

Synthesis of Carboxylic Acid-5-Hydroxy-Tryptamides with Saturated, Unsaturated, or Hydroxy Fatty Acids

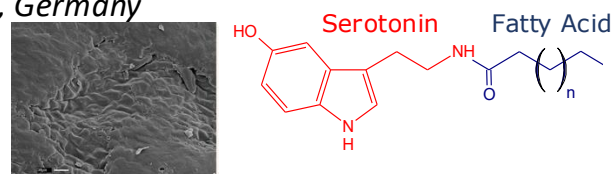
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Introduction

Coffee beans are covered by a thin waxy layer [1]. The main constituents are β -N-alkanoyl-5-hydroxytryptamides (C_n -5HTs), (Figure 1). They are known for causing stomach irritations. Steam treatment of the green coffee beans reduces their contents as well as the roasting or the decaffeination processes.

The C_n -5HTs have also gained importance from a medical perspective. The most important of all the positive properties described in the literature is the protection against Parkinson's disease and Alzheimer's disease [2-4].

For studying the behavior of the individual C_n -5HTs during the industrial processes or, in particular, for clinical studies, standard substances are necessary. A new synthesis method is presented.

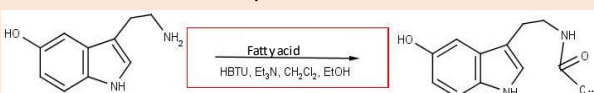


	Fatty Acid
Wurziger et al. (1969)	C_{20} , C_{22} , C_{24}
Folstar et al. (1979, 1980)	C_{20} -OH, C_{22} -OH, C_{18}
Kurzrock et al. (2004)	C_{21} , C_{23}
Hinkel et al. (2005, 2009)	C_{16} , $C_{18:2}$, $C_{20:1}$, $C_{20:1}$ -OH, $C_{22:1}$ -OH

Figure 1: Overview of the known C_n -5HTs

Synthesis and Clean-up

Figure 2 shows the HPLC chromatogram of an Arabica coffee. It is evident that the individual C_n -5HTs are present in fairly different amounts in coffee. Therefore, a new synthesis method for preparing fatty acid amides by reacting a saturated, hydroxylated or unsaturated fatty acid with serotonin is described (German Patent Nr. 10 2008 025 893).



The coupling reagent 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyl-uronium-hexafluoro-phosphate (HBTU) activates the carboxylic acid for the reaction, which is completed within 120 minutes. After washing and re-crystallization, a white powder will be retained.

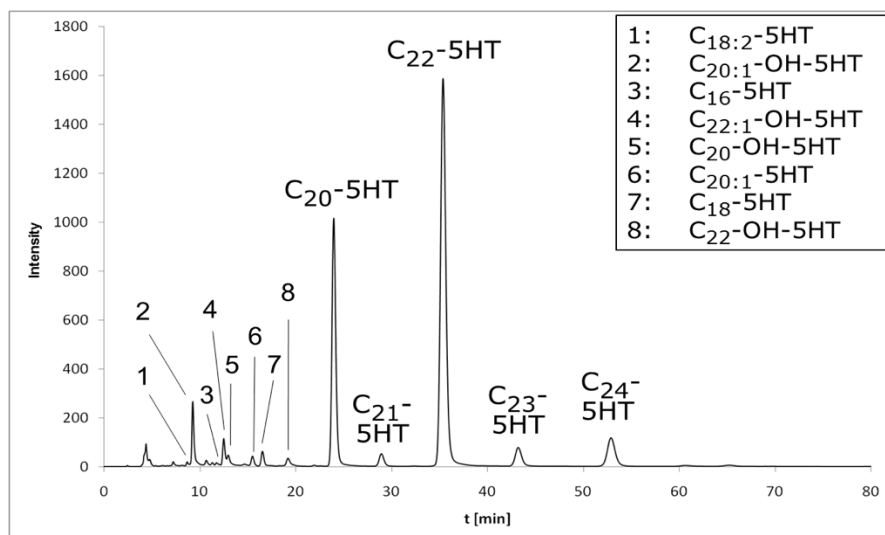


Figure 2: HPLC-FLD chromatogram of C_n -5HT, Arabica coffee

UV-Vis (Acetonitril/2-Propanol) $\lambda_{\max}$: 225, 276, 298 nm;

FL (Acetonitril/2-Propanol) $\lambda_{\text{ex}}/\lambda_{\text{em}}$: 275/330 nm;

LC/MS (APCI⁺): 469,3 [M+H]⁺, (EPI 469): 452,2 [M-16]⁺, 336,3 [M-132]⁺, 310,3 [M-158]⁺, 177,1/160,1;

HRMS: 468,3750 ($C_{30}H_{48}N_2O_2$);

¹H-NMR (500 MHz, CDCl₃+DMSO) δ /ppm: 7,98 (s, 1H, H-N₁), 7,21 (d, 1H, H-C₇), 7,03-6,96 (dd, 2H, H-C₄, H-C₂), 6,79 (dd, 1H, H-C₆), 5,66 (s, 1H, H-N₁₀), 5,33 (m, 2H, H-C_{21,22}), 3,54 (q, 2H, H-C₉), 2,87 (t, 2H, H-C₈), 2,11 (t, 2H, H-C₁₂), 1,99 (m, 4H, C_{20,23}), 1,56 (t, 2H, H-C₁₃), 1,25 (m, 26H, H-C_{14-19,24-29}), 0,87 (t, 3H, H-C₃₀);

Figure 3: Spectroscopic data of $C_{20:1}$ -5HT

Results/Discussion

In contrast to a formerly described multistage method [5], there now is no need to protect hydroxyl groups and other reactive groups in the amine. Saturated, hydroxylated as well as unsaturated fatty acids can directly be connected to serotonin for the first time. Yields over 90% were achieved with this simple and fast procedure. LC/MS and NMR data for eicosenoic acid ($C_{20:1}$) (Fig. 3) demonstrate the purity of the synthesised standard substance.

Conclusion/Perspectives

- A synthesis procedure for individual saturated, hydroxylated or unsaturated C_n -5HTs with high yields is developed.
- The study of the behavior of the individual C_n -5HT during roasting, steaming or decaffeination processes is now possible.
- Clinical studies with individual C_n -5HTs or mixtures thereof can be performed.

References:

- [1] Harms, U. and Wurziger, J. 1968 Zeitschrift fuer Lebensmittel-Untersuchung und -Forschung, 138, 75-80.
- [2] Brand, A.L.M. et al. 2023 Food Reviews International, 39:7, 4761-4780
- [3] Speer, K. and Kölling-Speer, I. 2006 Braz. J. Plant Physiol. 18 (1): 201-216
- [4] Speer, K. and Kölling-Speer, I. 2019 Lipids, Chapter 20, 458-504, in "Coffee Production, Quality and Chemistry" edited by Adriana Farah, The Royal Society of Chemistry
- [5] Hubert P. et al. 1977, Z. Anal. Chem. 285, 242-50