Research, Society and Development, v. 9, n. 10, e9739109419, 2020
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v9i10.9419

Bioreduction of α,β-unsaturated carbonyl compounds by *Lasiodiplodia pseudotheobromae*, endophytic fungus from *Morinda citrifolia* (RUBIACEAE)

Bioredução de compostos carbonílicos α,β-insaturados por *Lasiodiplodia pseudotheobromae*, fungo endofítico de *Morinda citrifolia* (RUBIACEAE)

Biorreducción de compuestos de carbonilo α,β-insaturados por *Lasiodiplodia pseudotheobromae*, hongo endofítico del *Morinda citrifolia* (RUBIACEAE)

Received: 10/19/2020 | Reviewed: 10/22/2020 | Accept: 10/26/2020 | Published: 10/29/2020

Mark Carvalho da Silva
ORCID: https://orcid.org/0000-0002-2343-6160
Universidade Federal do Sul e Sudeste do Pará, Brasil
E-mail: mark-k02@hotmail.com
Maricelia Lopes dos Anjos
ORCID: https://orcid.org/0000-0001-6837-0276
Universidade Federal do Pará, Brasil
E-mail: mariceliadosanjos@yahoo.com.br
Luana Cardoso de Oliveira
ORCID: https://orcid.org/0000-0002-3204-8194
Universidade Federal do Pará, Brasil
E-mail: luanacardoso.oliveira@hotmail.com
Patrícia Santana Barbosa Marinho
ORCID: https://orcid.org/0000-0002-9368-8574
Universidade Federal do Pará, Brasil
E-mail: pat@ufpa.br
Alessandra Keiko Nakasone
ORCID: https://orcid.org/0000-0002-6021-185X
Embrapa Amazônia Oriental, Brasil
E-mail: alessandra.nakasone@embrapa.br
Simone Yasue Simote Silva
ORCID: https://orcid.org/0000-0002-9421-5381
Universidade Federal do Sul e Sudeste do Pará, Brasil

E-mail: simote@unifesspa.edu.br
Heriberto Rodrigues Bitencourt
ORCID: https://orcid.org/0000-0002-0003-2876
Universidade Federal do Pará, Brasil
E-mail: heriberto.ufpa@gmail.com
Sebastião da Cruz Silva
ORCID: https://orcid.org/0000-0001-7436-0605
Universidade Federal do Sul e Sudeste do Pará, Brasil
E-mail: simotesilva@unifesspa.edu.br
Andrey Moacir do Rosario Marinho
ORCID: https://orcid.org/0000-0002-8981-0995
Universidade Federal do Pará, Brasil
E-mail: andrey@ufpa.br

Abstract

Biotransformations are reactions carried out by microorganisms that lead to changes in the structures of organic compounds, among the biotransformations there are bioreductions. Bioreductions are of great interest to the pharmaceutical and food industries, as they almost always lead to the formation of enantiomerically pure compounds. Thus, this work aimed to verify the ability of the fungus *Lasiodiplodia pseudotheobromae* in bioreduce α,β-unsaturated carbonyl compounds. Compounds (3E)-4-(2-methoxy-phenyl)-but-3-en-2-one (**1**), (1E, 4E)-1,5-diphenyl-pent-1,4-dien-3-one (**2**) and (1E, 4E)-1,5-bis-(2-methoxy-phenyl)-penta-1,4-dien-3-one (**3**) were used as substrates. The reactions were carried out on an orbital shaker for 8 days at room temperature. The products formed were characterized by analytical thin layer chromatography (ATLC), high performance liquid chromatography (HPLC) and hydrogen nuclear magnetic resonance (^{1}H NMR). For all products formed was observed reduction in double bonds C=C and C=O leading to the formation of the respective alcohols. This is the first report of biotransformation reactions using the fungus *Lasiodiplodia pseudotheobromae*.

Keywords: bioreduction; endophytic fungi; biotransformation; *Lasiodiplodia*

Resumo

Biotransformações são reações realizadas por microorganismos que levam a modificações nas estruturas de compostos orgânicos, dentre as biotransformações exitem as biorreduções. As

biorreduções são de grande interesse das indústrias farmacêuticas e de alimentos, pois quase sempre levam a formação de compostos enantiomericamente puros. Assim, este trabalho teve por objetivo verificar a capacidade do fungo *Lasiodiplodia pseudotheobromae* em biorreduzir compostos carbonílicos α,β-insaturados. Os compostos (3*E*)-4-(2-metoxi-fenil)-but-3-en-2-ona (**1**), (1*E*, 4*E*)-1,5-difenil-pent-1,4-dien-3-ona (**2**) e (1E, 4*E*)-1,5-bis-(2-metóxi-fenil)-penta-1,4-dien-3-ona (**3**) foram usados como substratos. As reações foram realizadas em agitador orbital por 8 dias a temperatura ambiente. Os produtos formados foram caracterizados por cromatografia em camada delgada analítica (CCDA), cromatografia líquida de alta eficiência (CLAE) e ressonância magnética nuclear de hidrogênio (RMN ^{1}H). Para todos os produtos formados foi observada a redução das ligações duplas C=C e C=O levando para a formação dos respectivos álcoois. Este é o primeiro relato de reações de biotransformação usando o fungo *Lasiodiplodia pseudotheobromae*.

Palavras-chave: biorredução, fungos endofíticos; biotransformação; *Lasiodiplodia*.

Resumen

Las biotransformaciones son reacciones llevadas a cabo por microorganismos que conducen a cambios en las estructuras de compuestos orgánicos, entre las biotransformaciones se encuentran las biorreducciones. Las biorreducciones son de gran interés para las industrias farmacéutica y alimentaria, ya que casi siempre conducen a la formación de compuestos enantioméricamente puros. Así, este trabajo tuvo como objetivo verificar la capacidad del hongo *Lasiodiplodia pseudotheobromae* en biorreductores de compuestos carbonílicos α,β-insaturados. Compuestos (3E)-4-(2-metoxi-fenil)-but-3-en-2-ona (1), (1E, 4E)-1,5-difenil-pent-1,4-dien-3-ona (2) y (1E, 4E)-1,5-bis-(2-metoxi-fenil)-penta-1,4-dien-3-ona (3) se utilizaron como sustratos. Las reacciones se llevaron a cabo en un agitador orbital durante 8 días a temperatura ambiente. Los productos formados se caracterizaron por cromatografía analítica en capa fina (CACF), cromatografía líquida de alta resolución (CLAR) y resonancia magnética nuclear de hidrógeno (RMN ^{1}H). Para todos los productos formados, se observó una reducción en los dobles enlaces C=C y C=O, lo que condujo a la formación de los respectivos alcoholes. Este es el primer informe de reacciones de biotransformación utilizando el hongo *Lasiodiplodia pseudotheobromae*.

Palabras clave: biorreducción, hongos endofíticos; biotransformación; *Lasiodiplodia*.

1. Introduction

Belonging to the genre *Lasiodiplodia*, family Botryosphariaceae, order Botryosphaeriales, class Dothideomycetes and phylum Ascomycota the fungus *Lasiodiplodia pseudotheobromae* arise of a split of the specie *Lasiodiplodia theobromae* (Adetunji and Oleke, 2013). The fungus *L. pseudotheobromae* is an opportunist pathogen, cause rottenness in seeds, decrease germinative potential of the plants and there are several host plants for it (Maciel et al., 2017; Machado and Pinho, 2013). The fungus *L. pseudotheobromae* has excellent herbicidal activity against weed (Adetunji et al., 2017; Adetunji et al., 2018).

The fungi have been widely used to search for bioactive secondary metabolites. Fungi from *Lasiopiplodia* genre have many kinds of secondary metabolites with different biological activities, such as jasmonic acid and its derivatives, polyketides, isocoumarins, sesquiterpenes, diketopiperazines, and others compounds have been reported (Wei et al., 2014; Nunes et al., 2008).

Biotransformations are chemical reactions carried out by microorganisms on organic substrates (Liu and Yu, 2010). Classic organic syntheses generally require special conditions, such as temperature and/or pressure controls, use of specific solvents and catalysts and other processes, that often making classic synthesis expensive and environmentally inadequate. On the other hand, biotransformation can be made in aqueous medium, it operate in mild conditions and products with greater enantioselectivity and regioselectivity have been obtained (Perkins et al., 2016). Thus, biotransformation can be considered a useful tool to produce new compounds in ecologically friendly conditions (Vasconcelos et al., 2015) and unusual reactions in classical synthesis can be made (Martins and Takahashi, 2010).

Microorganisms are well known for their abilities to catalyze different types of biotransformation reactions, including hydroxylation, reduction (double bonds and ketones), O-alkylation and dealkylations, glycosylation, and sulfatation (Cao et al., 2015). There are few studies about biotransformation potential of fungus of the *Lasiodiplodia* genre and this is the first study about biotransformation potential of fungus *Lasiodiplodia pseudotheobromae* using α,β-unsaturated carbonyl compounds as substrates.

2. Material and Methods

2.1 General procedures

The HPLC analyses were carried out on an Ultimate 3000 DIONEX chromatographic system. ^{1}H NMR spectra were recorded on an Ascend 400 (Bruker) spectrometer operating at 400 MHz, using $CDCl_3$ as solvent and reference. The chemical shifts are given in delta (δ) values and the coupling constants (*J*) in Hertz (Hz).

2.2 Microorganism

The fungus *Lasiodiplodia pseudotheobromae*, code NC5, was obtained from a collection of the Laboratório de Fitopatologia of the Embrapa Amazônia Oriental, Belém-PA, that contains endophytic fungi isolated from *M. citrifolia* (IAN 188703).

2.3 Substrates

2.3.1 Synthesis of Substrates procedures

(3E)-4-(2-methoxy-phenyl)-but-3-en-2-one (**1**): in a 250 mL Erlernmeyer flask were add 50 mL of acetone, 10 mL of NaOH solution 10% and shaken at room temperature. In other 50 mL Becker cup was add 3.67 g (20 mmol) of ortho-anisaldehyde and dissolved in 30 mL of methanol, then it was added and mixed in the solution of the 250 mL Erlenmeyer flask and shaken at room temperature for 40 min. After this time, the reaction was acidified with acetic acid solution 20% until acid pH and transferred to a 150 mL separation funnel and extracted with chloroform (50 mL, 3x). Then, the chloroform solution was washed with water (50 mL, 3x). Finally, the chloroform solution was evaporated and the solid result was recrystallized from methanol leading to yellow crystal yielding 56%.

(1E, 4E)-1,5-diphenyl-pent-1,4-dien-3-one (**2**): in a 250 mL Erlenmeyer flask were dissolved 3 mL of benzaldehyde and 1.2 mL of acetone in 30 mL of methanol. In this mixture was added 6 mL of the a NaOH 20 % solution and 25 mL of distillated water and shaken for 30 min at 22 °C, in ice bath. The compound formed was filtered on a Buchner funnel and washing with iced water. The product obtained was recrystallized from methanol yielding 65%.

(1E, 4E)-1,5-bis-(2-methoxy-phenyl)-pent-1,4-dien-3-one (**3**): to this substrate was applied same methodology for (**1**), but using 1.3 mL of acetone (11 mmol) and 2.9 mL (24 mmol) of 2-metoxy-benzaldehyde as starting materials. An yellow solid was obtained yielding 78 %.

(3E)-4-(2-methoxy-phenyl)-but-3-en-2-one (**1**): δ 6.90 (d, 1H, J=7.7, H-7), 7.35 (t, 1H, J=7.7, H-9), 6.97 (t, 1H, J=7.7, H-8), 7.54 (d, 1H, J=7.7, H-10), 7.87 (d, 1H, J=16.4, H-4), 6.74 (d, 1H, J=16.4, H-3), 3.88 (s, 3H, OMe-6), 2.07 (s, 3H, Me-1).

(1E, 4E)-1,5-diphenyl-pent-1,4-dien-3-one (**2**): δ 7.09 (d, 1H, J=15.9, H-2/ H-4), 7.75 (d, 1H, J=15.9, H-1/ H-5), 7.42 (m, 4H, H-7/H-7' and H-11/H-11'), 7.63 (m, 6H, H-8/H-8', H-9/H-9' and H-10/H-10').

(1E, 4E)-1,5 bis-(2-methoxy-phenyl)-pent-1,4-dien-3-one (**3**): δ 7.56 (d, 2H, J=7.8, H-8/H-8'), 7.31 (t, J=7.8, 2H, H-9/H-9'), 6.93 (t, 2H, J=7.6, H-10/H-10'), 6.86 (d, 2H, J=7.6, H-11/H-11'), 8.02 (d, 2H, J=16.8, H-1/H-5), 7.11 (d, 2H, J=16.8, H-2/H-4), 3.85 (s, 3H, OMe-7/ OMe-7').

2.4 Biotransformation procedures

Initially, the fungus *L. pseudotheobromae* NC5 was reactivated in a Petri dish, containing PDA culture medium, at room temperature for eight days. Then, for each substrate, six 500 mL Erlenmeyer flasks containing 200 mL of Czapeck culture medium were sterilized in a 75 L vertical autoclave (Prismatec) for 20 minutes at 121 ºC. After reaching room temperature, in a laminar flow hood (Panchane PA 320), three small pieces of 2 mm^3 of the fungus were added in five flasks. Three flasks were used as controls (one flask containing fungus plus culture medium, another flask containing culture medium plus substrate, and another flask containing only culture medium). The system was agitated on an orbital shaker (Quimis Q315IA) at 120 rpm on controlled temperature at 32 ºC for the growth of fungal colonies, for three days. Then, 20 mg (per flask) of each substrate were solubilized into 100 µL of DMSO and added into three Erlenmeyer flasks. Afterward all flasks were kept under agitation for five days. After, the flasks were filtered and the liquid-medium were extracting with ethyl acetate (75 mL, 3x). The formation of biotransformation products were verified through the analysis of bioreaction extracts by TLC chromatoplate, the mobile phase used was Hexane/AcOEt 1:1, observed at UV 365nm lamp (Boitton®). The HPLC analyzes were

carried out on an Ultimate 3000 DIONEX Chromatographic system equipped with automatic sampler and detector PDA, performed on a 250 mm x 4.6 mm Acclaim® 120 RP-C18 analytical column, 5 m particle sizes and 120 pore size, volume of the injected sample was 20 µL and the column temperature was fixed at 30 ºC. Elution was carried out in gradient linear MeOH/H_2O 10:90 to MeOH/H_2O 90:10 (60 min).

3. Results and Discussion

The biotransformation products formation were characterized by comparison between their ^{1}H NMR, TLC, HPLC data and respective substrate and literature (Figure 1).

The biotransformation products of substrates **1-3** were initially analyzed by TLC and HPLC. These analyzes allowed observe chromatographic bands with Rf and Rt different of substrates suggesting biotransformation products. In HPLC analyze to substrate **1** was observed a chromatographic band at 41 min, when this chromatogram was compared with that to the product **1a** an additional band at 43 min was observed showing the formation of biotransformation product **1a**. To the biotranformation products **2a** and **3a** were made similar comparison between their respective chromatograms and substrates **2** and **3**.

Through comparatives analyses between ^{1}H NMR data of the product **1a** and substrate **1** were observed structural modification (McConville et al., 2009). In the ^{1}H NMR spectrum of product **1a** were observed signals to aliphatic hydrogens at δ_H 2.67 (*t*, H-4, *J* = 7.32 Hz), δ_H 1.65 (*m*, H-3), δ_H 1.16 (d, H-1, J = 6.2 Hz) and δ_H 3.65 (*m*, H-2), this signals are compatible for system butan-2-ol moiety; signals in the aromatic hydrogens at 6.83-7.22 (m, 4H) were observed. Also the absence of doublet signals at δ_H 7.87 (d, 1H, J=16.4 Hz, H-4) and 6.64 (d, 1H, J=16.4 Hz, H-3) referent to olefinic hydrogens *trans* related at structure of substrate **1** permitted conclude a reduction in the C=C and C=O bonds by fungus leading to the alcohol **1a** (Boffi et al., 2011).

The product **2a** was characterized through comparative analyses between ^{1}H NMR spectra of substrate **2** and product **2a** (Hua et al., 2004). In the ^{1}H NMR spectrum of product **2a** was observed a multiplet signal at δ_H 3.72 referent for carbinolic hydrogen H-3; a multiplet signal at δ_H 2.80 to benzylic hydrogens H-1/H-5 and a signal at δ_H 1.80 referent for hydrogens H-2/H-4, these signals are compatible to secondary alcohol moiety. Signals to aromatic hydrogens at δ_H 7.23-7.33 (m, 10H) also were observed for **2a**. Thus, the **2a** was

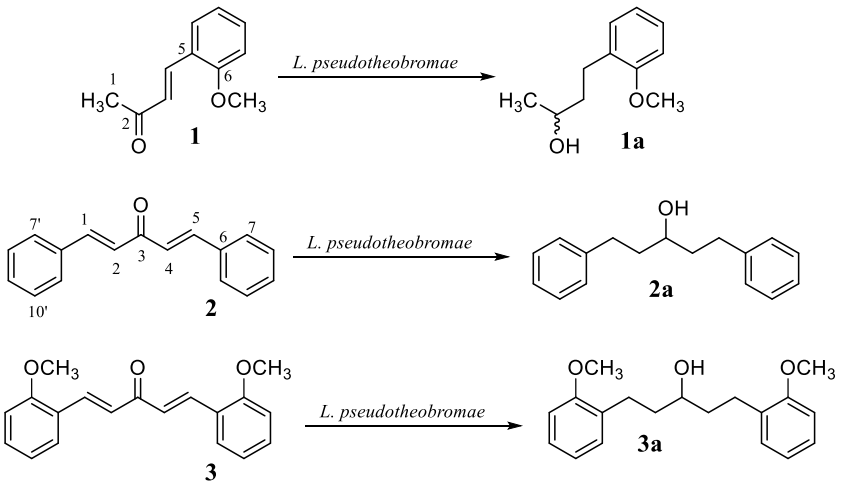
characterized as bioreduction product of C=C and C=O bonds leading to the alcohol (Kose and Saito, 2010).

The ^{1}H NMR spectrum to substrate **3** is similar to the substrate **2** showing major difference the signal for two methoxyl groups at δ_H 3.92. The comparison between **3** and product reaction **3a** ^{1}H NMR data showed bioreducton through of absence to double bond the signals for C=C at δ_H 8.02 (d, 2H, J=16.8 Hz, H-1/H-5) and 7.11 (d, 2H, J=16.8 MHz, H-2/H-4). The alcohol as major product was confirmed by signals at δ_H 1.75 (m, 4H, H-2/H-4), 2.80 (m, 4H, H-1/H-5), δ 3.75 (quint, 1H, H-3) for secondary alcohol moiety, the signals δ_H 7.23-7.33 (m, 10H, H-Ar) and 3.85 (s, 6H, OMe-7/OMe-7') were also observed (Yamakoshi at al., 2010).

Biotransformation reaction are related the modification of the chemical compounds by microorganisms, so that this reaction occur with high specificity, high selectivity and environmentally friendly (Labes and Wendhausen, 2008). Thus, there are increase in the search for new biocatalysts from fungi and yeast (Jesus et al., 2013).

Takahashi et al (2017) reported biotransformation of natural products procedures in academia are carried out in major by microorganism isolated from plant, principally using fungi instead pure enzymes, due to easy handle, low cost, and good reproducibility these fungi biotransformation.

Figure 1: Bioreduction of the α,β-unsaturated carbonyl compounds by *L. pseudotheobromae* leading to the respective alcohol.



Source: Authors.

In the literature are described several microorganisms used in biontransformation reaction of carbonyl compounds, but most frequently *Saccharomyces cerevisiae* yeast are used (Albuquerque, 2007). The microorganisms *Candida albicans*, *Rhodotorula glutinis*, *Geotrichum candidum*, *Micrococcus luteus* also have been used in biotransformation reaction of carbonyl compounds (Zampieri et al., 2013).

There is an increase in the search by enantiomerically pure compounds, that are of great interest to pharmaceutical and agrochemistry industry, it has boosted research in biocatalysis area (Labes and Wendhausen, 2008; Gallardo et al, 2013). The enzymes responsible by reduction of the double bonds C=C and C=O are called oxidoreductases and microorganisms are sources common of the dehydrogenases (Albuquerque, 2007).

Thus, it highlights the importance of fungi, such as *Lasiodiplodia pseudotheobromae*, in biotransformation procedures, once these microorganisms have enzymes in their biological system that can be used with efficiency and selectivity in biotransformation procedures more economically viable and less aggressive to environment.

4-(2-methoxy-phenyl)-butan-2-ol (**1a**): δ_H 2.73 (*t*, H-4, *J* = 7.32 Hz), δ_H 1.74 (*m*, H-3), δ_H 1.20 (d, H-1, J = 6,2 Hz), δ_H 3.74 (*m*, H-2), 3.89 (s, OMe), 6.83-7.22 (m, 4H, H-Ar).

1,5-diphenyl-pentan-3-ol (**2a**): δ 1.87 (m, 4H, H-2/H-4), 2.78 (m, 4H, H-1/H-5), δ 3.72 (quint, 1H, H-3), 7.23-7.33 (m, 10H, H-Ar).

1,5-bis-(2-methoxy-phenyl)-penta-3-ol (**3a**): δ 1.75 (m, 4H, H-2/H-4), 2.80 (m, 4H, H-1/H-5), δ 3.75 (quint, 1H, H-3), 7.23-7.33 (m, 10H, H-Ar), 3,85 (s, 6H, OMe-7/OMe-7').

4. Conclusion

The fungus *L. pseudotheobromae* showed as good biocatalyst selective for bioreduction reaction for double bond C=C and C=O of α,β-unsaturated carbonyl compounds leading to the respective alcohol. This kind of reaction is interesting for pharmaceutical and agrochemical industry for development of the new products. This is the first report of the biotransformation potential of *L. pseudotheobromae*. The present work can be continued to further exploration of the bioreduction potential of endophytic fungi.

Conflict of interest

The authors declare that there is no conflict of interest.

Acknowledgments

The authors would like to thank Brazilian agencies such as the National Council for Scientific and Technological Development (CNPq), the Commission for the Improvement of Higher Education Personnel (CAPES), the Amazon Foundation for Support in Studies and Research (FAPESPA) for the financial support for this research.

References

Adetunji, C. O. & Oloke, J. K. (2013). Effect of Wild and Mutant Strain of *Lasiodiplodia Pseudotheobromae* Mass Produced on Rice Bran as a Potential Bioherbicide Agents for Weeds under Solid state Fermentation. *J App Biol Biotech*, 1(2), 18-23. DOI: 10.7324/JABB.2013.1204

Adetunji, C. O., Adejumo, I. O., Oloke, J. K. & Akpor, O. B. (2018). Production of Phytotoxic Metabolites with Bioherbicidal Activities from *Lasiodiplodia pseudotheobromae* Produced on Different Agricultural Wastes Using Solid-State Fermentation. *Iran J Sci Technol Trans Sci*, 42(2), 1163-1175. https://doi.org/10.1007/s40995-017-0369-8

Adetunji, C., Kumar, J. O. A., Swaranjit, S. & Akpor, B. (2017). Synergetic effect of rhamnolipid from *Pseudomonas aeruginosa* C1501 and phytotoxic metabolite from *Lasiodiplodia pseudotheobromae* C1136 on Amaranthus hybridus L. and Echinochloa crus-galli weeds. *Environ Sci Pollut Res*, 24, 13700-13709. https://doi.org/10.1007/s11356-017-8983-8

Albuquerque, P. M. (2007). Utilização de *Saccharomyces cerevisiae* na redução de substratos carbonílicos. Tese de Doutorado, Universidade Federal de Santa Catarina, Florianópolis, Santa Catarina, Brasil.

Boffi, A., Cacchi, S., Ceci, P., Cirilli, R., Fabrizi, G., Prastaro, A., Niembro, S., Shafir, A. & Vallribera, A. (2011). The Heck Reaction of Allylic Alcohols Catalyzed by Palladium Nanoparticles in Water: Chemoenzymatic Synthesis of (R)-(-)-Rhododendrol. *ChemCatChem*, 3(2), 347-353. https://doi.org/10.1002/cctc.201000260

Cao H., Chen, X., Jassbi, A. R. & Xiao, J. (2015). Microbial biotransformation of bioactive flavonoids. *Biotechnol Adv*, 33(1), 214-223. doi: 10.1016/j.biotechadv.2014.10.012

Gallardo, Y. M., Soriano, M. P. C. & Santos, L. S. (2013). Stereoselective bioreduction of β-carboline imines through cell-free extracts from earthworms (*Eisenia foetida*). *Tetrahedron: Asymmetry*, 24(8), 440-443. https://doi.org/10.1016/j.tetasy.2013.03.003

Hu, Z. G., Liu, J., Zeng, P. L. & Dong, Z. B. (2004). Synthesis of α, α'-bis(substituted benzylidene)ketones catalysed by a SOCl2/EtOH reagent. *J Chem Res*, 55-56. https://doi.org/10.3184/030823404323000792

Jesus, I. S., Nogueira, F. B. & Fonseca, A. M. (2013). Redução de compostos carbonílicos: os talos de mamoeiro (*Carica papaya*) como reagente biocatalisador. *Scientia Plena*, 9(7), 077215.

Kose, O. & Saito, S. (2010). Cross-coupling reaction of alcohols for carbon–carbon bond formation using pincer-type NHC/palladium catalysts. *Org Biomol Chem*, 8(4), 896-900. DOI:10.1039/b914618k

Labes, J. R. & Wendhausen, R. (2008). Seleção de microorganismos com ação de compostos com ação sobre compostos carbonilados gerando álcoois quirais. *Dynamis*, 1, 73-79. http://dx.doi.org/10.7867/1982-4866.2008v14n1p73-79

Liu, J. H. & Yu, B. Y. (2010). Biotransformation of bioactive natural products for pharmaceutical lead compounds. *Curr Org Chem*, 14(14), 1400-1406. DOI:10.2174/138527210791616786

Machado, A. R, Pinho, D. B. & Perreira, O. L. (2014). Phylogeny, identification and pathogenicity of the Botryosphaeriaceae associated with collar and root rot of the biofuel plant Jatropha curcas in Brazil, with a description of new species of *Lasiodiplodia*. *Fungal Diversity*, 67, 231-247. https://doi.org/10.1007/s13225-013-0274-1

Maciel, C. G., Muniz, M. F. B., Rolim, J. M., Michelon, R. M. D. N., Paletto, T. & Rabuske, J. E. (2017). Uso da microbiolização contra *Lasiodiplodia theobromae* em sementes de *pinus* spp. *Floresta*, 47(1), 121-128. http://dx.doi.org/10.5380/rf.v47i1.44018

Martins, L. R. & Takahashi, J. A. (2010). Rearrangement and oxidation of β-amyrin promoted by growing cells of *Lecanicillium muscarinium*. *Nat Prod Res*, 24, 767-774. https://doi.org/10.1080/14786410903262865

McConville, M., Saidi, O., Blacker, J. & Xiao, J. (2009). Regioselective Heck Vinylation of Electron-Rich Olefins with Vinyl Halides: Is the Neutral Pathway in Operation? *J Org Chem*, 74(7), 2692-2698. https://doi.org/10.1021/jo802781m

Nunes, F. M., Oliveira, M. C. F., Arriaga, A. M., Lemos, T. L. G., Andrade-Neto, M., Mattos, M. C., Mafezoli, J., Viana, F. M. P., Ferreira, V. M., Rodrigues-Filho, E. & Ferreira, A. G. (2008). A new eremophilane-type sesquiterpene from the phytopatogen fungus *Lasiodiplodia theobromae* (Sphaeropsidaceae). *J Braz Chem Soc*, 19(3), 478-482. http://dx.doi.org/10.1590/S0103-50532008000300015

Perkins, C., Siddique, S., Puri, M. & Demain, A. L. (2016). Biotechnological applications of microbial bioconversions. *Crit Rev Biotechnol*, 36(6), 1050-1065. doi:10.3109/07388551.2015.1083943

Takahashi, J. A., Lima, G. S., Santos, G. F., Lyra, F. H., Silva-Hughes, A. F. & Gonçalves, F. A. G. (2017). Fungos Filamentosos e Química: Velhos Conhecidos, Novos Aliados. *Rev Virtual Quim*, 9(6), 2351-2382. DOI: 10.21577/1984-6835.20170141

Vasconcelos, D. H. P., Mafezoli, J., Uchôa, P. K. S., Saraiva, N. N., Lima, M. A. S., Silva-Júnior, J. N., Barbosa, F. G., Mattos, M. C., Oliveira, M. C. F., Lima, C. S. & Pessoa, M. N. G. (2015). Biotransformation of the Diterpene Ent-18,19-dihydroxytrachylobane by Rhizopus stolonifer. *J Braz Chem Soc*, 26(5), 1043-1047. https://doi.org/10.5935/0103-5053.20150070

Wei, W., Jiang, N., Mei, Y. N., Chu, Y. L., Ge, H. M., Song, Y. C., NG, S. W. & Tan, R. X. (2014). An antibacterial metabolite from *Lasiodiplodia pseudotheobromae* F2. *Phytochemistry*, 100, 103-109. https://doi.org/10.1016/j.phytochem.2014.01.003

Yamakoshi, H., Ohori, H., Kudo, C., Sato, A., Kanoh, N., Ishioka, C., Shibata, H. & Iwabuchi, Y. (2010). Structure–activity relationship of C5 curcuminoids and synthesis of their molecular probes thereof. *Bioorg Med Chem*, 18(3), 1083-1092. doi: 10.1016/j.bmc.2009.12.045

Zampieri, D. S., Paula, B. R. S., Zampieri, L. A., Vale, J. A., Rodrigues, J. A. R. & Moran, P. J. S. (2013). Enhancements of enantio and diastereoselectivities in reduction of (*Z*)-3-halo-4-phenyl-3-buten-2-one mediated by microorganisms in ionic liquid/water biphasic system. *J Mol Catal B- Enzym*, 85-86, 61-64. https://doi.org/10.1016/j.molcatb.2012.08.005

Porcentagem de contribuição de cada autor no manuscrito

Mark Carvalho da Silva -15%

Maricelia Lopes dos Anjos - 12%

Luana Cardoso de Oliveira - 8%

Patrícia Santana Barbosa Marinho - 8%

Alessandra Keiko Nakasone - 5%

Simone Yasue Simote Silva - 7%

Heriberto Rodrigues Bitencourt - 15%

Sebastião da Cruz Silva - 15%

Andrey Moacir do Rosario Marinho - 15%