6-Hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one—A degradable derivative of natural 6-Hydroxybenzoxazolin-2(3H)-one produced by Pantoea ananatis

Margot Schulza, Dieter Sickerb, Oliver Schackowb, Lothar Hennigb, Diana Hofmannf, Ulrich Diskoc, Marina Venturaa, and Kateryna Basyuk4

6-Hydroxybenzoxazolin-2(3H)-one is produced by many plants as an intermediate for subsequent glycosylation when exposed to the allelochemical benzoxazolin-2(3H)-one.1,2 The latter presents the compound was identified by NMR and mass spectrometric methods. In vitro synthesis succeeded with Pantoea protein, with isolated proteins from the Abutilon root surface or with horseradish peroxidase in the presence of nitrite and H2O2. Nitro-BOA-6-OH is completely degraded further by Pantoea ananatis and Abutilon root surface proteins. Under laboratory conditions, 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one inhibits Lepidium sativum seedling growth whereas Abutilon theophrasti is much less affected. Although biodegradable, an agricultural use of 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one is undesirable because of the high toxicity of nitro aromatic compounds to mammals.
performed using standard 2D techniques (HSQC, HMBC). Characteristic shift differences in $^1$H and $^{13}$C were found between a neutral and ionic form of the compound. Additionally, line broadening of C-5, C-6 and C-7 was observed in the carbon spectrum of the salt. A bathochromic shift in the spectrum from 383 nm to 418 nm occurred as a result of salt formation. According to these data, the colored compound produced by *Pantoea ananatis* was identified as 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one. It exists in the medium first in a yellow neutral and than in an orange anionic form due to the increasing pH during continued culturing (Fig. 1).

**In vitro synthesis of 6-hydroxy-5-nitrobenzo[d] oxazol-2(3H)-one**

BOA-6-OH was converted to 6-hydroxy-5-nitrobenzo[d] oxazol-2(3H)-one by proteins isolated from *P. ananatis* in presence of nitrite and H$_2$O$_2$. Replacing nitrite with nitrate decreased product formation (Fig. 2). Thus, we concluded that nitrate present in the Czapek medium is reduced by bacterial nitrate reductase and the resulting nitrate is used for the nitrilation of BOA-6-OH by a peroxidase. Secretion of peroxidase and periplasmic nitrate reductase by certain bacteria is known. $^7,8$ *Pantoea ananatis* possesses genes for nitrate reductase (UniProtKB-A0A0H3KVM0 (A0A0H3KVM0_PA-NAA) and catalase/hydroperoxidase (NCBI Reference Sequence: WP_014592998.1)). $^9,10$ Nitrate reductase may be located within the periplasmic space of the Gram-negative *Pantoea ananatis*.

To determine whether peroxidase activity is able to perform the nitrilation step, commercial horseradish peroxidase (HRP) was investigated. This enzyme was successfully used by Sakihama et al. $^{11}$ for nitrilation of p-coumaric acid and cinnamic acids. Similar to the observations of Sakihama et al. $^{11}$ with other acceptor molecules, nitrilation of BOA-6-OH in position 5 was almost immediately accomplished after application of horseradish peroxidase (Fig. 2) resulting in a product identical to the previously identified compound. The OH group at C-6 might increase electron density at C-5 and C-7 due to its own donor effect, which facilitates nitrilation. For steric reasons, C-5 should be preferred for electrophilic attacks and is therefore favored for nitrilation of BOA-6-OH. Since benzoxazolin-2(3H)-one (BOA) lacks the OH group, nitrilation with horseradish peroxidase failed when BOA was used as a substrate in the assay. Aromatic nitro compounds are rare in nature $^{12}$ and natural nitrated benzoxazolinones have not been previously

![Figure 1](image1.png)

**Figure 1.** The color of 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one depends on pH: pH 3 greenish; pH 7 yellow; pH 8 orange; pH 9–10 wine-red. *Pantoea ananatis* cultures, producing the compound from BOA-6-OH, change the color from yellow to orange due to the pH value which increases over time. The anionic, orange form of the compound is degraded, as shown by the HPLC chromatograms (left: analysis of the yellow medium immediately after adding synthetic nitro-BOA-6-OH (black points) before the medium turned to orange. After 3 h (right), only traces of the compound are left.

![Figure 2](image2.png)

**Figure 2.** Enzymatic nitrilation by *Pantoea ananatis* (P.a.) exuded protein, horseradish peroxidase (HRP) and *Abutilon* (Ab) root surface proteins in presence of nitrite; P.a. and HRP also in the presence of nitrate. No enz. = no enzyme was added to the assay. Ab/B-6-OH: root surface proteins from seedlings pre-incubated with BOA-6-OH. Means ± SD are shown; asterisk(s) indicate significant differences (t-test, $^{*}p < 0.05; ^{**}p < 0.0001$).
reported. Zikmundova et al.13 who identified N-(2-hydroxy-5-nitrophenyl)acetamide and N-(2-hydroxy-3-nitrophenyl)acetamide as fungal detoxification products of benzoxazolone-derived 2-aminophenol, assumed an enzymatic reduction of nitrate, a constituent of the culture medium, and use of the resulting nitrite for nitration. This mechanism was also suggested by Rousseau et al.14 for tocopherol nitration by *Streptomyces catenulae*.

A question was whether the compound would be formed at the root surface. Therefore, the root surface proteins were collected and assayed for peroxidase-dependent synthesis in the presence of nitrite. After 3 min, approximately 30 nmol of nitro compound could be extracted from the assay mixture; when seedlings were pre-incubated with 2 mM BOA-6-OH (Fig. 2) more product was formed.

**Degradation of 6-Hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one**

Since the compound disappeared during prolonged cultivation of *P. ananatis*, biological degradation was considered because the isolated, purified compound did not show any indication of instability. To elucidate whether *P. ananatis* can metabolize 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one when existing in the anionic form, the bacterium was taken from a previous culture grown in the presence of BOA-6-OH and incubated with the purified, *in vitro* synthesized compound. Aliquots of the media revealed that anionic 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one is almost completely metabolized within 3 h (Fig. 1). The compound is also degraded by proteins collected from the *Abutilon* root surface colonized by the microbial community (shown in the supplemental online material). Thus, 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one presents an intermediate of a catabolic sequence.

The nitration of 6-hydroxybenzoxazolin-2(3H)-one and its subsequent degradation presents a hitherto unknown possibility for the elimination of benzoxazolone by a plant-bacterium cooperation. For BOA-6-OH, nitration seems to be a necessary step to initiate degradation. Electron-withdrawing NO₂-group substitution at the aromatic ring position 5 may facilitate enzymatic attacks by destabilizing the heterocyclic molecule and starting the decomposition. It is known that nitro aromatic compounds can be completely degraded by several bacteria such as *Pseudomonas*, *Ralstonia* and *Comamonas* species resulting in small biooxidizable molecules that can enter the TCA cycle.15

**Bioassays**

The purified compound was tested for its effects on germinating seeds of *Abutilon theophrasti* and *Lepidium sativum* using the bioassay procedure of Macias and
coworkers. Since the water solubility of the compound changes with pH, the bioassays were performed at pH 4, 5, 6 and 7.0. *Abutilon* root growth was, however, reduced with increasing pH, the growth of *Lepidium* roots only at pH 7.0. *L. sativum* exhibits a higher sensitivity to nitrated-BOA-6-OH than *Abutilon theophrasti* at all pH values (Fig. 3). Exposure to low amounts of nitro-BOA-6-OH results in shoot growth stimulation of *Abutilon* (significant with 86 μM at pH 7.0.). Taken together, nitro-BOA-6-OH is less toxic for *Abutilon* than for *Lepidium*. The results of the bioassays obtained under laboratory conditions indicate that only sensitive plant species such as *L. sativum* may be considerably inhibited, but it is questionable whether the compound has any phytotoxic effects under field conditions when bacteria able to degrade the compound are present. An agricultural use of nitro-BOA-6-OH is undesirable because of the known toxicity of nitro aromatic compounds against animals due to their mutagenic, carcinogenic and teratogenic properties. The results are in line with the formerly observed insensitivity of *A. theophrasti* against benzoxazinoids. It is assumed that root associated microorganisms can trigger effects of benzoxazolinone derived allelochemicals by molecule modifications and by shortening the time of exposure due to degradation processes.

**Materials and methods**

*Pantoea ananatis* was isolated from a microbial micro-colony colonizing *Abutilon theophrasti* roots. The identity of the bacterium was confirmed by the DMSZ (Leibniz-Institut - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Braunschweig). The bacterium was pre-cultured in LB medium for 2 weeks. One ml of the cultures was added to 50 ml flasks with 25 ml liquid Czapek medium supplemented with 1–5 mg BOA-6-OH (stocks from Dieter Sicker, University of Leipzig). Subsequent culturing was without shaking at 23 °C. The culture media were filtered as soon as the color of the medium had turned luminous yellow and the filtrate was extracted with ethyl acetate. The organic phase was evaporated to dryness in vacuo and the yellow residue was dissolved in ethyl acetate. The organic phase was evaporated to dryness in vacuo and the yellow residue was dissolved in ethyl acetate. The fraction was passed through silica gel (Macherey-Nagel). The fractions were analyzed for products by HPLC-DAD (Shimadzu) using a 0–100% methanol gradient as described. The results of the bioassays obtained under laboratory conditions indicate that only sensitive plant species such as *L. sativum* may be considerably inhibited, but it is questionable whether the compound has any phytotoxic effects under field conditions when bacteria able to degrade the compound are present. An agricultural use of nitro-BOA-6-OH is undesirable because of the known toxicity of nitro aromatic compounds against animals due to their mutagenic, carcinogenic and teratogenic properties. The results are in line with the formerly observed insensitivity of *A. theophrasti* against benzoxazinoids. It is assumed that root associated microorganisms can trigger effects of benzoxazolinone derived allelochemicals by molecule modifications and by shortening the time of exposure due to degradation processes.

**Pantoea ananatis** was isolated from a microbial micro-colony colonizing *Abutilon theophrasti* roots. The identity of the bacterium was confirmed by the DMSZ (Leibniz-Institut - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Braunschweig). The bacterium was pre-cultured in LB medium for 2 weeks. One ml of the cultures was added to 50 ml flasks with 25 ml liquid Czapek medium supplemented with 1–5 mg BOA-6-OH (stocks from Dieter Sicker, University of Leipzig). Subsequent culturing was without shaking at 23 °C. The culture media were filtered as soon as the color of the medium had turned luminous yellow and the filtrate was extracted with ethyl acetate. The organic phase was evaporated to dryness in vacuo and the yellow residue was dissolved in ethyl acetate. The fraction was passed through silica gel (Macherey-Nagel). The fractions were analyzed for products by HPLC-DAD (Shimadzu) using a 0–100% methanol gradient as described. The results of the bioassays obtained under laboratory conditions indicate that only sensitive plant species such as *L. sativum* may be considerably inhibited, but it is questionable whether the compound has any phytotoxic effects under field conditions when bacteria able to degrade the compound are present. An agricultural use of nitro-BOA-6-OH is undesirable because of the known toxicity of nitro aromatic compounds against animals due to their mutagenic, carcinogenic and teratogenic properties. The results are in line with the formerly observed insensitivity of *A. theophrasti* against benzoxazinoids. It is assumed that root associated microorganisms can trigger effects of benzoxazolinone derived allelochemicals by molecule modifications and by shortening the time of exposure due to degradation processes.

**Pantoea ananatis** was isolated from a microbial micro-colony colonizing *Abutilon theophrasti* roots. The identity of the bacterium was confirmed by the DMSZ (Leibniz-Institut - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Braunschweig). The bacterium was pre-cultured in LB medium for 2 weeks. One ml of the cultures was added to 50 ml flasks with 25 ml liquid Czapek medium supplemented with 1–5 mg BOA-6-OH (stocks from Dieter Sicker, University of Leipzig). Subsequent culturing was without shaking at 23 °C. The culture media were filtered as soon as the color of the medium had turned luminous yellow and the filtrate was extracted with ethyl acetate. The organic phase was evaporated to dryness in vacuo and the yellow residue was dissolved in ethyl acetate. The fraction was passed through silica gel (Macherey-Nagel). The fractions were analyzed for products by HPLC-DAD (Shimadzu) using a 0–100% methanol gradient as described. The results of the bioassays obtained under laboratory conditions indicate that only sensitive plant species such as *L. sativum* may be considerably inhibited, but it is questionable whether the compound has any phytotoxic effects under field conditions when bacteria able to degrade the compound are present. An agricultural use of nitro-BOA-6-OH is undesirable because of the known toxicity of nitro aromatic compounds against animals due to their mutagenic, carcinogenic and teratogenic properties. The results are in line with the formerly observed insensitivity of *A. theophrasti* against benzoxazinoids. It is assumed that root associated microorganisms can trigger effects of benzoxazolinone derived allelochemicals by molecule modifications and by shortening the time of exposure due to degradation processes.

**Materials and methods**

*Pantoea ananatis* was isolated from a microbial micro-colony colonizing *Abutilon theophrasti* roots. The identity of the bacterium was confirmed by the DMSZ (Leibniz-Institut - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Braunschweig). The bacterium was pre-cultured in LB medium for 2 weeks. One ml of the cultures was added to 50 ml flasks with 25 ml liquid Czapek medium supplemented with 1–5 mg BOA-6-OH (stocks from Dieter Sicker, University of Leipzig). Subsequent culturing was without shaking at 23 °C. The culture media were filtered as soon as the color of the medium had turned luminous yellow and the filtrate was extracted with ethyl acetate. The organic phase was evaporated to dryness in vacuo and the yellow residue was dissolved in ethyl acetate. The fraction was passed through silica gel (Macherey-Nagel). The fractions were analyzed for products by HPLC-DAD (Shimadzu) using a 0–100% methanol gradient as described. The results of the bioassays obtained under laboratory conditions indicate that only sensitive plant species such as *L. sativum* may be considerably inhibited, but it is questionable whether the compound has any phytotoxic effects under field conditions when bacteria able to degrade the compound are present. An agricultural use of nitro-BOA-6-OH is undesirable because of the known toxicity of nitro aromatic compounds against animals due to their mutagenic, carcinogenic and teratogenic properties. The results are in line with the formerly observed insensitivity of *A. theophrasti* against benzoxazinoids. It is assumed that root associated microorganisms can trigger effects of benzoxazolinone derived allelochemicals by molecule modifications and by shortening the time of exposure due to degradation processes.

**Pantoea ananatis** was isolated from a microbial micro-colony colonizing *Abutilon theophrasti* roots. The identity of the bacterium was confirmed by the DMSZ (Leibniz-Institut - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Braunschweig). The bacterium was pre-cultured in LB medium for 2 weeks. One ml of the cultures was added to 50 ml flasks with 25 ml liquid Czapek medium supplemented with 1–5 mg BOA-6-OH (stocks from Dieter Sicker, University of Leipzig). Subsequent culturing was without shaking at 23 °C. The culture media were filtered as soon as the color of the medium had turned luminous yellow and the filtrate was extracted with ethyl acetate. The organic phase was evaporated to dryness in vacuo and the yellow residue was dissolved in ethyl acetate. The fraction was passed through silica gel (Macherey-Nagel). The fractions were analyzed for products by HPLC-DAD (Shimadzu) using a 0–100% methanol gradient as described. The results of the bioassays obtained under laboratory conditions indicate that only sensitive plant species such as *L. sativum* may be considerably inhibited, but it is questionable whether the compound has any phytotoxic effects under field conditions when bacteria able to degrade the compound are present. An agricultural use of nitro-BOA-6-OH is undesirable because of the known toxicity of nitro aromatic compounds against animals due to their mutagenic, carcinogenic and teratogenic properties. The results are in line with the formerly observed insensitivity of *A. theophrasti* against benzoxazinoids. It is assumed that root associated microorganisms can trigger effects of benzoxazolinone derived allelochemicals by molecule modifications and by shortening the time of exposure due to degradation processes.

Materials and methods

*Pantoea ananatis* was isolated from a microbial micro-colony colonizing *Abutilon theophrasti* roots. The identity of the bacterium was confirmed by the DMSZ (Leibniz-Institut - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Braunschweig). The bacterium was pre-cultured in LB medium for 2 weeks. One ml of the cultures was added to 50 ml flasks with 25 ml liquid Czapek medium supplemented with 1–5 mg BOA-6-OH (stocks from Dieter Sicker, University of Leipzig). Subsequent culturing was without shaking at 23 °C. The culture media were filtered as soon as the color of the medium had turned luminous yellow and the filtrate was extracted with ethyl acetate. The organic phase was evaporated to dryness in vacuo and the yellow residue was dissolved in ethyl acetate. The fraction was passed through silica gel (Macherey-Nagel). The fractions were analyzed for products by HPLC-DAD (Shimadzu) using a 0–100% methanol gradient as described. The results of the bioassays obtained under laboratory conditions indicate that only sensitive plant species such as *L. sativum* may be considerably inhibited, but it is questionable whether the compound has any phytotoxic effects under field conditions when bacteria able to degrade the compound are present. An agricultural use of nitro-BOA-6-OH is undesirable because of the known toxicity of nitro aromatic compounds against animals due to their mutagenic, carcinogenic and teratogenic properties. The results are in line with the formerly observed insensitivity of *A. theophrasti* against benzoxazinoids. It is assumed that root associated microorganisms can trigger effects of benzoxazolinone derived allelochemicals by molecule modifications and by shortening the time of exposure due to degradation processes.
Abutilon theophrasti seeds were purchased from Herbiseed (UK). They were germinated and grown hydroponically under greenhouse conditions for 10 d on cheesecloth-covered containers filled with tap water. The seedlings were transferred successively with their roots to 5 ml 50 mM phosphate buffer pH 5.8 supplemented with protease inhibitor cocktail (Sigma) and sonicated for 5 sec. The resulting protein solution was centrifuged for 10 min at 10000 g and 4 °C. The supernatant was assayed for 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one synthesis using the assay conditions described for the P. ananatis protein for 3 min. All EtOAc phases of the assays were analyzed by HPLC. Calculations of the product amounts based on standard curves established with the purified 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one.

For the degradation of 6-hydroxy-5-nitrobenzo[d] oxazol-2(3H)-one, BOA-6-OH primed Pantoea ananatis cultures were supplemented with 500 μl 40 μM 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one and incubated at 25 °C. Aliquots of the culture medium were taken directly after addition of the nitro-compound and then every hour over a period of 3 h and analyzed by HPLC. The Abutilon root surface protein fraction was assayed for compound degradation by adding 5 μl of 10 mM 6-hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one to 50 μl phosphate buffer (pH 6.5).

The inhibitory activity of the nitro compound was bioassayed with Abutilon theophrasti and Lepidium sativum. Lepidium sativum seeds were purchased from a local garden supplier. Abutilon and Lepidium seedlings (Abutilon 8; Lepidium 15 germinating seeds/ dish) with emerging radicles were transferred on filter paper placed in Petri dishes. The bioassays were performed as described by Macias and coworkers.16 at pH 4.0, 5.0, 6.0 (all 100 mM Mes buffers) and 7.0 (100 mM Hepes buffer) with each 0, 8.6, 86, 430 and 860 μM 6-hydroxy-5-nitrobenzo[d] oxazol-2(3H)-one. Root and shoot lengths were measured after 1.5 d. The bioassays were repeated 5 times. IC50 values were determined as described by Baerson and coworkers.19 The t-test was used for statistical analysis of all data. The error bars are based on the SD. In figures, the data are presented as the mean ± standard deviation. Each data point is based on at least 3 biologic replicates from 3 independent experiments, if not otherwise noted.

Abbreviations

6-Hydroxy-5-nitrobenzo[d]oxazol-2(3H)-one  NO2-BOA-6-OH

BOA-6-OH  6-hydroxybenzoxazolin-2(3H)-one

UPLC-ESI-MS  Ultra Performance Liquid Chromatography- Electrospray Ionisation Mass Spectrometry

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

References

[1] Schulz M, Tabaglio V, Marocco A, Macias FA, Molinillo JMG. Benzoazainoids in rye allelopathy – from discovery to application in sustainable weed control and organic farming. J Chem Ecol 2013; 39:154-74; PMID:23385365; https://doi.org/10.1007/s10886-013-0235
[2] Schulz M, Wieland I. Variations in metabolism of BOA among species in various field communities - biochemical evidence for co-evolutionary processes in plant communities? Chemoecology 1999; 9:133-41; https://doi.org/10.1007/s000490050044
[3] Tabaglio V, Gavazzi C, Schulz M, Marocco A. Alternative weed control using the allelopathic effect of natural benzoazainoids from rye mulch. Agron Sustain Dev 2008; 28:397-401; https://doi.org/10.1051/agro:2008004
[4] Schulz M, Marocco A, Tabaglio V. BOA detoxification of four summer weeds during germination and seedling growth. J Chem Ecol 2012; 38:933–46; PMID:22614450; https://doi.org/10.1007/s10886-012-0156-4
[5] Haghi Kia S, Schulz M, Ayah E, Schouten A, Mullerborn C, Paetz C, Schneider B, Hofmann D, Disko U, Tabaglio V, et al. Abutilon theophrasti defense against the allelochemical benzoxazolin-2(3H)-one: Support by Actinomucor elegans. J Chem Ecol 2014; 40:128-98; PMID:25432667; https://doi.org/10.1007/s10886-014-0529-7
[6] Walterson A M, Stavrinides I. Pantocea: insights into a highly versatile and diverse genus within the Enterobacteriaceae. FEMS Microbiol Rev 2015; 39:968-84; PMID:26109597; https://doi.org/10.1093/femsre/fuv027
[7] Barloy-Hubler F, Cheron A, Helléguarch A, Galibert F. Smc01944, a secreted peroxidase induced by oxidative stresses in Sinorhizobium meliloti 1021. Microbiology 2004; 150:657-64; PMID:14993315; https://doi.org/10.1099/mic.0.26764-0
[8] Madec S, Pichereau V, Jacq A, Paillard M, Boisset C, Gourlard F, Paillard C, Nicolas JL. Characterization of the secretomes of two vibrios pathogenic to mollusks. PLoS one 2014; 9:e113097; PMID:25401495; https://doi.org/10.1371/journal.pone.0113097
[9] De Maayer P, Chan WY, Rubagotti E, Venter SN, Toth I, Burch PRJ, Coutinho TA. Analysis of the Pantoea ananatis pan-genome reveals factors underlying its ability to colonize and interact with plant, insect and vertebrate hosts. BMC Genomics 2014; 15:404; PMID:24884520; https://doi.org/10.1186/1471-2164-15-404
[10] Hara Y, Kadotani N, Izu H, Katakshina JL, Kuvaeva TM, Andreeva IG, Golubeva LI, Malko DB, Makeev VJ, Mashko SV, et al. The complete genome sequence of Pantoea ananatis AJ13355, an organism with great biotechnological potential. Appl Microbiol Biotechnol 2012;
[11] Sakihamaa Y, Tamakia R, Shimojia H, Ichibac T, Fukushib Y, Taharab S, Yamasakia H. Enzymatic nitration of phytophenolics: Evidence for peroxynitrite-independent nitration of plant secondary metabolites. FEBS Letters 2003; 553:377-80; PMID:14572654; https://doi.org/10.1016/S0014-5793(03)01059-7

[12] Winkler R, Hertweck C. Sequential enzymatic oxidation of aminoarenes to nitroarenes via hydroxylamines. Angew Chem 2005; 4:4083-7; https://doi.org/10.1002/anie.200500365

[13] Zikmundova M, Drandarov K, Bigler L, Hesse M, Werner C. Biotransformation of 2-benzoazolinone and 2-hydroxy-1,4-benzoxazin-3-one by endophytic fungi isolated from Aphelandra tetragona. Appl Environ Microbiol 2002; 68:4863-70; PMID:12324332; https://doi.org/10.1128/AEM.68.10.4863-4870.2002

[14] Rousseau B, Dostal L, Rosazza JPN. Biotransformations of tocopherols by Streptomyces catenulae. Lipids 1997; 32:79-84; PMID:9075197

[15] Ju KS, Parales RE. Nitroaromatic compounds, from synthesis to biodegradation. Microbiol Molec Biol Rev 2010; 74:250-72; PMID:20508249; https://doi.10.1128/MMBR.00006-10

[16] Macías FA, Marin D, Oliveros-Bastidas A, Castellano D, Simonet AM, Molinillo MGJ. Degradation studies on benzoxazinoids. Soil degradation dynamics of (2r)-2-O-β-D-glucopyranosyl-4-hydroxy-(2h)-1,4-benzoxazin-3(4h)-one (DIBOA-Glc) and its degradation products, phytotoxic allelochemicals from gramineae. Agric Food Chem 2005; 53:538-48; PMID:15686401; https://doi.10.1021/jf048702l

[17] Bruhn C, Lenke H, Knackmuss J. Nitrosubstituted aromatic compounds as nitrogen source for bacteria. Appl Environ Microbiol 1987; 53:208-10; PMID:16347259

[18] Sax IR, Lewis RJ. Dangerous Properties of Industrial Material. 7th ed., vol. II; New York: Van Nostrand Reinhold; 1989.

[19] Baerson SR, Sanchez-Moreira A, Pedrol-Bonjoch N, Schulz M, Kagan IN, Agarwal AK, Reigosa MI, Duke SO. Detoxification and transcriptome response in Arabidopsis seedlings exposed to the allelochemical benzoxazolin-2(3H)-one. J Biol Chem 2005; 280:21867-81; PMID:15824099; https://doi.10.1074/jbc.M500694200