IMPURITIES IN ILLICIT AMPHETAMINE. 7. IDENTIFICATION OF BENZYL METHYL KETONE PHENYLISOPROPYLIMINE AND BENZYL METHYL KETONE BENZYLIMINE IN AMPHETAMINE

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Summary

The identification of the Schiff bases benzyl methyl ketone phenylisopropylimine and benzyl methyl ketone benzylimine by both high- and low-resolution mass spectrometry is reported. Both substances are found in amphetamine produced illegally by a reductive amination of benzyl methyl ketone.

Introduction

It is well known that impurities in illegally prepared amphetamine can be of great help in the characterization and comparison of this type of drug [1 - 5]. As these impurities can originate from precursor chemicals, incomplete reactions and side-reactions, it is obvious that a lot of information can be gathered about the method of preparation and the chemicals used merely by studying the by-products to be found in illicitly produced amphetamine.

Up to now amphetamine has been made illegally in The Netherlands by Leuckart synthesis, in which benzyl methyl ketone is reacted with formamide at an elevated temperature. Quite recently, however, a production location was discovered where amphetamine was prepared in another way. The amphetamine was synthesized by means of a reductive amination of benzyl methyl ketone. The general procedure (Fig. 1) was as follows. In a vessel kept at room temperature benzyl methyl ketone dissolved in methanol was brought together with a suspension of Raney nickel. A mixture of ammonia gas and hydrogen was bubbled through the solution at a slight overpressure. After a short time the reaction was finished and the amphetamine was purified by repeated crystallization.

In this report the major and minor impurities found as by-products in this method of preparing amphetamine are described.

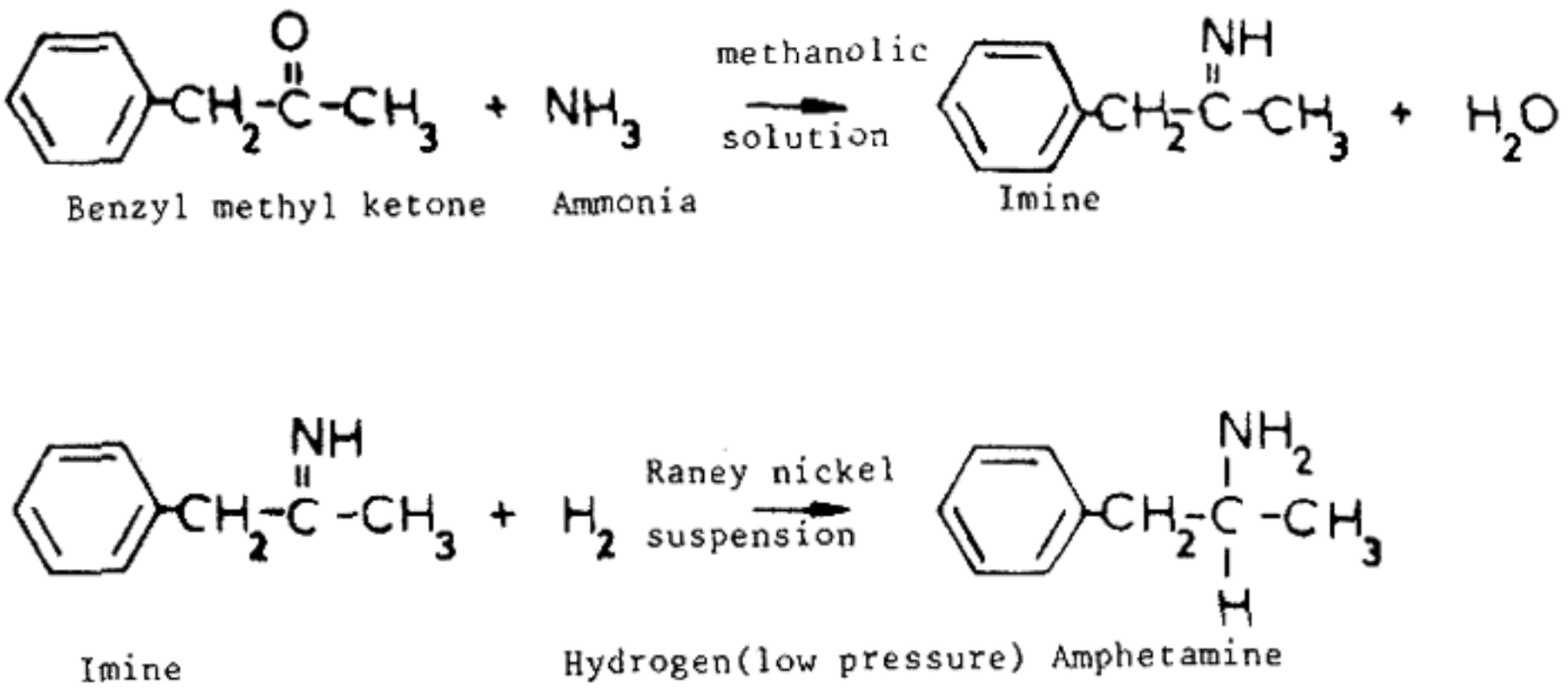


Fig. 1. Reaction scheme of the reductive animation of benzyl methyl ketone.

Experimental

General

Due to the small quantities of the impurities in the amphetamine seized by the police, it was decided to use for identification purposes the reaction mixture found at the production location, in which the impurities occurred in a much higher amount. A portion of the reaction mixture was made alkaline, extracted with diethyl ether, concentrated and injected into the gas chromatograph–mass spectrometer combination. Afterwards the same procedure was applied to a fair quantity of amphetamine found in the workshop. The presence of the impurities, of which the identification is to be described below, could then be established without difficulty.

Synthesis

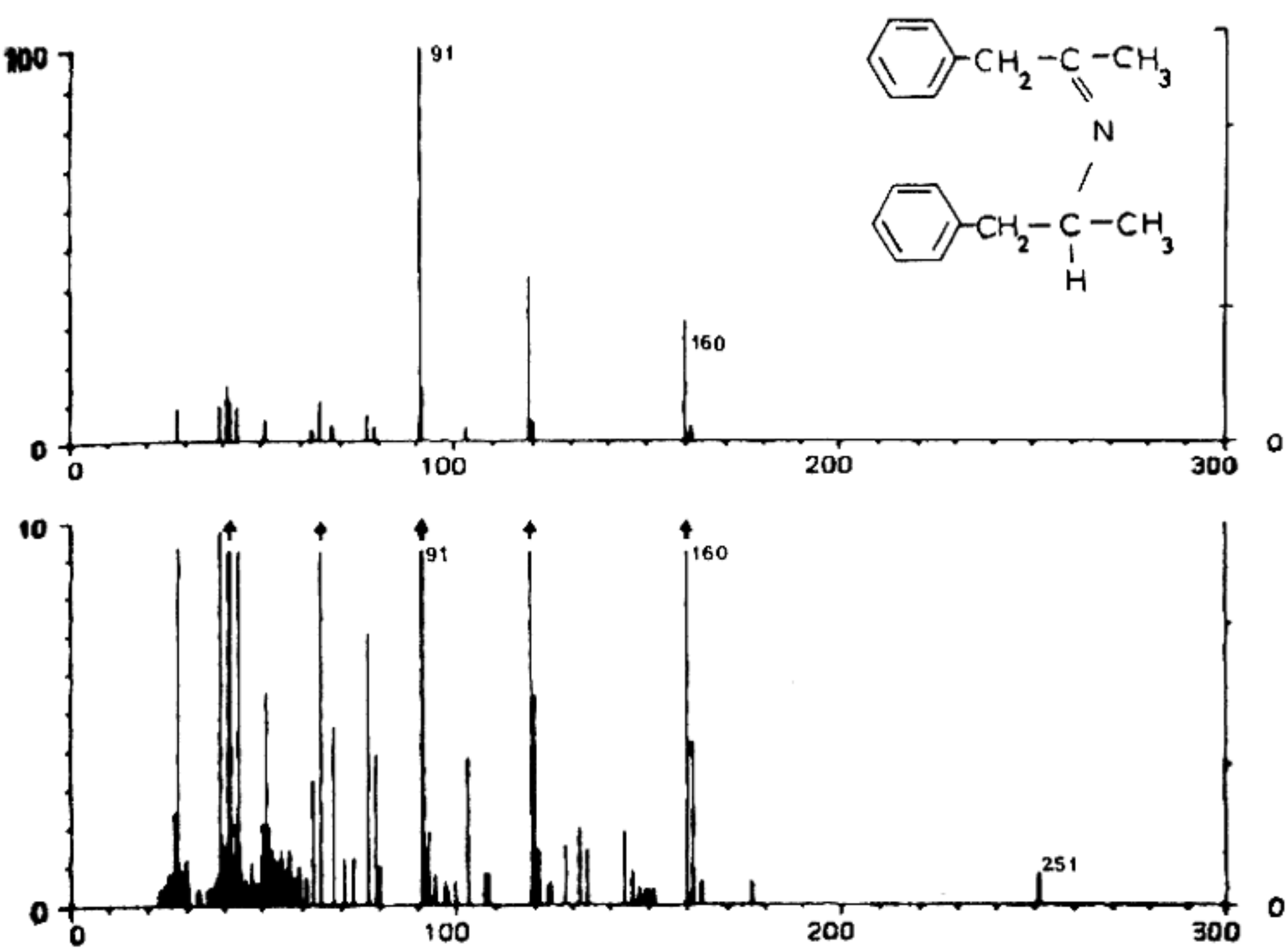
For comparative purposes the Schiff bases of benzyl methyl ketone and amphetamine and of benzaldehyde and amphetamine were prepared according to the methods of Buth *et al.* [6] and of Hanus *et al.* [7], respectively. The substances were not purified.

Spectroscopy

Electron-impact spectra at 70 eV were taken on Varian MAT 111 and 212 spectrometers, coupled to Varian MAT SpectroSystems 100 MS and 200, respectively. The chromatographic conditions were: column 2 m × 1/8 inch stainless steel filled with Apiezon L/KOH 10%/10% on Chromosorb G DMCS; carrier gas helium, flow-rate 10 ml/10 min; the oven temperature was programmed from 100 °C to 200 °C at 4 °C/min.

Results and discussion

The major and minor compounds were identified by interpretation of the low- and high-resolution mass spectra of the impurities. With high-resolu-



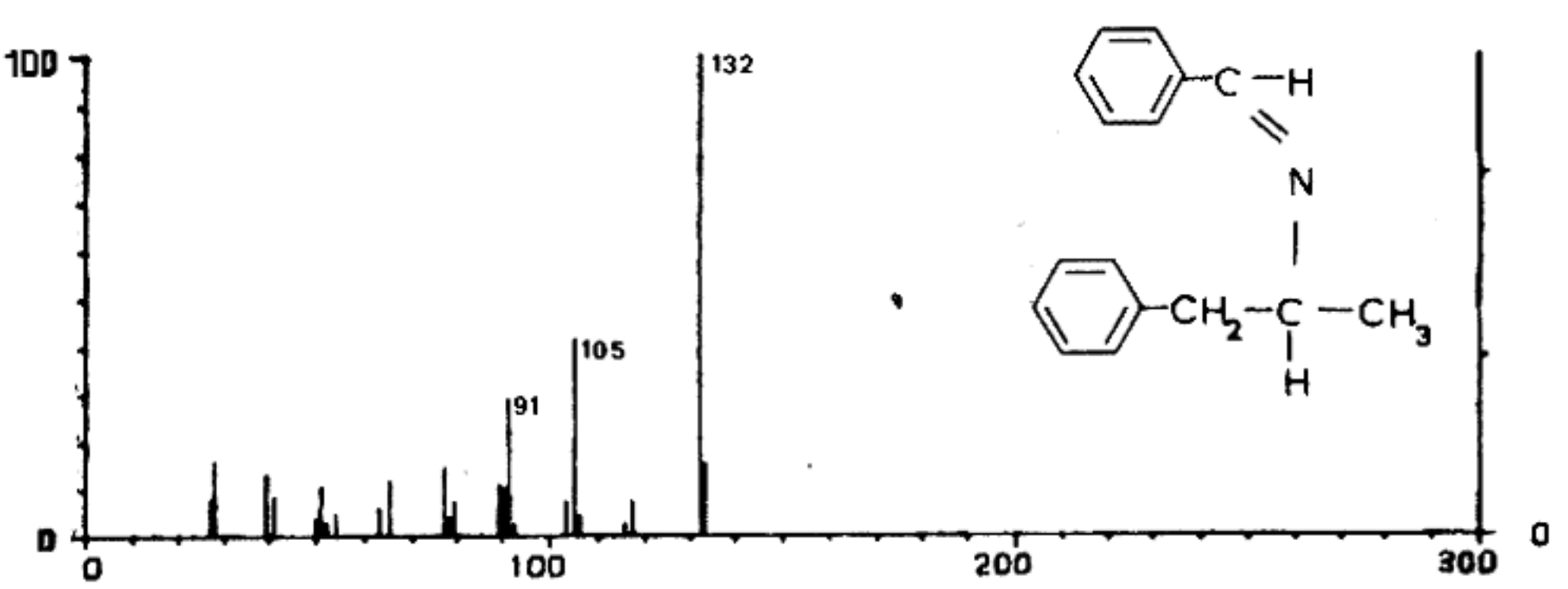
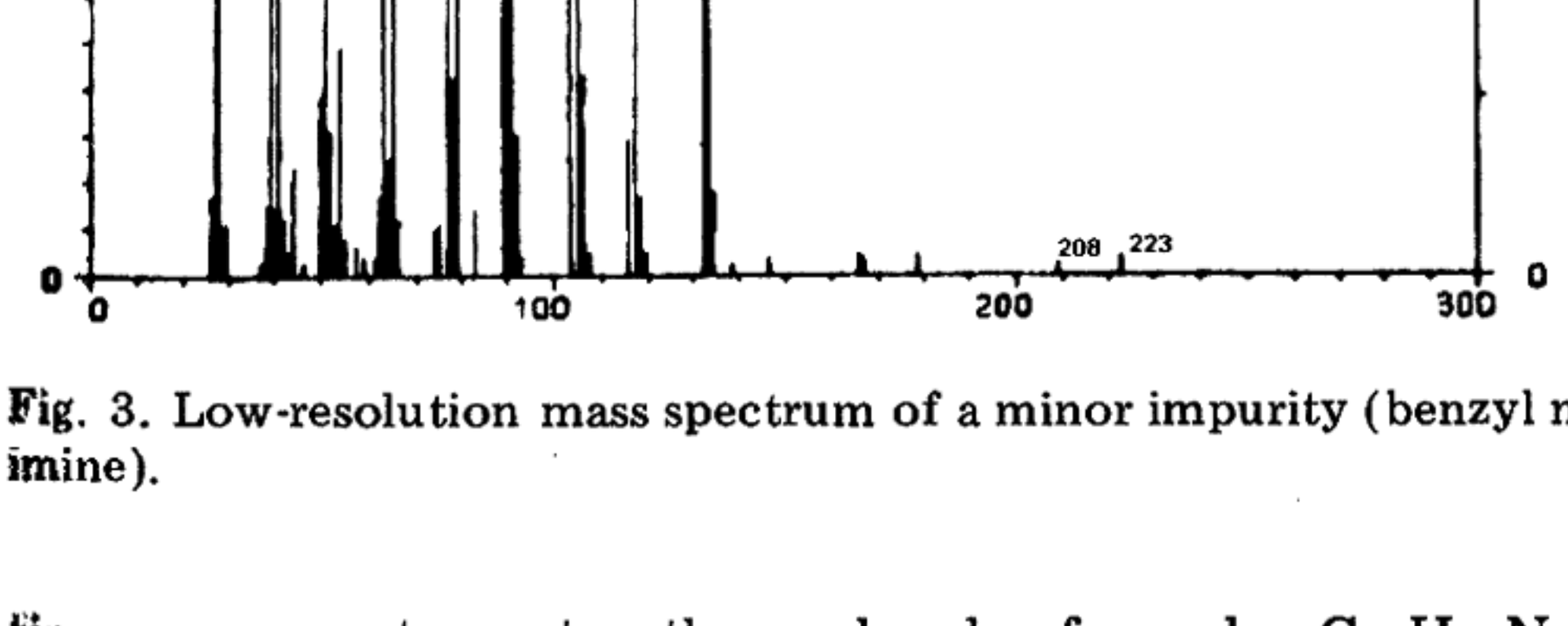


Fig. 2. Low-resolution mass spectrum of the major impurity (benzyl methyl ketone phenylisopropylimine).



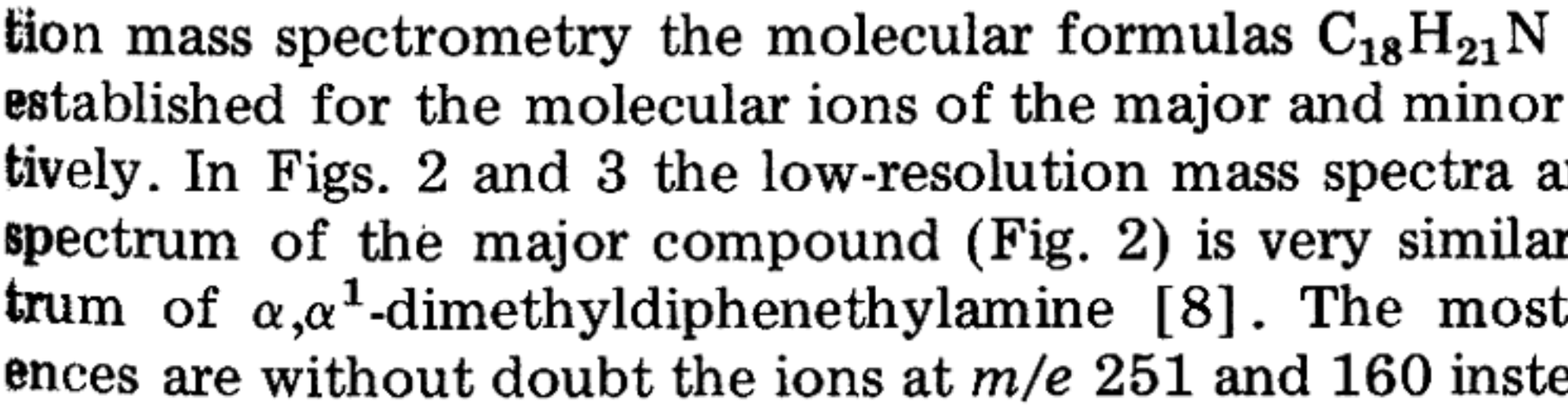
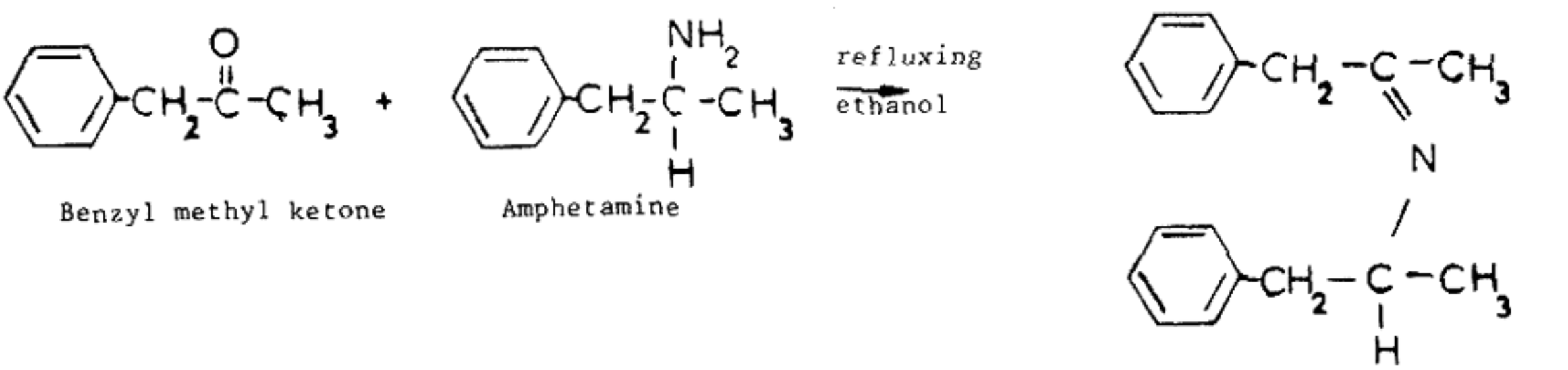


Fig. 3. Low-resolution mass spectrum of a minor impurity (benzyl methyl ketone benzylimine).

tion mass spectrometry the molecular formulas $C_{18}H_{21}N$ and $C_{16}H_{17}N$ were established for the molecular ions of the major and minor impurities, respectively. In Figs. 2 and 3 the low-resolution mass spectra are given. The mass spectrum of the major compound (Fig. 2) is very similar to the mass spectrum of α,α^1-dimethyldiphenethylamine [8]. The most significant differences are without doubt the ions at *m/e* 251 and 160 instead of *m/e* 253 and



Benzyl methyl ketone

Amphetamine

Benzyl methyl ketone phenyl isopropylimine

Fig. 4. Reaction scheme of the condensation of an amine and a ketone to form a Schiff base.

162. Thus the evidence of both high- and low-resolution mass spectrometry points to a compound with the same structure as α,α^1-dimethyldiphenethylamine with the loss of two hydrogen atoms. For this reason the Schiff base of amphetamine and benzyl methyl ketone was synthesized, and this compound appeared to behave in a similar way to the major impurity in both gas chromatography and mass spectroscopy.

The minor component presented more difficulties. It is clear from the mass spectrum that a phenyl group attached to at least two carbon atoms must be a part of the molecule. Besides this, benzyl must play an important part, because of the $(M - 91)$ peak, and m/e 132 → m/e 105 points to HCN removal. Combining this evidence, the structure of the Schiff base of benzaldehyde and amphetamine was tentatively adopted for this impurity.

This compound was also synthesized, and the mass-spectroscopic and gas-chromatographic properties conformed to those of the minor impurity, as well to evidence from the literature [7]. The explanation for the occurrence of the major impurity is straightforward; it is the condensation product of benzyl methyl ketone and amphetamine (Fig. 4) which is not yet hydrogenated. The minor impurity could be thought to be the condensation product of benzaldehyde and amphetamine or perhaps the product of the condensation of benzylamine with benzyl methyl ketone. In our view the latter two possibilities do not seem very likely, as the minor impurity was also found, to our surprise, as a by-product in the condensation of amphetamine with benzyl methyl ketone. This preparation was done under laboratory conditions, using the reaction conditions described by Buth *et al.* [6]. Thus, in our opinion, the two compounds described could be found in any synthesis of amphetamine from benzyl methyl ketone provided: (1) water originating in the condensation can escape from the reaction mixture, and (2) hydrogenation of the imines in the reaction mixture is not fully effective.

References

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