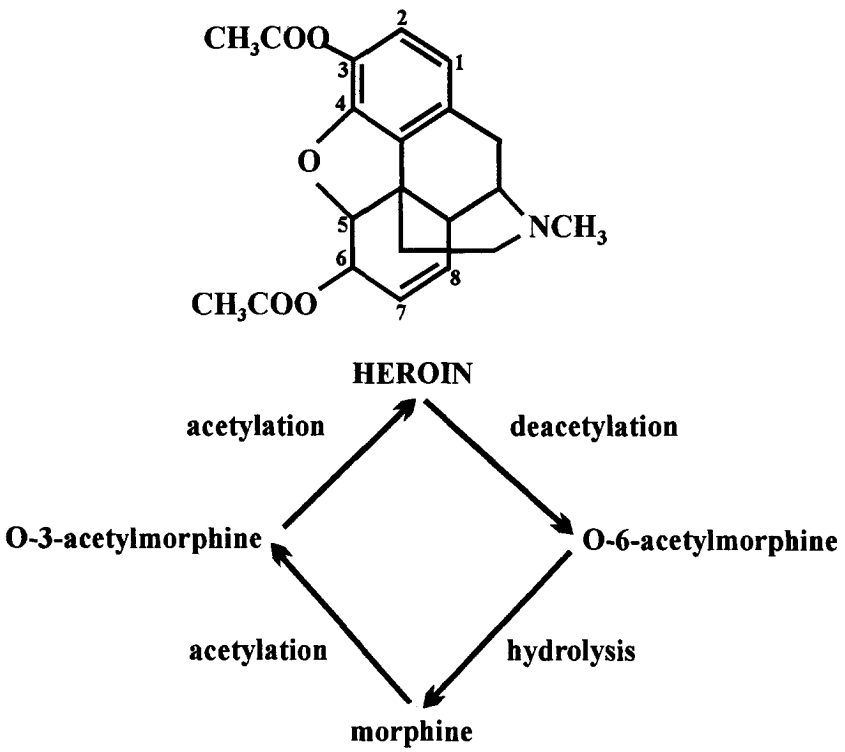

Fig. 1. The partial acetylation of morphine with acetic anhydride to produce *O*-3-acetylmorphine (3AM), and the partial hydrolysis of heroin to produce *O*-6-acetymorphine (6AM).

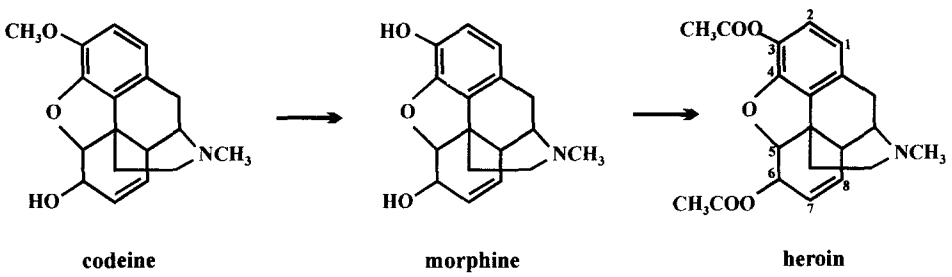

Fig. 2. The 'homebake' demethylation of codeine to produce morphine followed by the acetylation of morphine to produce heroin.

extraction and crystallisation of the morphine base, and its acetylation to heroin (Fig. 2).

However, 'homebakers' do not always prepare their own morphine from codeine, but use any available source of morphine. This may be opium from homegrown *Papaver somniferum* poppies, or crushed morphine sulphate tablets. Slow release morphine sulphate tablets, known as MST Continus in New Zealand, are used to treat the pain of cancer patients. Recently, MST Continus tablets have been widely abused and connected with many cases of 'homebaking'.

In the 'homebake' procedure, the conversion of morphine to heroin is usually carried out with a few millilitres of an acetylating agent and sufficient morphine for a single heroin dose. The mixture is gently heated, with ignition, in a spoon, often using a spirit burner. The heroin produced is most often used immediately. The most common acetylating agent is acetic anhydride, but recent seizures of 'homebakers' reagents, submitted to our laboratory by the police for analysis, have shown an increased use of acetyl chloride.

To determine whether or not the effects of acetyl chloride are different from those of acetic anhydride in the 'homebake' procedure, the following preliminary study was performed. Our aim was to simulate acetylation reactions under typical 'homebaking' conditions and observe the variety of reaction products.

2. Materials

Morphine base was prepared either from morphine sulphate, or from codeine using the 'homebake' procedure. The morphine sulphate used was B.P. Powder manufactured by May & Baker. MST Continus tablets were a case sample. Heroin was a case sample of heroin hydrochloride which contained the equivalent of 80% heroin base with traces of acetyl codeine and 6AM. Heroin base, 3AM and 6AM were synthesised in this laboratory. Heroin base was prepared in the following way: heroin hydrochloride was dissolved in 0.02M sodium tetraborate buffer and immediately extracted into chloroform. The chloroform was dried over sodium sulphate, filtered, and evaporated at room temperature to leave white crystalline heroin base. The 3AM, in the form of its sulphamate salt, was prepared in this laboratory using

the method of Welsh [9]. The 6AM, in the form of its hydrochloride salt, was prepared in this laboratory using the method of Wright [10]. The acetyl chloride used was laboratory reagent grade, manufactured by Ajax Chemicals of Australia. The acetic anhydride was laboratory reagent grade manufactured by BDH.

An electroplated nickel silver (E.P.N.S.) spoon, and a stainless steel spoon were used as vessels for the acetylation reactions. An ethanol spirit burner obtained from a dental supply company was used for heating the spoons. Reaction products were dissolved in analytical reagent grade methanol manufactured by Rhône-Poulenc.

3. Method

All experiments were performed in duplicate. Reaction mixtures were analysed by GC/MS using a Hewlett Packard HP 5890 Gas Chromatograph in split mode equipped with a 10 m HP-Ultra-1 capillary column (0.22 mm I.D., 0.11 μm film thickness) with helium as carrier gas and a column head pressure of 16 kPa. The flow at the split valve was 39 ml per min. Oven temperature 200 to 280°C at 10/degC per min. Injector temperature 280°C. The GC was connected to a Hewlett Packard 5970 Series Mass Selective Detector, 2200 EM volts, scanning 40 to 500 mHz with MS Chem Station software. Retention times were: morphine 3.1 min; 3AM 3.5 min; 6AM 3.6 min; heroin 4.2 min.

Small samples (about 2–5 mg each) of morphine base, morphine sulphate, heroin hydrochloride or heroin base were placed in spoons. Small volumes (0.2–10 ml) of acetic anhydride or acetyl chloride were added and the mixtures were simmered, usually with ignition, to dryness. The residues were dissolved immediately in methanol to give solutions containing about 1 mg of residue per ml. Two μl were immediately injected into the GC/MS. The acetylchloride experiments were repeated on a larger scale using 100–300 mg of morphine sulphate, or morphine base, with 5–40 ml of acetyl chloride. The components of the residues were identified by GC retention times and mass spectra.

The relative amounts of morphine, 3AM, 6AM and heroin were assessed by their relative peak areas. While this is an extremely imprecise measure of their relative concentrations, it was sufficient to identity differences between the residues.

4. Results and discussion

As expected, morphine acetylated with acetic anhydride gave major peaks of 3AM and heroin, as well as unreacted morphine. Only traces of 6AM were detected (Fig. 3).

However, numerous experiments in which varying amounts of both morphine sulphate or morphine base were reacted with acetyl chloride produced 6AM peaks which were almost always larger than the 3AM peaks.

The production of 6AM was much more pronounced with morphine sulphate powder and with crushed MST Continus morphine sulphate tablets than it was

with morphine base. In the most pronounced case, about 2 mg of morphine sulphate powder was warmed with about 0.2 ml of acetyl chloride, in an E.P.N.S. spoon, the resulting residue contained virtually all 6AM and unreacted morphine. Only traces of 3AM and heroin were detected (Fig. 4).

Most of our experiments were in E.P.N.S. spoons but we carried out three in stainless steel spoons. In these spoons, the acetylation of morphine sulphate with acetyl chloride consistently produced both 6AM and 3AM, as well as heroin.

Replicate injections gave consistent results. To determine whether the proportions of the reaction products in the solutions varied with the strength of the solution, one of the solutions was diluted up to ten times. No significant variation of the proportions of the reaction products in the solution was found.

In order to prove that the 6AM was not being produced from the hydrolysis of heroin, samples of heroin hydrochloride or heroin base were treated with acetyl chloride. The residues contained heroin with no detectable 6AM (Fig. 5). The 6AM present in the other residues, therefore, was not a result of heroin hydrolysis but was formed by the acetylation of morphine.

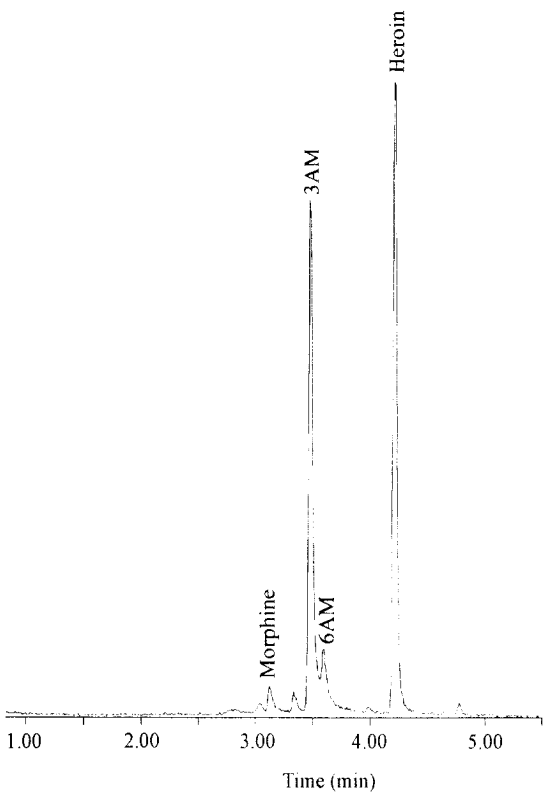

Fig. 3. A typical total ion chromatogram of the product obtained from the reaction of 2 mg of morphine sulphate with 2 ml of acetic anhydride.

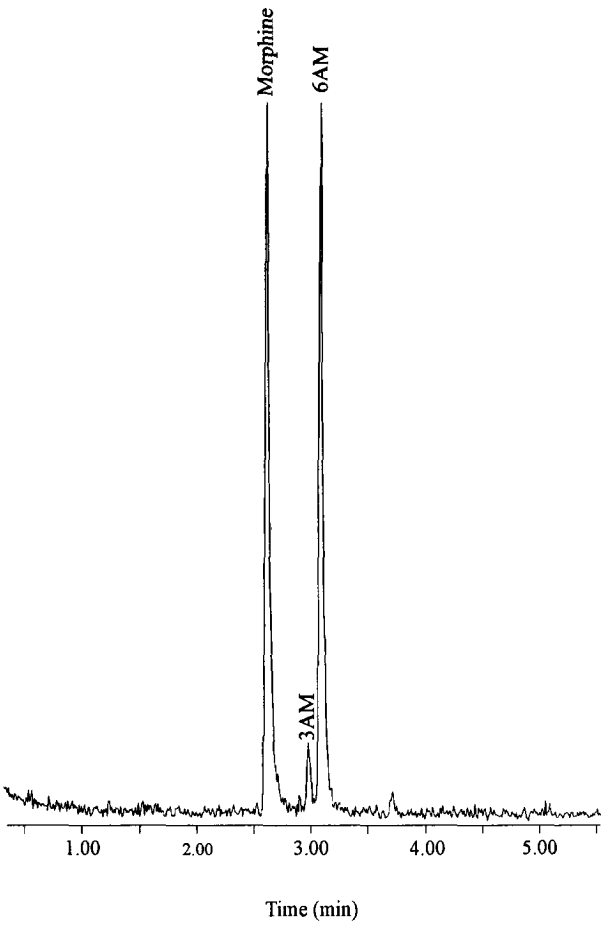

Fig. 4. Total ion chromatogram of the product obtained from the reaction of 2 mg of morphine sulphate with 0.2 ml of acetyl chloride in an E.P.N.S. spoon.

We have not yet attempted to establish why using acetyl chloride to acetylate morphine, particularly the sulphate salt of morphine, produces 6AM. Obviously a further, more systematic, quantitative study is needed.

5. Conclusions

In the 'homebake' acetylation of morphine with acetic anhydride, mainly heroin and 3AM are produced. In the 'homebake' acetylation of morphine, with acetyl chloride, large amounts of 6AM are produced. Some 3AM may also be produced. The 6AM is not a result of heroin hydrolysis.

The acetylation of morphine sulphate produced more 6AM than did the acetylation of morphine base. Some acetylations of morphine sulphate produced only

6AM with little or no detectable heroin. Therefore, the presence of 6AM should not be used as evidence that heroin has been present in a sample.

Two tables are included which show the results of the experiments with acetic anhydride (Table 1) and acetyl chloride (Table 2).

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Fig. 5. Total ion chromatogram of the reaction product obtained from the reaction of 2 mg of heroin hydrochloride with 2 ml of acetyl chloride.

Table 1
Results of experiments with acetic anhydride[a]

Acetic anhydride (ml)	Peak areas relative to morphine			
	M	3AM	6AM	H
0.2	1.0	0.28	nd	nd
0.2	1.0	0.06	nd	nd
5	1.0	4.55	0.77	1.14
5	1.0	14.28	2.86	16.71

M = morphine, 3AM = *O*-3-acetylmorphine, 6AM = *O*-6-acetylmorphine, H = heroin, nd = not detected.
[a]2 mg portions of morphine sulphate were warmed with acetic anhydride in an E.P.N.S. spoon.

Table 2
Results of experiments with acetyl chloride

Type of morphine	Weight of powder (mg)	Approximate volume of acetyl chloride (ml)	Approximate time heated (s)	Spoon type	Peak areas relative to 6AM			
					M	3AM	6AM	H
MST	20	5	170	EPNS	0.19	0.31	1.00	1.19
Continuous	20	5	170	EPNS	0.34	0.23	1.00	0.54
tablet	10	10	250	EPNS	0.22	0.34	1.00	1.05
	10	10	250	EPNS	nd	0.38	1.00	2.69
Morphine	2	0.2	10	EPNS	3.10	0.12	1.00	nd
sulphate	2	0.2	10	EPNS	1.14	0.09	1.00	nd
	2	0.2	10	EPNS	1.19	0.10	1.00	0.09
	2	2	60	EPNS	0.31	0.26	1.00	0.55
	2	5	170	EPNS	1.90	0.47	1.00	0.18
	300	5	170	EPNS	0.17	0.28	1.00	0.64
	300	5	170	EPNS	0.10	0.31	1.00	0.90
	300	10	250	EPNS	nd	1.43	1.00	11.7
	300	10	250	EPNS	nd	1.11	1.00	6.87
	2	2	60	StSt	2.27	1.02	1.00	0.23
	2	2	60	StSt	2.04	0.64	1.00	0.40
	2	2	60	StSt	nd	0.85	1.00	2.03
Morphine	2	2	60	EPNS	9.53	3.14	1.00	nd
base	2	2	60	EPNS	4.58	3.80	1.00	0.51
	2	2	60	EPNS	0.58	0.46	1.00	0.34
	110	40	1000	EPNS	0.62	0.27	1.00	0.70
	110	10[a]	850	EPNS	0.11	trace	1.00	3.80

[a]This mixture stood for 10 min before it was heated.
EPNS = electroplated nickel silver spoon, StSt = stainless steel spoon.
M = morphine, 3AM = *O*-3-acetylmorphine, 6AM = *O*-6-acetylmorphine, H = heroin, nd = not detected.

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