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α-Phenylethylamine in illegally produced amphetamine

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Abstract

The possibility of simultaneous synthesis of α-phenylethylamine and amphetamine from mixture of acetophenone and benzylmethylketone was studied. The structures of specific impurities were predicted and these compounds were synthesized and finally found in reaction mixtures, as well as in the final product. The data collected by gas chromatography, proton and carbon magnetic resonance, Fourier transform infrared spectrometry and mass spectrometry are presented. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: α-Phenylethylamine; Fourier transform infrared spectrometry; Mass spectrometry

1. Introduction

In the recent years, the availability of amphetamine and its analogues in Poland has increased significantly. In the last 5 years, numerous illegal laboratories for the production of these compounds were discovered. Central nervous stimulants (CNS) — amphetamine and methamphetamine, as well as *N*-alkyl derivatives of 3,4-methylenedioxyamphetamine (MDA): 3,4-methylenedioxymethamphetamine (MDMA) and 3,4-methylenedioxyethylamphetamine (MDE) are perhaps the most widely produced and abused drugs of this family. Incidentally, *N*-methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (MBDB), *p*-methoxyamphetamine (PMA) and *p*-methoxymethamphetamine (PMMA) are encountered in street samples.

The amphetamine sulfate is rarely seen on the street market in a pure state. Many traffickers mix their supply with physiologically active or inactive compounds. The most commonly encountered in illicit samples are solid dilutents: lactose, glucose, citric acid and adulterants: phenacetine, acetylsalicylic acid, caffeine. Sometimes, other drugs are mixed with amphetamine sulfate. Illicit tablets, containing other controlled substances, including MDMA or MDE were also examined in our laboratory.

In the last decade, a lot of samples of amphetamine sulfate containing α-phenylethylamine salts were encountered on the polish illicit market.

The α-phenylethylamine concentration in analyzed samples ranged from 2 to 90%. In several cases, pure α-phenylethylamine sulfate was offered on the market as an amphetamine drug [1]. The presence of hydrochloride or sulfate salts of this amine as adulterants in amphetamine samples was also reported by several authors [2–4].

2. Chemistry

The synthesis of amphetamine from benzylmethylketone (BMK) and formamide or ammonium formate is still without doubt, a most popular method utilized in clandestine laboratories in Poland. During the first step, BMK is treated with formamide or ammonium formate to give intermediate product, formylamphetamine. Refluxing formylamphetamine with hydrochloric acid solution produces crude amphetamine which can be purified by extraction and/or steam distillation. Sometimes, vacuum distillation is utilized in purification of the free base. In these cases, especially pure product can be obtained.

Generally, there are two ways for the preparation of the mixture of amphetamine and α-phenylethylamine salts. First, commercially available α-phenylethylamine base can be transformed into an appropriate salt (hydrochloride, sulfate) and subsequently added to the drug. Secondly, the

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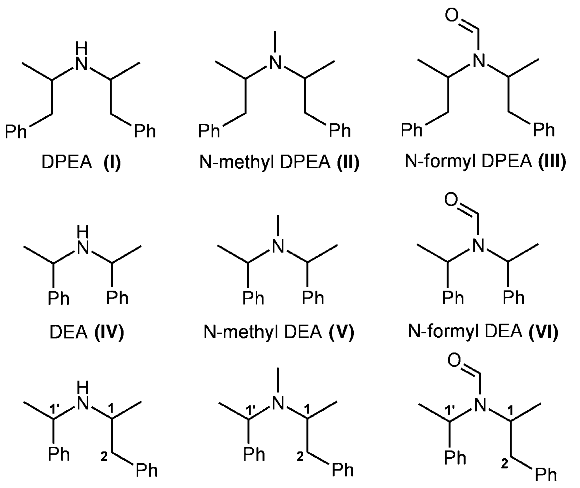

Fig. 1. Structures of the impurities found in amphetamine and α-phenylethylamine samples originated from the illegal synthesis.

amine can be prepared in illegal laboratory in a simple Leuckart reaction using readily available and uncontrolled acetophenone. In our opinion, another possible route to obtain the mixture of both amines has to be considered. This approach involves the use of mixture of acetophenone and benzylmethylketone in the simultaneous Leuckart synthesis. Furthermore, it can be expected that the mixture prepared in this way may contain contaminants and/or by-products that were unique to this method, such as compounds α-methyl-*N*-(1-phenylethyl)-benzenethanamine (**VII**), α,*N*-dimethyl-*N*-(1-phenylethyl)-benzenethanamine (**VIII**) and α-methyl-*N*-formyl-*N*-(1-phenylethyl)-benzenethanamine (**IX**) (Fig. 1). It therefore creates a valuable tool in the forensic analysis of the samples.

Many impurities and by-products found in amphetamine of illicit origin have been mentioned in the literature [5,6]. The by-products characteristic for the Leuckart synthesis such as di-(β-phenylisopropyl)amine (**I**) [7], *N*,*N*-di-(β-phenylisopropyl)methylamine (**II**) [8] and *N*,*N*-di-(β-phenylisopropyl)formamide (**III**) [9] have been described. Recently, the corresponding secondary amine, di-(1-phenylethyl)-amine (**IV**) as well as formamide derivative (**VI**) were identified in illegally produced α-phenylethylamine [2]. As shown on the Fig. 2, impurity **I**, **II**, **III** and **IV**, **VI** were formed probably in the similar manner. The secondary amine DPEA (**I**) and DEA (**IV**) can be formed from amphetamine/BMK and acetophenone/α-phenylethylamine condensation to the corresponding imines, and subsequent reduction. Formylation of **I** and **IV** gives *N*-formyl DPEA (**III**) and *N*-formyl DEA (**VI**), respectively. The formation of *N*-methyl DPEA (**II**) and *N*-methyl DEA (*N*,*N*-di-(1-phenylethyl)methylamine) (**V**) can be explained by the reduction of *N*-formyl derivatives.

We assumed that during simultaneous Leuckart synthesis of mixture of α-phenylethylamine and amphetamine the by-products **VII**, **VIII** and **IX** were formed. The explanation for the occurrence of these compounds is straightforward: they are the cross-reaction products of amphetamine/acetophenone and α-phenylethylamine/BMK condensation. As was shown on the Fig. 3, intermediary imines, **X** and **XI** once formed were reduced to the amine **VII**.

In order to verify our hypothesis, we carried out series of simultaneous amphetamine and α-phenylethylamine syntheses from the mixture of acetophenone and benzylmethylketone. We also synthesized amino compound **VII**, **VIII** and *N*-formyl derivative (**IX**). The structure confirmation of these compounds was based on their MS, FT-IR, ^{1}H NMR, ^{13}C NMR data. We also prepared *N*,*N*-di-(1-phenylethyl)methylamine (**V**) and confirmed its structure as mentioned above. Amine **V** was identified as a new by-product in the Leuckart synthesis of α-phenylethylamine. The preparation of PIEA (**VII**) and *N*-methyl DEA (**V**) has been previously reported [10,11]; however, to our knowledge, *N*-methyl PIEA (**VIII**) and *N*-formyl PIEA (**IX**) have never been synthesized previously.

3. Experimental

3.1. Reagents and chemicals

The amphetamine sulfate was obtained from Sigma Chemicals Co., (*R*)-(+)-1-phenylethylamine, (*S*)-(−)-1-phenylethylamine, benzylmethylketone, formamide, 36%

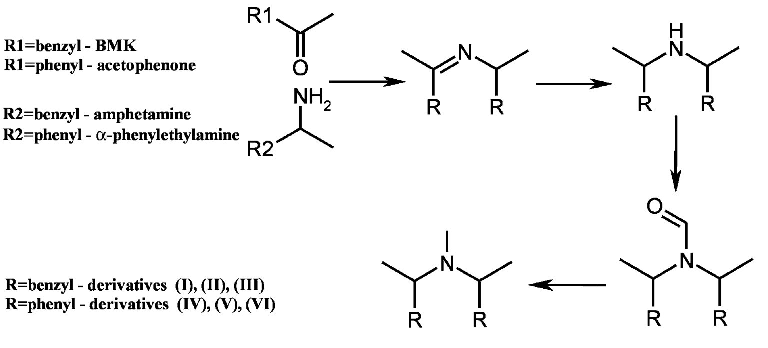

Fig. 2. The impurity pattern formation during Leuckart synthesis of amphetamine or α-phenylethylamine.

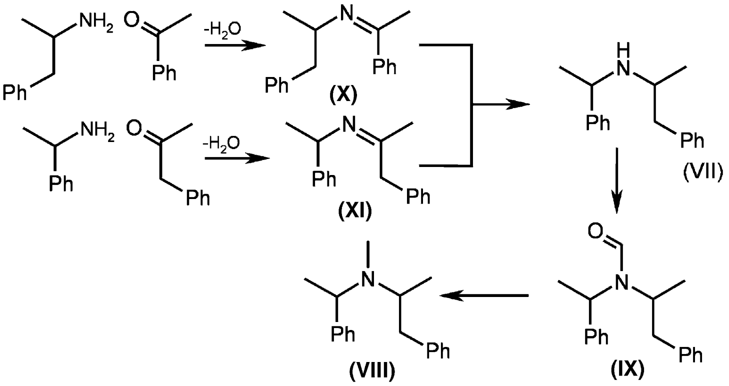

Fig. 3. The impurity pattern formation during Leuckart synthesis of mixture of amphetamine and α-phenylethylamine from the mixture of appropriate ketones.

formaldehyde solution, formic acid, sodium borohydride were obtained from Merck, Schuchard. The amphetamine base was prepared via Leuckart synthesis and vacuum distilled prior to use. Formamide (p.a. Merck) was further purified by passing through acidic alumina, basic alumina (both Merck), distilled and stored under argon over acidic alumina. Warning: when this special purification procedure was omitted, only *N*-methylation during *N*-formylation of the starting amine PIEA (**VII**) was observed.

All other solvents and reagents were analytical grade and were purchased from their representative manufacturers and used without further purification.

3.2. Synthesis

3.2.1. The Leuckart synthesis of mixture of amphetamine and α-phenylethylamine

The mixture of 20 g (0.17 mol) of acetophenone, 20 g (0.15 mol) of benzylmethylketone and 97.6 g of (1.6 mol) anhydrous ammonium formate was refluxed for 6 h. Next, 80 ml of concentrated HCl was added to the mixture and the resulting solution was heated under reflux. After 2 h, the mixture was cooled down, combined with 250 ml of water and made alkaline with NaOH pellets. The amines were separated, mixed with 650 ml of water, steam distilled until no more amines distilled with water. The distillate was extracted with chloroform (3 × 150 ml). The extracts were combined, dried over magnesium sulfate and evaporated yielding a colorless oil. Amines in the mixture were converted to their corresponding sulfates by treatment with 30% sulfuric acid in ethanol. Collected precipitate consisted of the mixture of 14.4 g (yield 52%) α-phenylethylamine sulfate and 15 g of (yield 55%) amphetamine sulfate (for quantitation methods: see Sections 3.3 and 3.4).

3.2.2. Preparation of α-methyl-N-(1-phenylethyl)-benzenethanamine (PIEA) (*VII*)

The racemic α-methyl-*N*-(1-phenylethyl)-benzenethanamine was synthesized from racemic α-phenylethylamine and benzylmethylketone using a method of Lindeke and coworkers [12].

Analytical data for compound **VII**: mp (hydrochloride) 227–229°C (reported 229–230 and 231–232°C for *S,S*-(−) and *R,R*-(+) form, respectively [11]; ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 0.97 (d, 3H, $J = 7$ Hz, CH_3 at C-1); 1.29 (d, 3H, $J = 7$ Hz, CH_3 at C-1′); 1.39 (s, 1H, disappeared with D_2O, NH); 2.50 (dd, 1H, $J_1 = 7.5$ Hz, $J_2 = 13$ Hz, H-2); 2.68 (dt, 1H, $J_1 = 7$ Hz, $J_2 = 7.5$ Hz, H-2); 2.86 (dd, 1H, $J_1 = 6$ Hz, $J_2 = 13$ Hz, H-2), 3.92 (q, 1H, $J = 7$ Hz, H-1′); 7.05–7.35 (m, 10H, H_{arom}); ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 21.16, 24.57, 42.59, 51.88, 55.31, 125.96, 126.53, 126.81, 128.20, 128.29, 128.42, 139.59, 146.21; IR (ν_{max}): 3026, 2965, 2924, 1602, 1493, 1451, 1372, 1206, 1130, 1027, 760, 701 cm^{-1}.

3.2.3. Preparation of α-N-dimethyl-N-(1-phenylethyl)-benzenethanamine (*VIII*)

A sample of 5 g (20.9 mmol) of α-methyl-*N*-(1-phenylethyl)-benzenethanamine (**VII**), 28 g (0.48 mol) of 80% formic acid and 20.8 g (0.25 mol) of 36% formaldehyde were combined and resulting solution was heated under reflux for 10 h. The cooled mixture was acidified with 20 ml of concentrated HCl and excess of formic acid and formaldehyde was removed under vacuum. The cooled mixture was poured into 250 ml of water and the mixture was made alkaline with 40% NaOH. Next, the product of reaction was extracted with dichloromethane (3 × 100 ml). Extracts were combined, dried and evaporated under vacuum to give yellow oil. The crude amine **VIII** was distilled under vacuum to give 3.92 g (74%) of colorless oil, bp 117–125°C (0.4 mmHg). All attempts to convert base into a solid hydrochloride salt failed. However, after storage in refrigerator, the part of the oil solidified. Solid material was separated and washed with cold cyclohexane to provide 1.15 g of soft, colorless material with mp below 15°C.

Spectral data for compound **VIII**: for major isomer ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 0.90 (d, 3H, $J = 6$ Hz, CH_3 at C-1); 1.31 (d, 3H, $J = 7$ Hz, CH_3 at C-1′); 2.24 (s, 3H, N–CH_3); 2.37 (dd, 1H, $J_1 = 9$ Hz, $J_2 = 13$ Hz, H-2); 2.92 (dd, 1H, $J_1 = 5$ Hz, $J_2 = 12.5$ Hz, H-2); 3.04–3.09 (m, 1H, H-1); 3.68 (q, 1H, $J = 6.5$ Hz, H-1′); 7.01–7.32 (m, 10H, H_{arom}) ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 21.96, 30.17, 32.35, 38.11, 55.78, 62.10, 125.57, 126.66, 127.24, 128.07, 128.31, 129.19, 141.10, 146.50; for minor isomer: ^1H NMR (500 MHz, $CDCl_3$, δ, ppm): 0.86 (d, 3H, $J = 6.5$ Hz, CH_3 at C-1); 1.31 (d, 3H, $J = 7$ Hz, CH_3 at C-1′); 2.24 (s, 3H, N–CH_3); 2.43 (dd, 1H, $J_1 = 8.5$ Hz, $J_2 = 13$ Hz, H-2); 2.82 (dd, 1H, $J_1 = 6$ Hz, $J_2 = 13.5$ Hz, H-2); 2.95–3.00 (m, 1H, H-1); 3.62 (q, 1H, $J = 7$ Hz, H-1′); 7.01–7.32 (m, 10H, H_{arom}); ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 22.01, 26.90, 31.84, 40.59, 55.92, 61.98, 125.58, 126.50, 127.22, 127.98, 128.16, 129.30, 140.89, 146.30; IR (ν_{max}): 3026, 2971, 2785, 1602, 1492, 1452, 1369, 1230, 1073, 1028, 740, 700 cm^{-1}.

3.2.4. Preparation of α-methyl-N-formyl-N-(1-phenylethyl)-benzenethanamine (**IX**)

A sample of 530 mg amine (**VII**) hydrochloride (1.83 mmol) was dissolved in 30 ml of CH_2Cl_2 and washed with 30 ml 10% NaOH. A dichloromethane solution of a free base thus obtained was dried over K_2CO_3 and evaporated. To the residue 20 ml of formamide was added and the mixture was refluxed under argon for 14 h. The resulting dark solution was cooled to room temperature and poured onto 50 ml of sat. NaCl solution. The water layer was extracted with 3 × 10 ml of toluene. Organic extracts were combined, washed with water and dried. After evaporation of the solvent, the residue was chromatographed over silica gel (230–400 mesh, Merck) using 5% ethylacetate in cyclohexane. The final *N*-formyl derivative was obtained in 48% yield.

Spectral data for compound **IX** (stable conformers present): ^1H NMR (200 MHz, $CDCl_3$, δ, ppm): 1.25 and 1.30 (2d, 3H each, $J = 7$ Hz, CH_3 at C-1′); 1.54 and 1.57 (2d, 3H each, $J = 7$ Hz, CH_3 at C-1); 2.48 (m, 2H, H-2); 2.64 (dd, 1H, $J_1 = 5$ Hz, $J_2 = 13$ Hz, H-2); 3.0 (dd, 1H, $J_1 = 9$ Hz, $J_2 = 13$ Hz, H-2); 3.28 and 3.47 (2m, 1H each, H-1); 4.62 and 5.94 (2q, 1H each, $J = 7$ Hz, H-1′); 6.58–7.44 (m, 20H, H_{arom}); 8.40 and 8.42 (2br, s, 1H each, C–H at CHO); ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 16.44, 17.31, 19.91, 21.75, 40.47, 44.72, 49.82, 51.20, 53.55, 57.08, 126.14, 126.52, 127.24, 127.82, 127.95, 128.12, 128.28, 128.44, 128.54, 128.92, 129.12, 138.15, 139.44, 139.82, 140.35, 161.53, 162.52); IR (ν_{max}): 3026, 2976, 2937, 1713, 1668, 1650, 1636, 1496, 1452, 1378, 1217, 1203, 971, 748, 702 cm^{-1}.

3.2.5. Preparation of N,N-di-(1-phenylethyl)-methylamine (V)

Di-(1-phenylethyl)amine (**IV**) was synthesized from acetophenone by Borch et al. [13] method. During this synthesis also α-phenylethylamine was formed as a by-product.

A resulting mixture of 1.9 g (10 mmol) α-phenylethylamine and 4.2 g (18.7 mmol) of di-(1-phenylethyl)amine (**IV**) was refluxed with 43 g (0.746 mol) of 80% formic acid and 28 g (0.336 mol) of 36% formaldehyde solution for 8 h.

The reaction mixture was allowed to cool to room temperature, and next treated with 36% HCl (20 ml) and the solvents were removed under vacuum. The residue was diluted with water (200 ml) and made alkaline with 40% NaOH. The solution was extracted with dichloromethane (3 × 100 ml), combined extracts were dried ($MgSO_4$) and solvents were evaporated under vacuum. *N*,*N*-dimethyl-α-phenylethylamine was separated from *N*,*N*-di-(1-phenylethyl)methylamine (**V**) by fractional distillation under vacuum using apparatus equipped with short Vigreoux column. *N*,*N*-di-(1-phenylethyl)methylamine distilled second at 155–161°C (3 mmHg), yielding 1.56 g (35%) of **V** as a colorless oil. All our attempts to convert base into solid hydrochloride salt failed.

Spectral data for compound **IX**: mixture of diastereomers (∼1:1): ^1H NMR (200 MHz, $CDCl_3$, δ, ppm): 1.29 and 1.33 (2d, 3H each, $J = 7$ Hz and $J = 6.5$ Hz); 2.00 and 2.10 (2s, 3H each, 2 × N−CH_3); 3.71–3.87 (m, 2 × 1H, −$C\underline{H}$); 7.24–7.39 (m, 2 × 10 H_{arom}); ^{13}C NMR (50 MHz, $CDCl_3$, δ, ppm): 16.01, 18.62, 32.34, 32.88, 55.98, 59.15, 126.55, 126.58, 127.44, 127.75, 128.08, 128.15, 144.38, 145.43; IR (ν_{max}): 3028, 2973, 2786, 1601, 1492, 1451, 1370, 1209, 1072, 1029, 761, 733, 700 cm^{-1}.

3.3. Sample preparation

Amine bases **VII**, **VIII**, **V** and *N*-formyl derivative (**IX**) were dissolved in ethanol (1–2 mg/ml). Samples taken from reaction mixtures were diluted with water, made alkaline with 5% Na_2CO_3 solution and extracted with chloroform.

Extraction of impurities [14]: a sample of 200 mg of α-phenylethylamine sulfate and amphetamine sulfate was dissolved in 2 ml of 0.1 M phosphate buffer (pH 7.0). The solution was extracted by vigorous shaking with 200 μl of *n*-octane containing diphenylamine (35 μg/ml) as an internal standard. After separation, 2 μl of the *n*-octane was injected into the GC–MS.

N-propylamphetamine hydrochloride as an internal standard in GC analysis was used when the samples were analyzed for contents of α-phenylethylamine and amphetamine sulfates.

3.4. Instruments and chromatographic conditions

GC–MS was performed on the HP 5973 mass selective detector interfaced with a HP 6890 series GC. The mass spectrometer was operated in the electron impact mode at 70 eV. The source temperature was maintained at 230°C. The samples (1–2 μl) were introduced manually into the GC–MS system equipped with SPB-1 25 m × 0.25 μm i.d. × 0.25 μm capillary column. The column temperature was held at 100°C for 1 min and next gradually increased to 290°C at rate of 10°C/min. The injector port was 250°C.

Helium was used as a carrier gas at 0.6 ml/min. The gas chromatograph was operated in the split mode with split ratio of 30:1. During analysis of impurity extracts, GC was operated in the splitless mode.

Quantitative analysis of mixture of α-phenylethylamine and amphetamine sulfates was performed on HP 5890 series II chromatograph equipped with flame ionization detector. Split ratio 100:1, injector temperature 250°C and detector temperature 280°C were used. The oven was operated in isothermal mode at 120°C. A SE-30 capillary column (12 m × 0.32 mm i.d. × 0.5 μm capillary column) was used.

NMR spectra were recorded on a Varian Unity Plus spectrometer operating at 500 or 200 MHz for ^{1}H NMR and at 125 or 50 MHz for ^{13}C NMR, respectively.

Infrared spectra were obtained using Brucker FT-IR 113v equipped with IR microscope. Spectra of amine bases were prepared working in a reflection mode.

4. Results

4.1. Synthesis

As shown on the Fig. 3, both imine compounds **X** and **XI** are condensation products of amphetamine with acetophenone and α-phenylethylamine with benzylmethylketone. Regardless the double bond position these intermediate imines were reduced with $NaBH_4$ to afford the same amine **VII**. This approach was employed in our study, but we found that imine **X** is formed in a far less amount. GC–MS data clearly show that both imines can be readily reduced to give PIEA (**VII**). Analytical sample was obtained after column chromatography, precipitation as a hydrochloride salt, recrystalization from 2-propanol and recovery as a free base. The tertiary amines *N*-methyl PIEA and *N*-methyl DEA were analyzed as free bases.

Table 1
Retention indices of synthesized compounds

Compounds[a]	Retention index
PIEA	1740, 1770
N-methyl PIEA	1847, 1855
N-formyl PIEA	2151, 2169
N-methyl DEA	1781, 1792

[a] Both diasteroisomers.

4.2. Gas chromatography

All four synthesized product **V**, **VII**, **VIII** and **IX** posses two stereogenic centers, and therefore, they exist in four enantiomeric forms. The enantiomers *RR*/*SS* are diasteroisomeric with respect to the *RS*/*SR* pair. Diasteroisomeric forms possess different chemical and physical properties. For this reason, each compound appeared to give two baseline resolved peaks with similar mass spectra. It should be noted that PIEA after recrystalization showed diasteroisomeric purity with ratio about 92/8. Also investigation by GC analysis of the diasteroisomeric composition *N*-methyl PIEA, which was separated as a solid base showed diasteroisomeric purity about 93/7. The Kovat's indices for synthesized compounds are presented in Table 1.

4.3. Mass spectra

Mass spectra resulting from the GC–MS analysis of intermediary imines **X** and **XI** and derivatives **V**, **VII**, **VIII** and **IX** are presented on Figs. 4–9. Inserts in the figures of

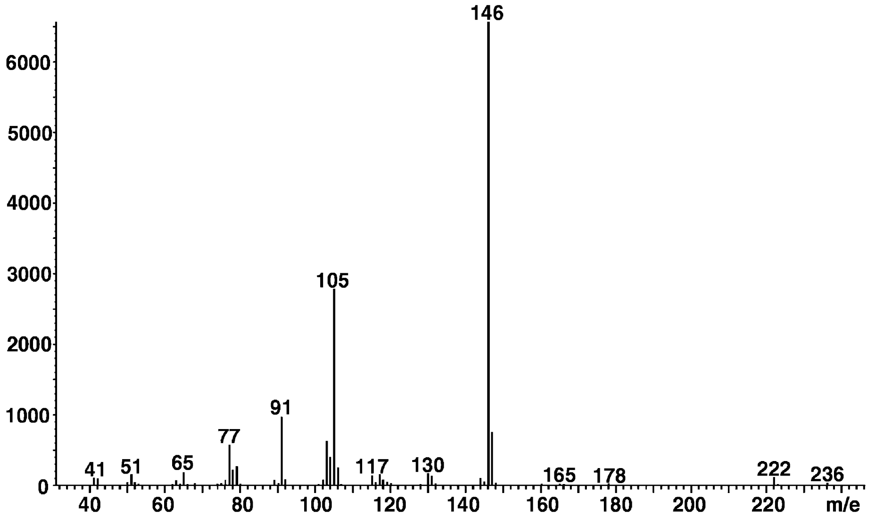

Fig. 4. The mass spectra of imine **X**.

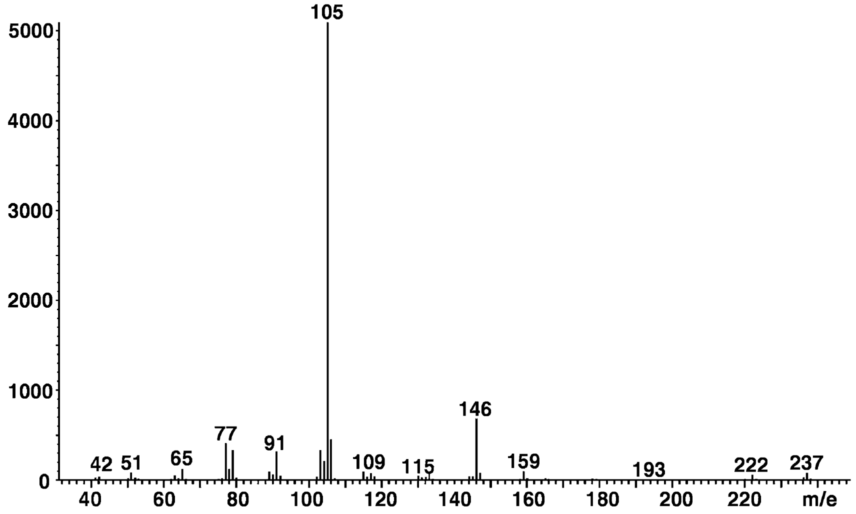

Fig. 5. The mass spectra of imine **XI**.

amine spectra describe a major fragments originated from the fragmentation process. Molecular ions or ions corresponding to $M - 1$ fragments were detected in all the spectra of the synthesized compounds.

The β-fission process is expected to produce fragment *m/e* 148 for **VII**, fragment *m/e* 162 for **VIII** and fragment *m/e* 176 for **IX** [15,16]. The predominant abundance of ion *m/e* 105 in the case of compounds **VII**, **VIII** and **IX** could be explained by C–N cleavage of the ion derived from the β-fission process and charge transfer to the phenylalkyl moiety [16,17]. The α,β-cleavage with hydrogen rearrangement produces *m/e* 44 fragment for structure **VII** and *m/e* 58 fragment for structure **VIII** [15,18]. In the case of tertiary amine **V** ion *m/e* 224 originates from methyl loss from the parent ion *m/e* 239. Fragment *m/e* 120 is produced probably during C–N cleavage of the ion 224 with proton rearrangement to nitrogen atom.

4.4. Fourier transform infrared spectroscopy

The FT-IR spectra of amino compounds were taken for free bases. The apparent similarity of the 1600–900 cm^{-1} region results from spectra are dominated by the intense amino, aromatic, and methyl functional group vibrations. The tertiary amine are readily differentiated from secondary amine by a characteristic absorbance at 2786 cm^{-1}. The two moderate strong absorption band at 760 and 700 cm^{-1} are indicative of a monosubstituted aromatic ring. Relatively

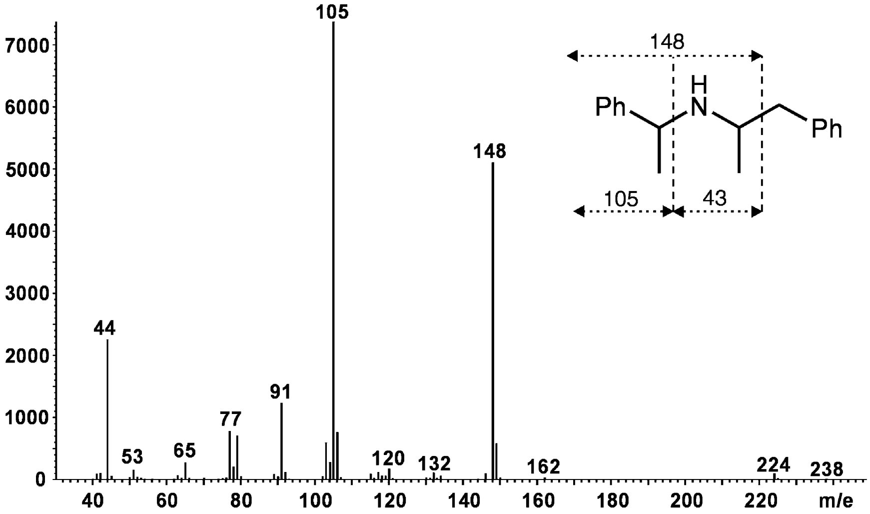

Fig. 6. The mass spectra of α-methyl-*N*-(1-phenylethyl)-benzenethanamine (**VII**).

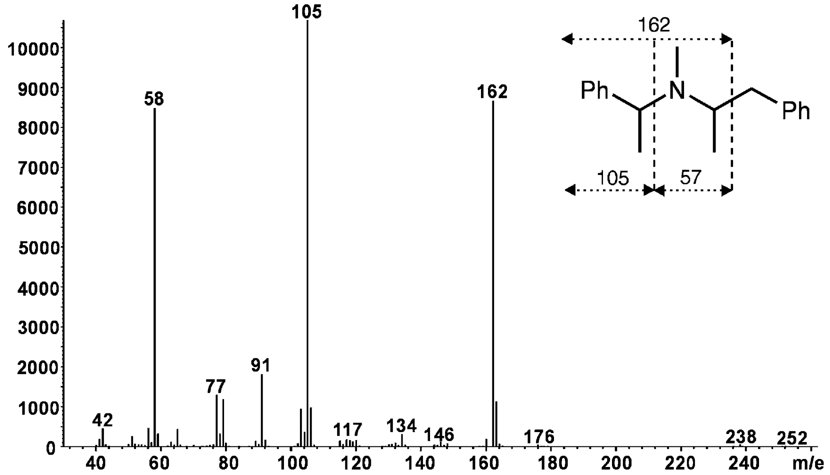

Fig. 7. The mass spectra of α-*N*-dimethyl-*N*-(1-phenylethyl)-benzenethanamine (**VIII**).

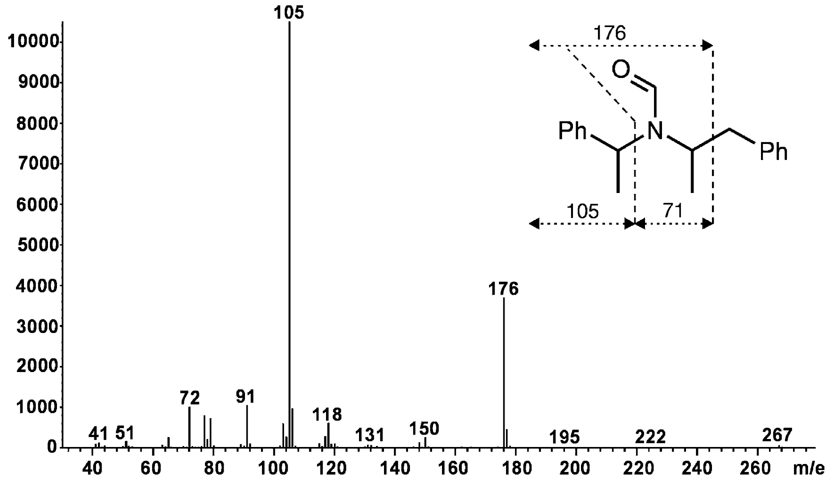

Fig. 8. The mass spectra of α-methyl-*N*-formyl-*N*-(1-phenylethyl)-benzenethanamine (**IX**).

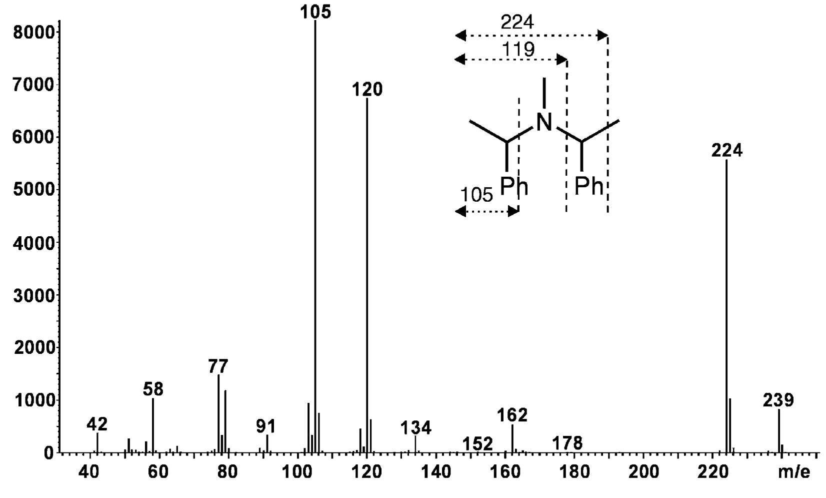

Fig. 9. The mass spectra of *N*,*N*-di-(1-phenylethyl)methylamine (**V**).

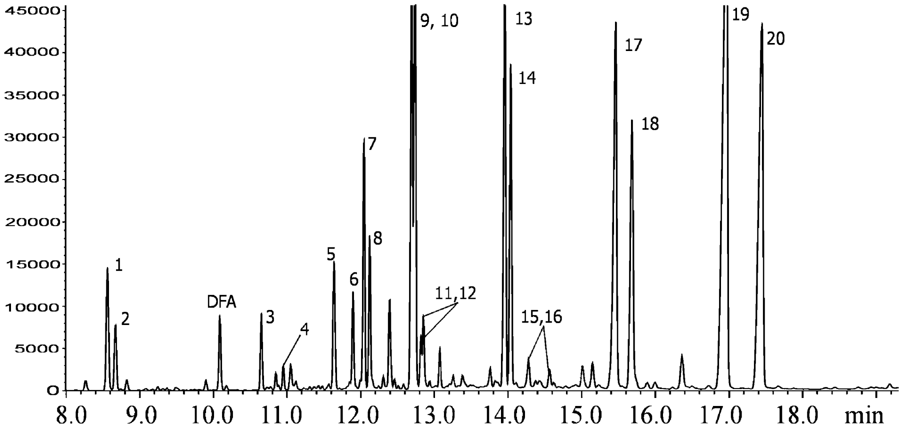

Fig. 10. GC–MS analysis of impurity extract of mixture of amphetamine and α-phenylethylamine produced from the mixture of appopriate ketones.

Table 2
Retention data of compounds identified in examined extract

Peak numbers	Retention times[a] (min)	Compounds	Molecular weight
1	8.56	4-Phenylpyrimidine[b]	156
2	8.67	4-Methyl-5-phenylpyrimidine[c]	170
3, 4	10.65, 10.95	DEA (**IV**)[b]	225
5, 6	11.64, 11.89	PIEA (**VII**)[d]	239
7, 8	12.04, 12.12	*N*-methyl DEA (**V**)[b]	239
9, 10	12.64, 12.69	*N*-methyl PIEA (**VIII**)[d]	253
11, 12	12.84, 12.87	DPEA (**I**)[c]	253
13, 14	13.96, 14.04	*N*-methyl DPEA (**II**)[c]	267
15, 16	14.28, 14.57	*N*-formyl DEA (**VI**)[b]	253
17, 18	15.46, 15.68	*N*-formyl PIEA (**IX**)[d]	267
19, 20	16.96, 17.45	*N*-formyl DPEA (**III**)[c]	281

[a] Retention data of diasteroisomeric pairs (except 1 and 2).

[b] Impurities in α-phenylethylamine synthesized by the Leuckart method.

[c] Impurities in amphetamine synthesized by the Leuckart method.

[d] Impurities in mixture of α-phenylethylamine and amphetamine synthesized simultaneously by the Leuckart method from the mixture of appopriate ketones.

complicated character of the spectrum of **IX**, especially at the carbonyl absorption region, may be connected with the presence of stable conformers due to a restricted rotation over the amide bond. This effect is clearly seen in both ^{1}H and ^{13}C NMR spectra of **IX**.

4.5. Amphetamine and α-phenylethylamine synthesis

During Leuckart synthesis from a mixture of acetophenone and BMK, was converted into the corresponding amines. Both amphetamine and α-phenylethylamine were obtained in a good yields. For the isolation of those ''Leuckart impurities'' we were interested in, we employed an extraction procedure routinely used in our laboratory for classification of seized samples. Thus, the impurities from the mixture were concentrated and analyzed by GC–MS. Chromatographic data, as well as mass spectrometric data of extracted impurities were compared to those, obtained for synthesized reference compounds **V**, **VII**, **VIII** and **IX**. The mass chromatogram of extracted impurities is presented in Fig. 10. The retention data and mass spectra of impurities matched perfectly with those of synthesized compounds. The identified compounds and their retention times are presented in Table 2.

5. Summary

We found that mixture of α-phenylethylamine and amphetamine can be easily obtained directly from the mixture of acetophenone and benzylmethylketone. With the help of knowledge of the cross-reaction possibilities, the structures of specific impurities were predicted. Next, these impurities were found in final product and their identity was confirmed by comparison with synthesized reference compounds.

We believe that data presented here will be helpful in analysis of amphetamine samples containing α-phenylethylamine. In this respect the detection of described impurities presents a good proof that the amphetamine/α-phenylethylamine mixture was produced by the Leuckart synthesis from the mixture of corresponding ketones. Moreover, the peak area ratios of these impurities can give additional information that will be useful for comparative purposes. The knowledge of described impurities is also essential for another reasons. One important reason is the possible additional toxic effect caused by the impurities.

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