Microwave-Assisted Reductive Amination under Heterogeneous Catalysis for the Synthesis of β-Adrenergic Agonist and Related Structures

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Supplementary Information

As mentioned in the main text, the reaction crudes were firstly analysed via GC-MS after derivatisation with BSTFA to convert the hydroxyls groups into silyl ethers. The procedure was performed in pyridine with 5 eq. of BSTFA leaving the samples to stir at 60 °C for 1 h in an oil bath.

Firstly, we injected the standard of the reagents (raspberry ketone and octopamine) and the product (ractopamine) to assess their fragmentation and retention time.

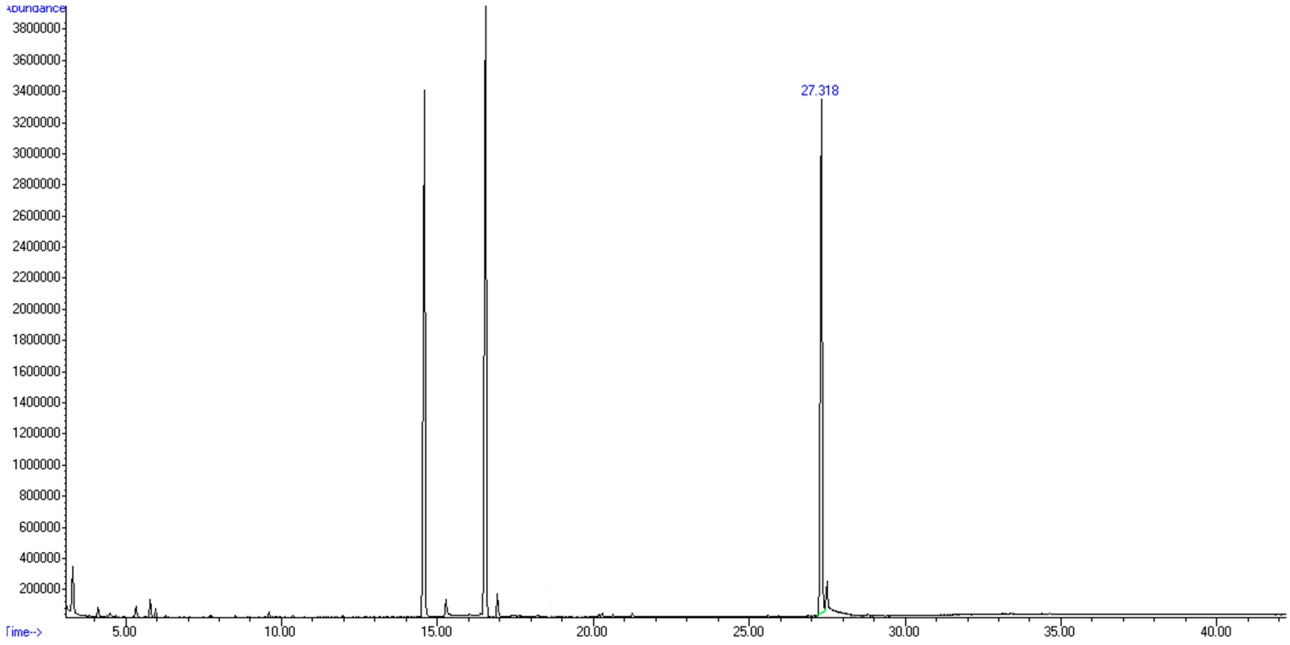

Figure S1: chromatogram of the reaction standards. The peaks correspond to raspberry ketone (14.6'), octopamine (16.5'), ractopamine (27.3').

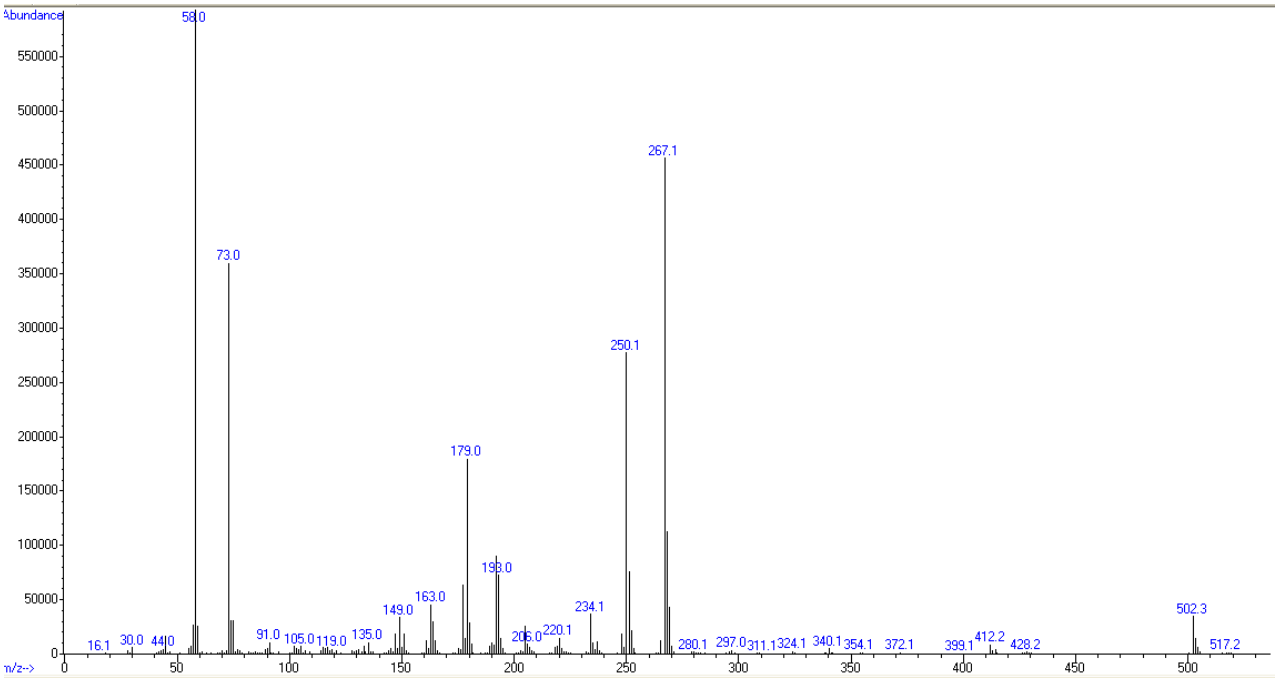

Figure S2: fragmentation pattern of the standard ractopamine.

The expected mass for the derivatised ractopamine should be of 563 m/z, however 517 m/z was observed both in the standard and in the crudes. This might be due to the loss of methyl groups from the four silyl ethers.

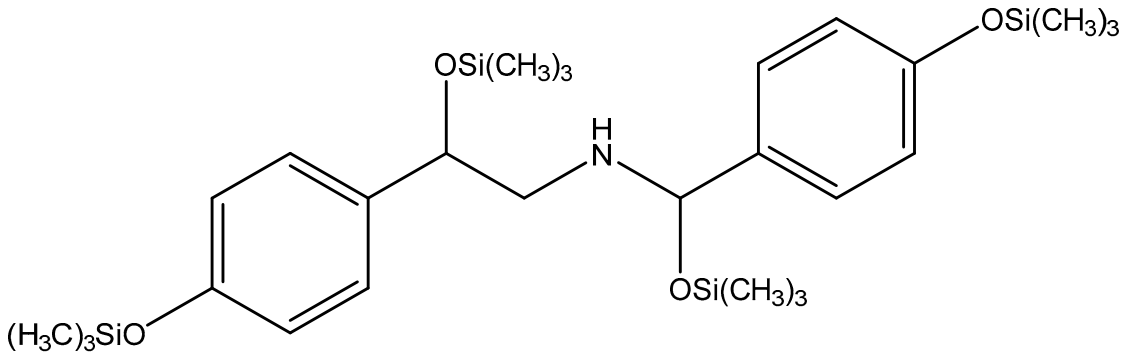

Figure S3: structure of the derivatised ractopamine (563 m/z).

Here follow the chromatograms for the reaction products in the optimized conditions, leading to ractopamine.

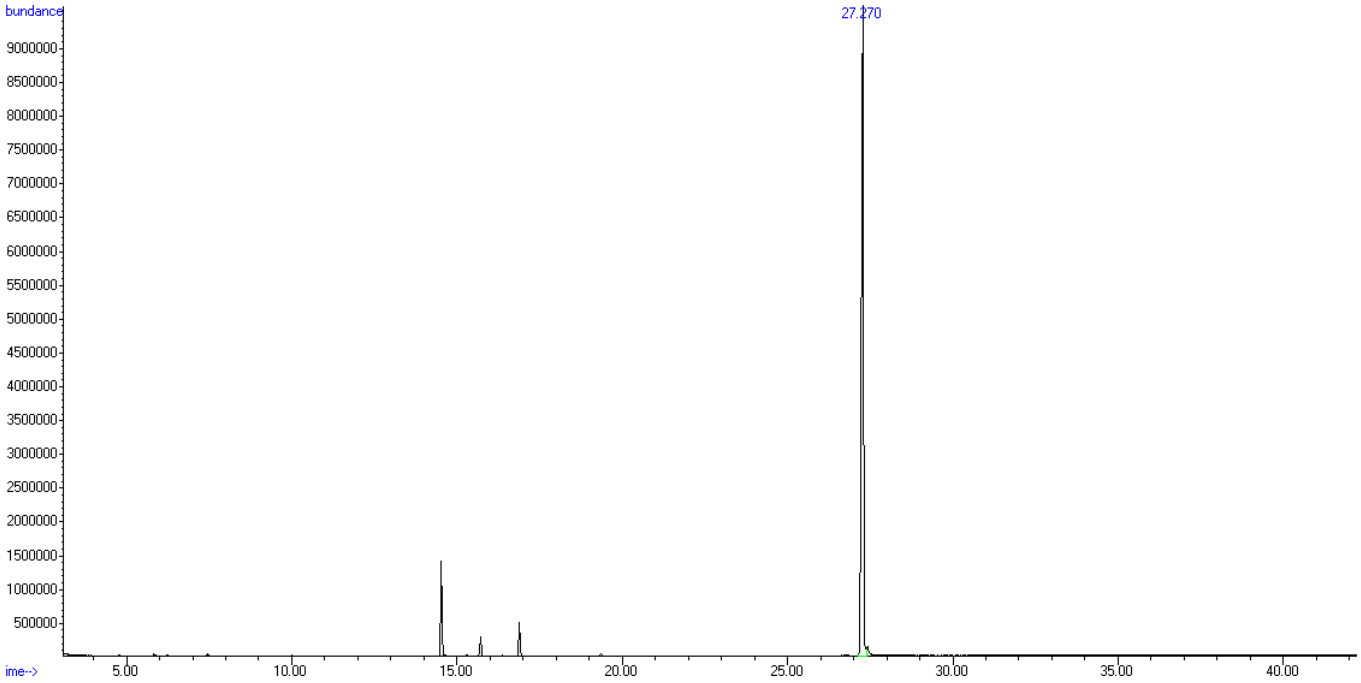

Figure S4: reaction between octopamine and raspberry ketone over Pt/C 5 wt.%, 50 °C, 3 h, 10 bar H_2.

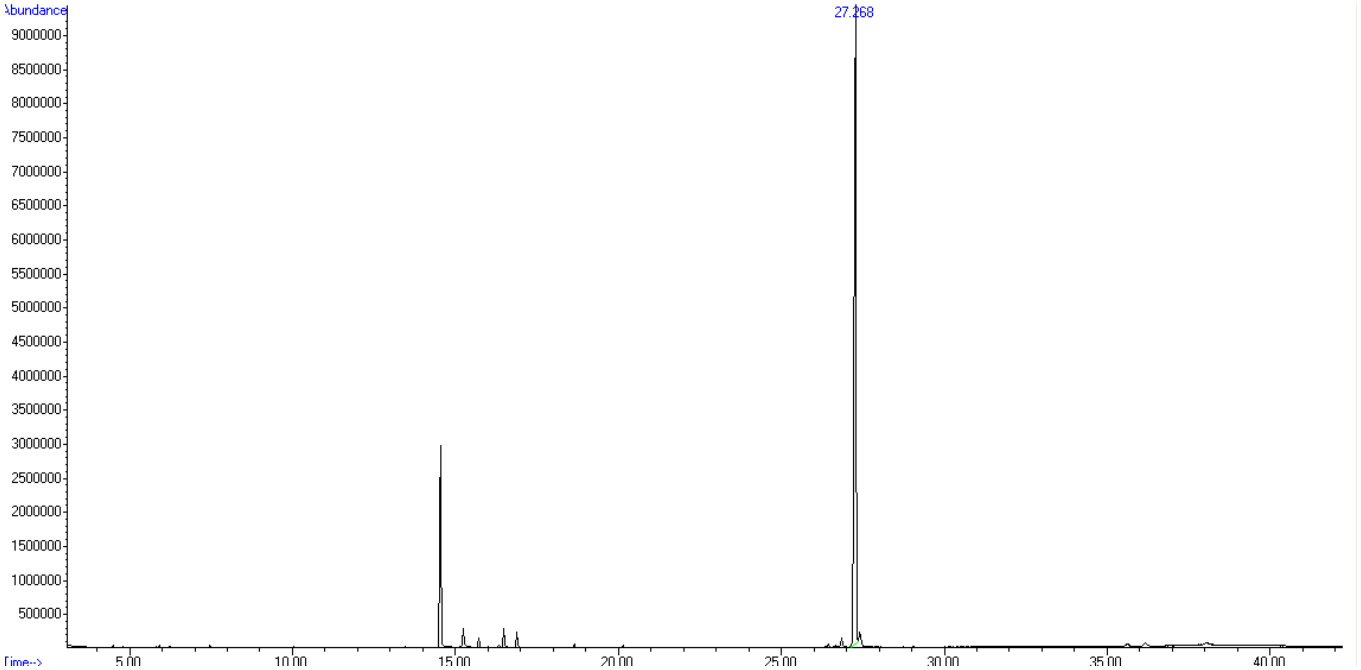

Figure S5: reaction between octopamine and raspberry ketone over Rh/C 5 wt.%, 50 °C, 3 h, 10 bar H_2.

The fragmentation of the synthetized ractopamine corresponds to the standard (figure S6).

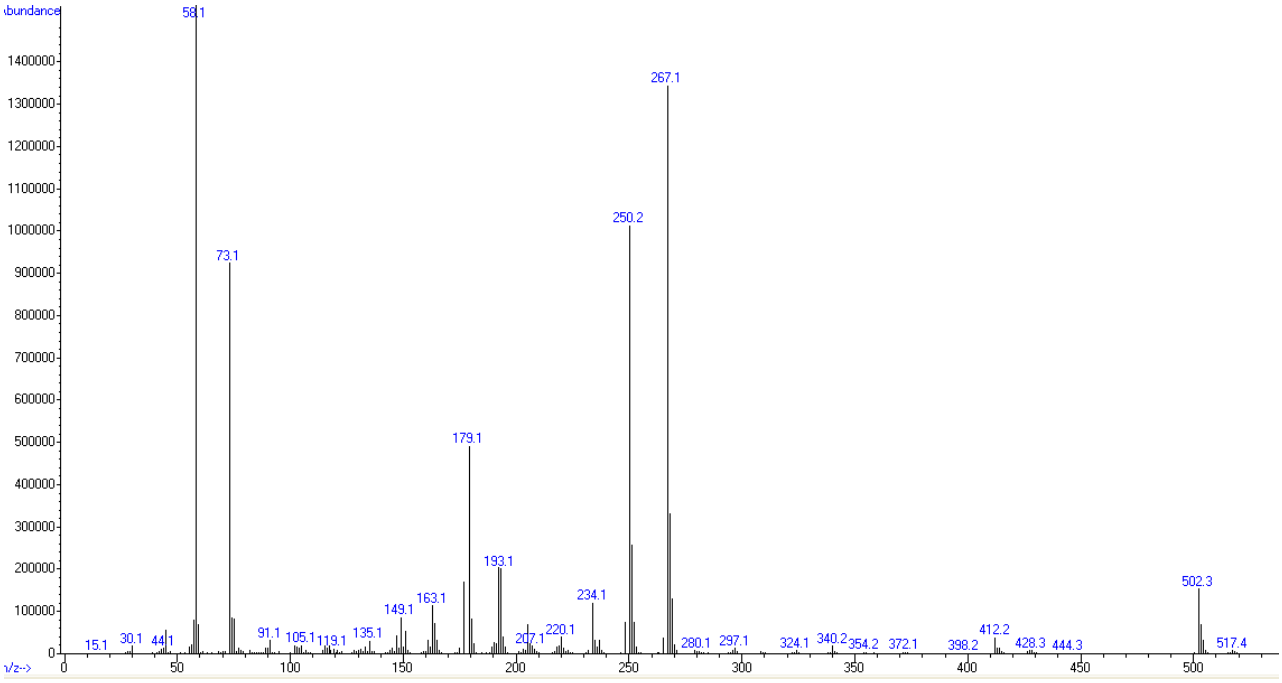

Figure S6: fragmentation pattern of the synthetised ractopamine.

Here follows the chromatogram of the reaction over Ru/C 5 wt.% in the same conditions. As shown (figure S7 and S8) both the retention time and the observed m/z (515 m/z) lead to the assumption that the imine was obtained instead.

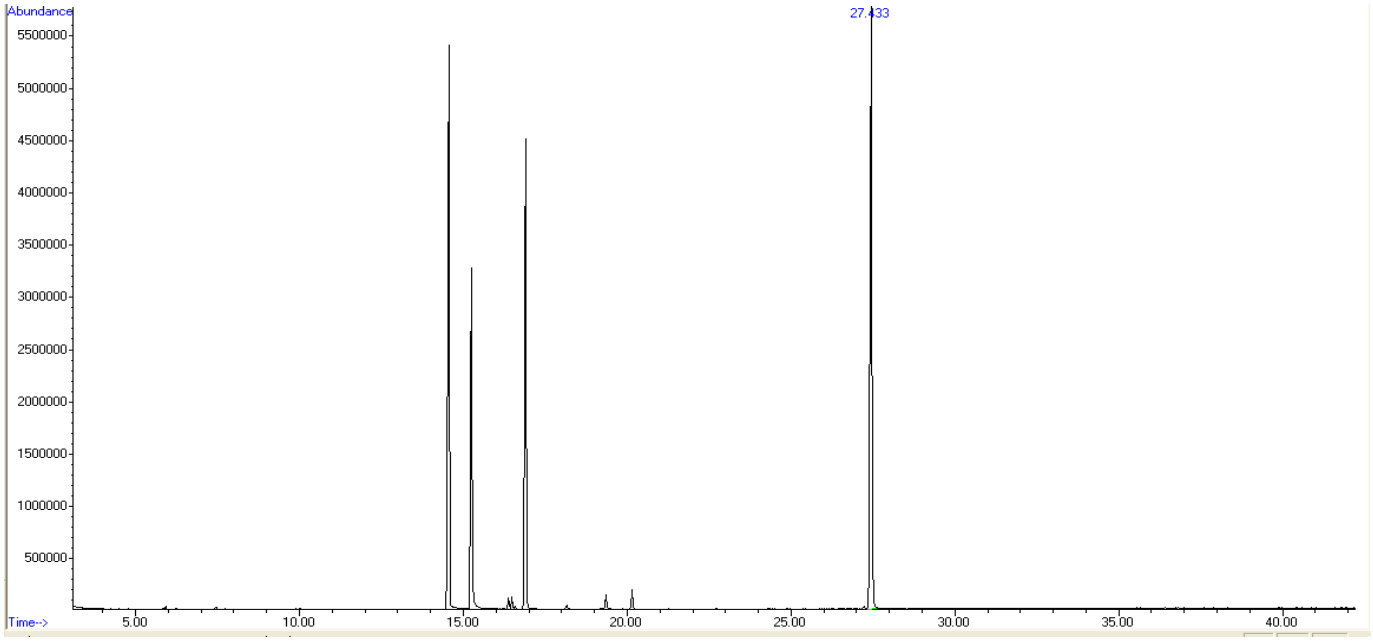

Figure S7: chromatogram for the reaction between octopamine and raspberry ketone over Ru/C 5 wt.%, 50 °C, 3 h, 10 bar H_2. As shown, the retention time of the main product shifts from 27.3' to 27.4'.

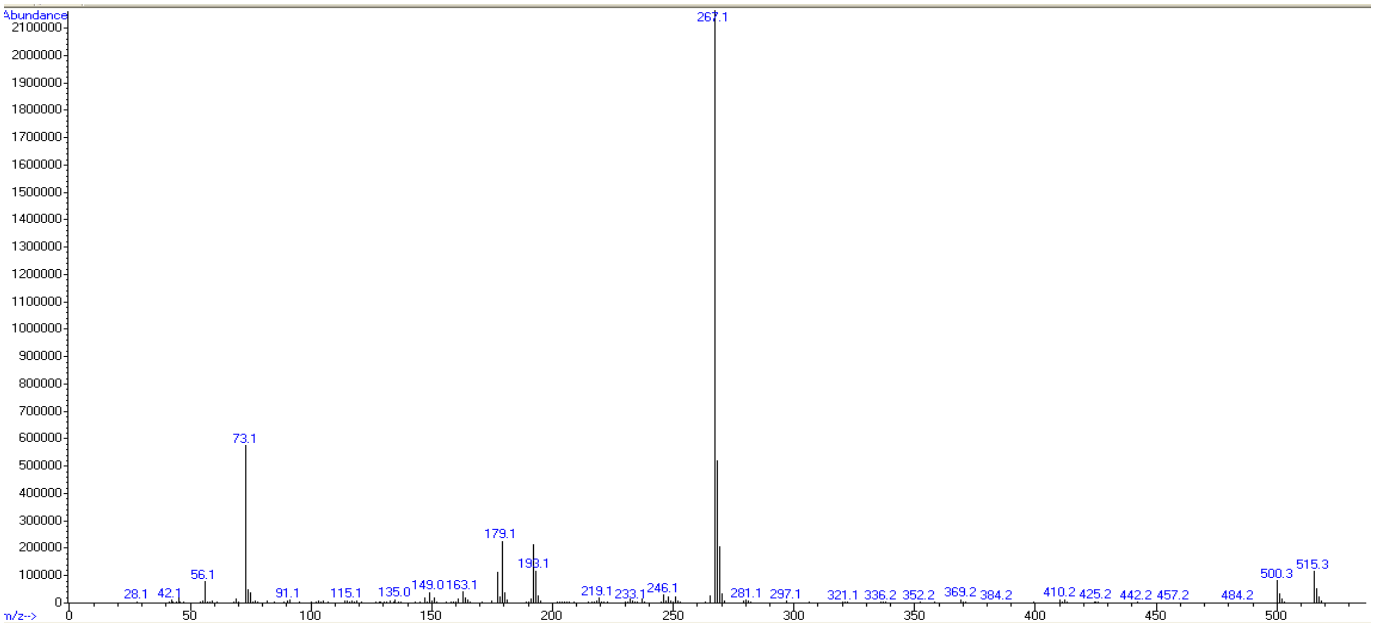

Figure S8: fragmentation pattern of the main product from the Ru/C reaction.

The reductive amination between octopamine and other ketones was also explored. Here follows the result of the reaction between octopamine and acetophenone, run over Pt/C 5 wt.% with 10 bar of H_2. Despite it being the best result for acetophenone, selectivity is still low, and conversion is incomplete. Nonetheless, the product was observed as reported below (figure S10 and S11).

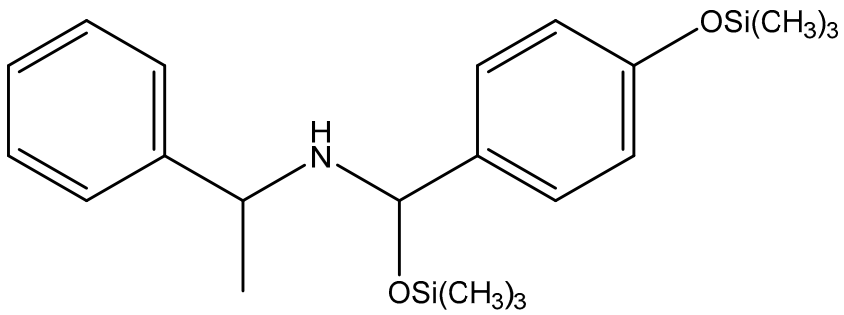

Figure S9: structure of the wanted product from acetophenone (m/z 387).

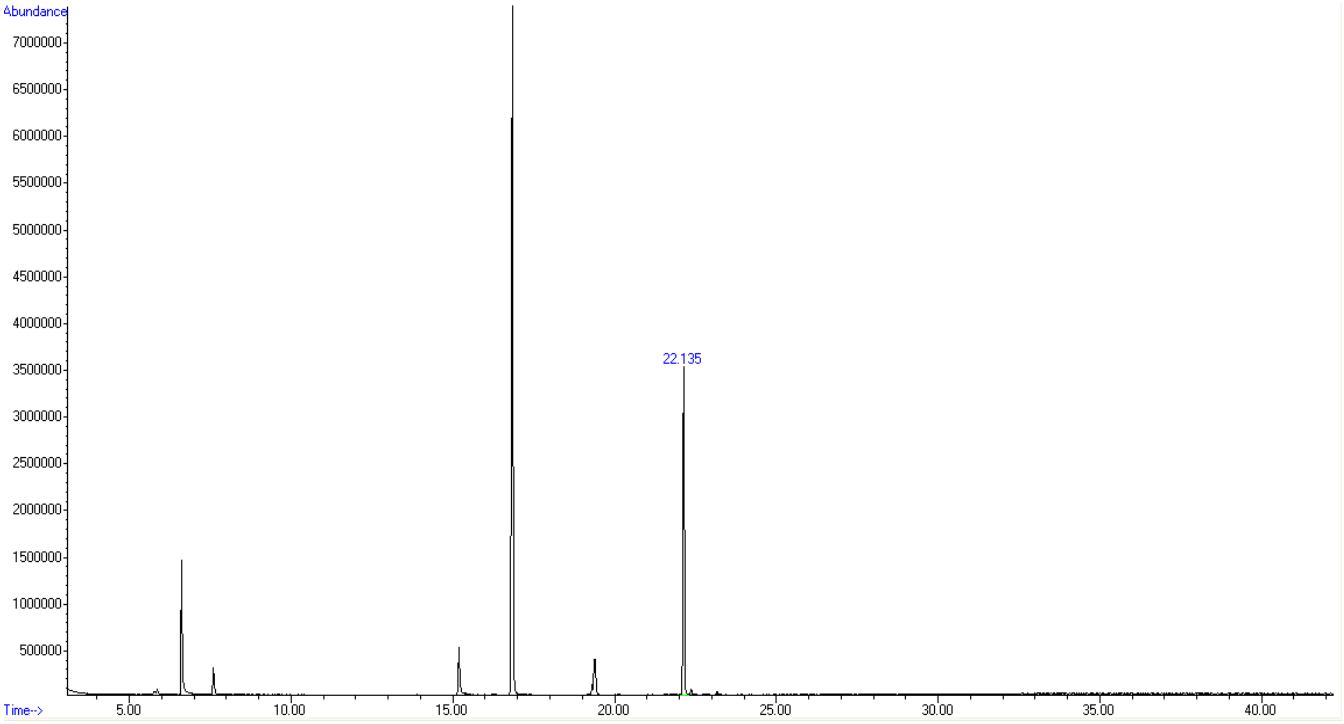

Figure S10: chromatogram for the reaction between octopamine and raspberry ketone over Pt/C 5 wt.%, 50 °C, 3 h, 10 bar H_2.

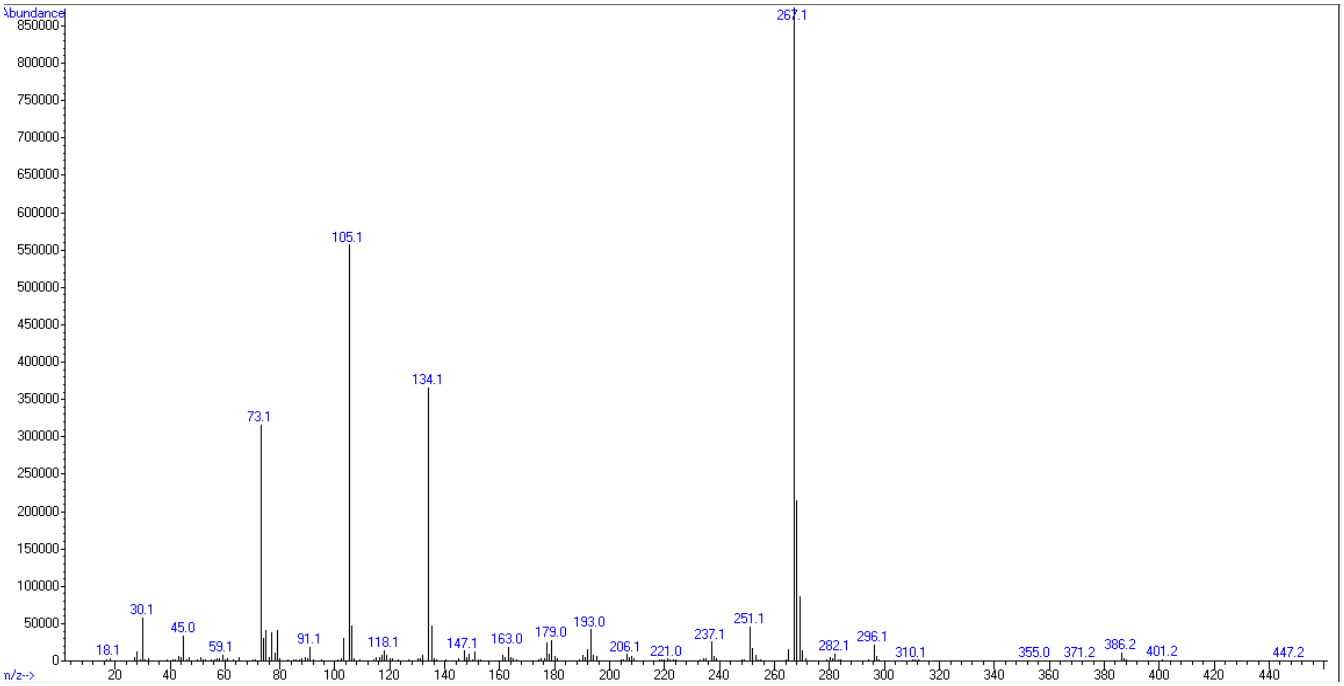

Figure S11: fragmentation pattern of the acetophenone reductive animation product.

Here follow the chromatograms of the reactions run over both Pt/C and Rh/C 5 wt.% starting from octopamine and cyclohexanone, which were both successful.

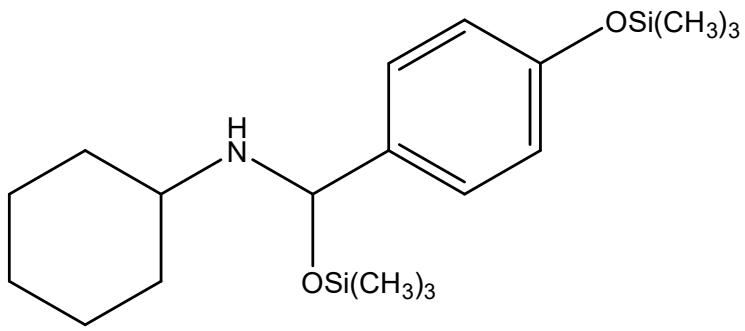

Figure S12: structure of the desired product from cyclohexanone (m/z 365).

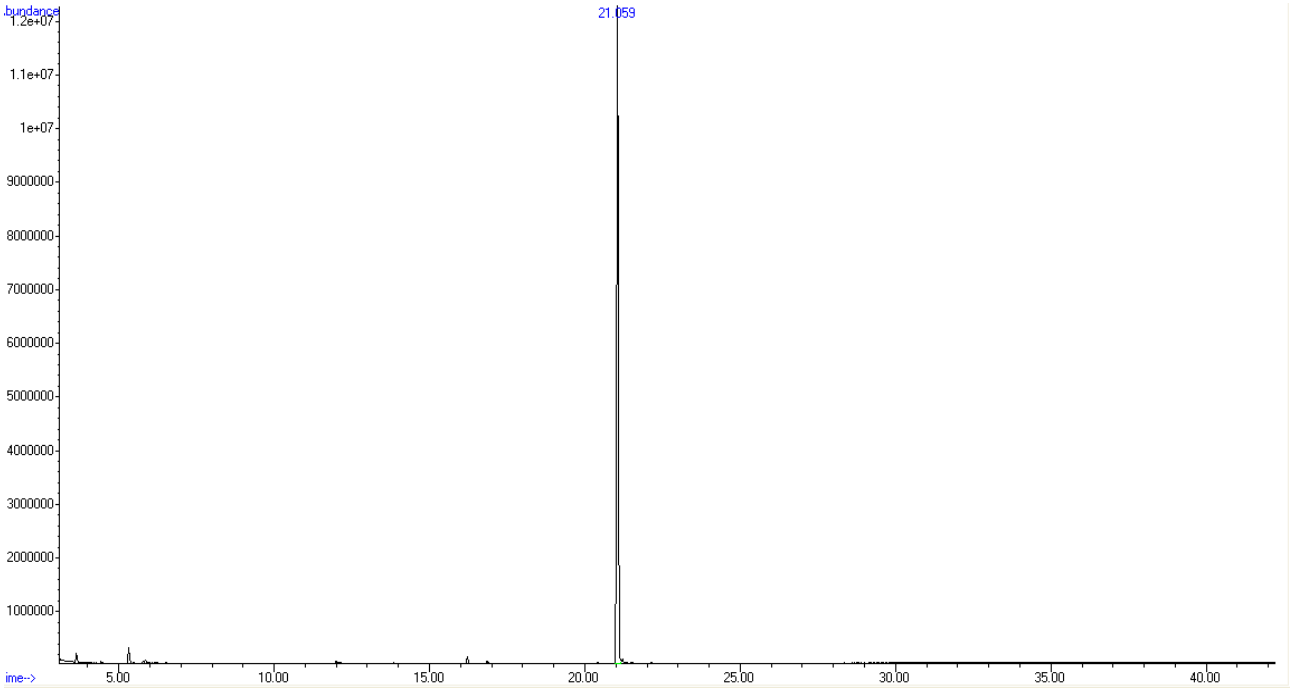

Figure 13: chromatogram for the reaction between octopamine and cyclohexanone over Pt/C 5 wt.%, 50 °C, 3 h, 5 bar H_2.

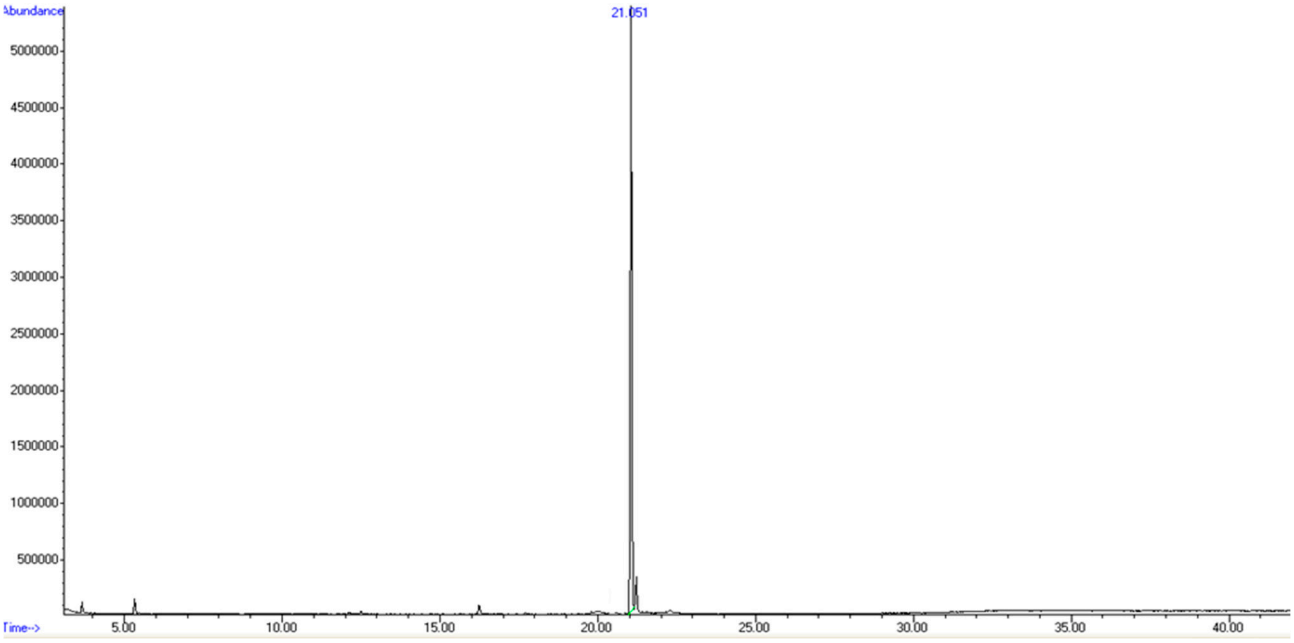

Figure S14: chromatogram for the reaction between octopamine and cyclohexanone over Rh/C 5 wt.%, 50 °C, 3 h, 5 bar H_2.

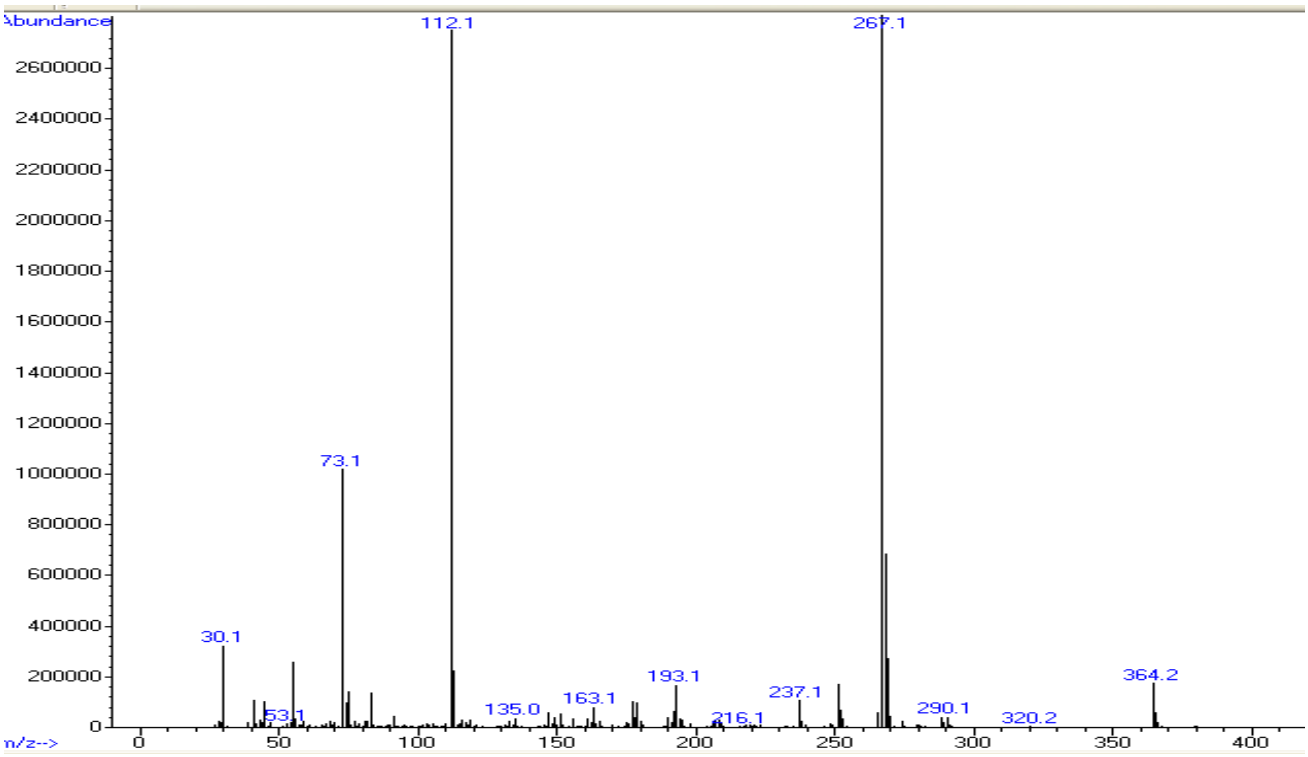

Figure S15: fragmentation pattern of the cyclohexanone reductive animation product.

At last, we report the chromatograms of the reductive amination between octopamine and 2-butanone run over both Pt/C and Rh/C 5 wt.%.

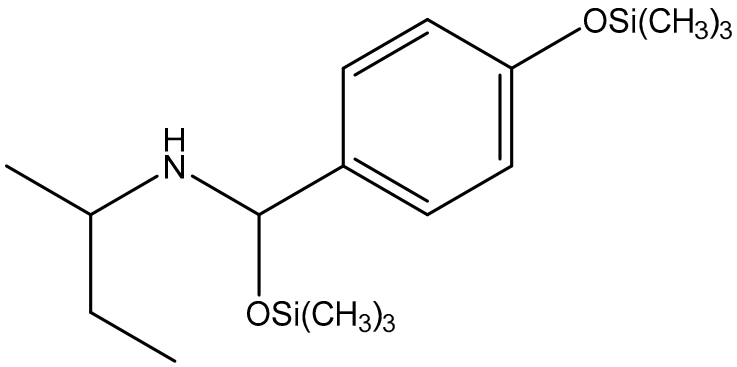

Figure S16: structure of the desired product from 2-butanone (m/z 339).

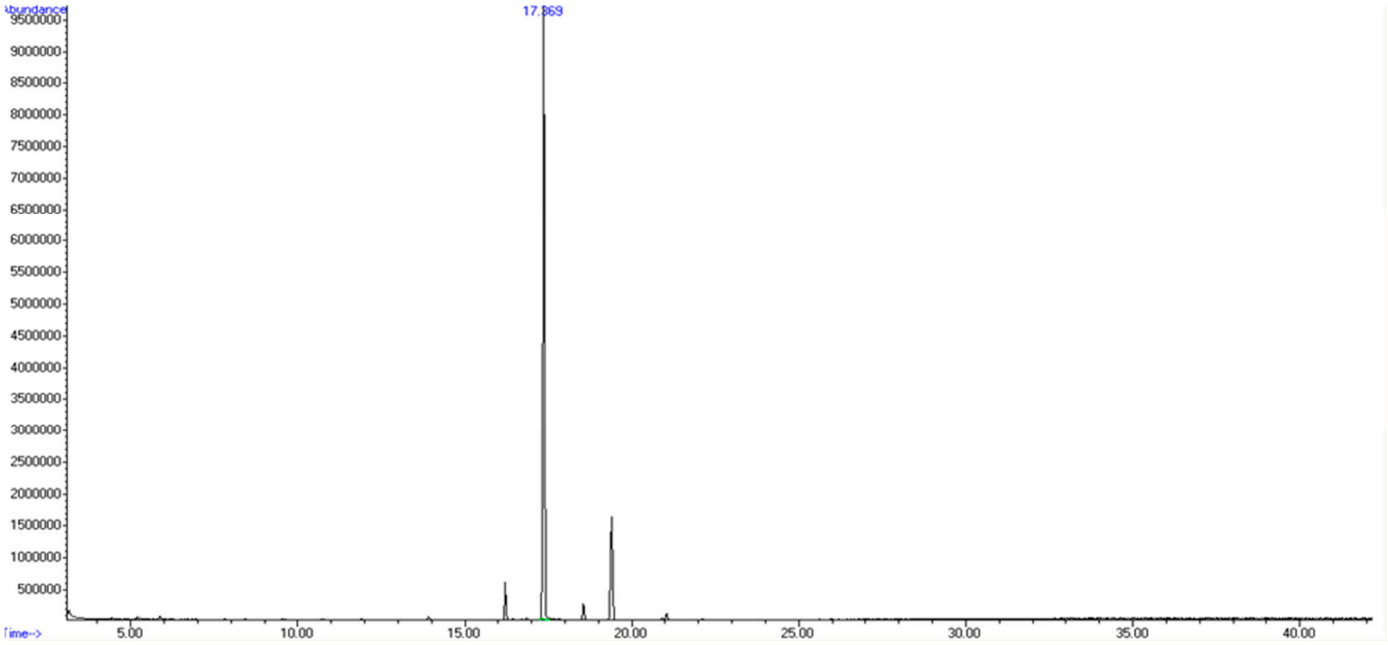

Figure S17: chromatogram for the reaction between octopamine and 2-butanone over Pt/C 5 wt.%, 50 °C, 3 h, 5 bar H_2.

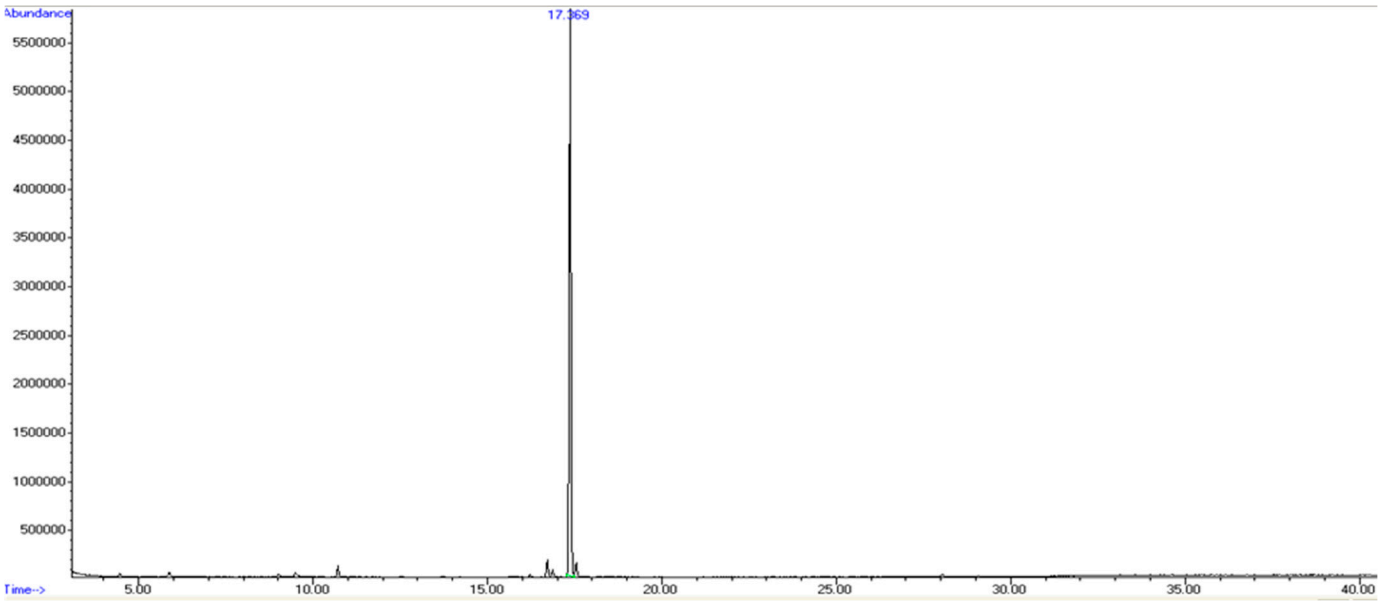

Figure S18: chromatogram for the reaction between octopamine and 2-butanone over Rh/C 5 wt.%, 50 °C, 3 h, 5 bar H_2.

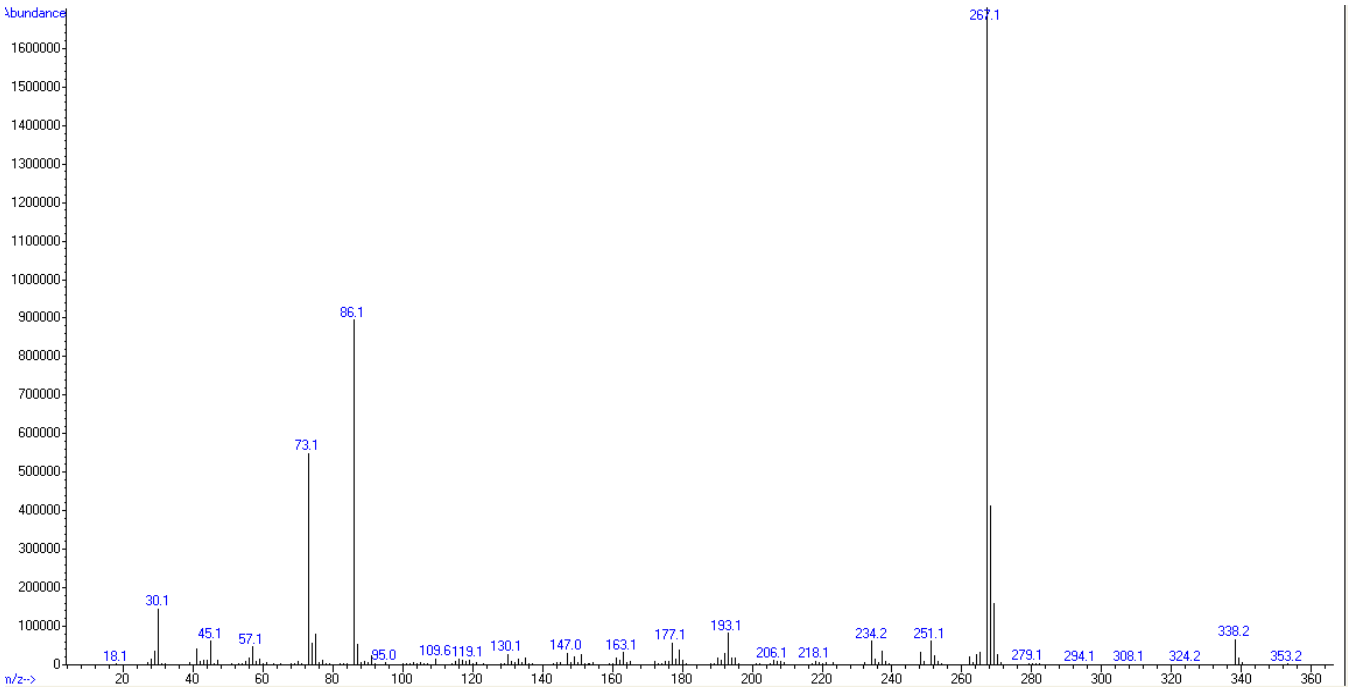

Figure S19: fragmentation pattern of the 2-butanone reductive animation product.