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Synthesis of 4-Hydroxy-7,8-dimethoxyisochroman-3-one and Its Plant Growth-Regulating Properties on Tobacco (*Nicotiana tabacum* cv. Petit Havana)

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The synthesis of 6,7-dimethoxy-4-hydroxyisochroman-3-one **10** from 2,3-dimethoxytoluene (**11**) via glyoxylate **12** is reported. Compound **10** strongly inhibited vegetative growth of tobacco plants, whereas developmental patterns (protein levels, protein profile, pigments, and chlorophylls) were not affected. Morphological changes were observed in the leaves of the treated plants.

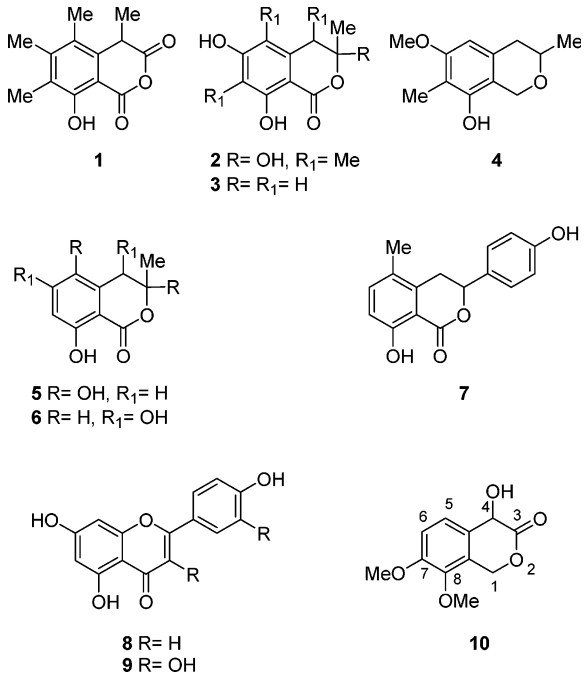
KEYWORDS: Synthesis; plant growth regulation; isochroman-3-one; tobacco (*Nicotiana tabacum* cv. Petit Havana)

INTRODUCTION

Several natural and synthetic benzopyran derivatives (isochromanes, isocoumarines, flavonoids, chromones) have demonstrated interesting effects on plant growth. Sclerin (**1**) and sclerotinin A (**2**) promote seed germination and shoot elongation of castor bean, mung bean, rice, and other plants (*1*, *2*), while 6-hydroxymellein (**3**) is an inhibitor of pollen development (*3*) and several of its derivatives impaired the germination of *Setaria italica* and *Lepidium sativum* (*4*).

Cutler et al. (*5*) reported that isochromane **4** (*6*) significantly inhibits etiolated wheat coleoptile growth; they also prepared derivatives and analogues of **4**, many of which were found to act as auxin polar transport inhibitors (*7*, *8*). More recently, Michel (*9*) isolated dihydroisocoumarin **5** and the known phytotoxin **6** from the culture broth of the fungus causing Dutch elm disease, a vascular disease that kills the trees; the presence of phytotoxic compound **5** in infected trees has also been detected. In addition, it has been shown that hydrangenol (**7**), isolated from the flowers of *Hydrangea hortensia*, has synergistic effects on elongation caused by gibberellin (*10*), and the effects of coumarin and substituted coumarins on plant growth have long been known (*11*).

On the other hand, Taniguchi and co-workers tested the activity of 1- and 4-substituted isochroman-3-ones as plant growth inhibitors (*12*), after demonstrating that 2-substituted phenylacetic acid derivatives are capable of inducing antigeotropism and inhibition of radicle and hypocotyl elongation of seedling plants (*13*, *14*). These authors found that most isochroman-3-ones without substituent at C-1 had no significant growth-regulating activity on rice seedlings.



It has also been reported that the flavonoids apigenin (**8**) and quercetin (**9**) are able to perturb auxin transport (*15*−*18*). These natural products have been proposed as endogenous auxin polar transport regulators. Finally, Tobler et al. (*19*) have shown that certain 4-substituted isochroman-3-ones can act as antidotes, being capable of reducing the damage caused to wheat by the herbicide clodinafop, thus allowing the selective control of weeds in useful plant cultivations.

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Herein, we report the synthesis of 7,8-dimethoxy-4-hydroxyisochroman-3-one (**10**) from commercially available 2,3-dimethoxytoluene (**11**) and its growth-regulating properties on tobacco (*Nicotiana tabacum* cv. Petit Havana) plants. This is of importance because although certain isochromans have demonstrated influence on plant growth, the activity of 4-hydroxyisochroman derivatives has not been tested. Interestingly, the presence of a benzylic oxygen substituent has been linked to the biological activity of certain natural products bearing an isochroman moiety such as the pyranonaphthoquinone antibiotics (*20*).

MATERIALS AND METHODS

The melting point (uncorrected) was taken on an Ernst Leitz Wetzlar model 350 hot-stage microscope. Fourier transform infrared (FT-IR) spectra were determined with a Bruker IFS 25 FT-infrared spectrophotometer. The ^{1}H and ^{13}C NMR spectra were acquired with a Bruker AC200-E spectrometer (200.13 MHz for ^{1}H), employing $CDCl_3$ as solvent; the chemical shifts are expressed in parts per million (ppm) downfield from the internal standard (TMS). High-resolution mass spectral data were obtained from the Kent Mass Spectrometry Unit 1 (Kent, U.K.). Reagents and solvents were used as received; dry MeOH was obtained by distillation from magnesium methoxide. Starting glyoxylate **12** was prepared in 77% yield (three steps) from commercially available (Aldrich Chemical Co.) 2,3-dimethoxytoluene (**11**) by Friedel−Crafts acylation with ethyl oxalyl chloride, followed by *N*-bromosuccinimide- (NBS-) mediated benzylic bromination and subsequent nucleophilic displacement of the bromide with sodium acetate in hexamethylphosphoramide (HMPA)−toluene (1:3) mixed solvent (*21*). Flash column chromatographies were carried out with silica gel 60 H and eluted with hexanes−EtOAc employing gradient techniques. All new compounds gave single spots on thin-layer chromatography (TLC) plates (Merck, art. 5554) run in different hexanes−ethyl acetate solvent systems. Chromatographic spots were detected by exposure to UV light (254 nm) followed by spraying with ethanolic *p*-anisaldehyde/sulfuric acid reagent and careful heating of the plates for better selectivity.

Ethyl {2-[(Acetoxy)methyl]-3,4-dimethoxyphenyl}(hydroxy)-acetate (13). Under a nitrogen atmosphere, a solution of keto ester **12** (*21*) (1001.4 mg, 3.23 mmol) in absolute ethanol (40 mL) was successively treated with glacial acetic acid (0.184 mL, 3.23 mmol) and sodium cyanoborohydride (223.7 mg, 3.55 mmol), and the mixture was stirred overnight at room temperature. The reaction was quenched with 1 N NaOH (5 mL), diluted with brine (10 mL), and extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed once with brine (5 mL), dried (Na_2SO_4), concentrated under reduced pressure, and chromatographed, providing mandelate **13** (918 mg, 91%), as an oil; R_f = 0.33 (hexanes−EtOAc 1:1); IR (film, ν) 3460, 2980, 2850, 1740, 1730, 1600, 1500, 1460, 1280, 1090 and 810 cm^{-1}; ^{1}H NMR (δ) 1.22 (s, 3H, J = 8.6 Hz, OCH$_2$*Me*), 1.60 (br s, 1H, OH), 2.07 (s, 3H, *Me*CO$_2$), 3.84 (s, 3H, OMe), 3.86 (s, 3H, OMe), 4.20 (dq, 2H, J = 1.0 and 8.6 Hz, OC*H*$_2$Me), 5.35 (s, 2H, ArC*H*$_2$O), 5.40 (br s, 1H, ArC*H*OH), 6.92 (d, 1H, J = 8.6 Hz, ArH) and 7.10 (d, 1H, J = 8.6 Hz, ArH); ^{13}C NMR (δ) 13.88 (*Me*CH$_2$), 20.86 (*Me*CO$_2$), 55.56 (OMe-7), 57.60 (ArCH$_2$O), 61.20 (OMe-8), 61.97 (MeCH$_2$O), 69.77 (ArCHOH), 112.71 (C-5), 122.97 (C-6), 128.03 (C-2), 130.88 (C-1), 148.46 (C-4), 152.65 (C-3), 170.73 (C═O), and 173.60 (C═O). HRMS for $C_{15}H_{20}O_7$: calcd, 312.12087; found, 312.12087.

4-Hydroxy-7,8-dimethoxyisochroman-3-one (10). A mixture of mandelate **13** (250 mg, 0.80 mmol) and camphorsulfonic acid (93 mg, 0.4 mmol) in anhydrous MeOH (8 mL) was warmed to 40 °C and stirred for 6 h. After cooling, the reaction mixture was diluted with brine (10 mL) and extracted with EtOAc (3 × 10 mL); the organic extracts were washed with brine (10 mL) and dried over Na_2SO_4. Concentration of the solvent *in a vacuum* afforded a residue, which was purified by column chromatography to give α-hydroxylactone **10** (160 mg, 89%), as a white solid, mp 126−128 °C (hexanes−EtOAc); R_f = 0.38 (hexanes−EtOAc 1:1). IR (KBr, ν) 3466, 2980, 2870, 1734, 1496, 1456, 1380, 1276, 1258, 1206, 1142, 1086, 1024, 818, and 806 cm^{-1}; ^{1}H NMR (δ) 3.62 (br s, 1H, $w_{1/2}$ = 8 Hz, OH), 3.87 (s, 3H, OMe), 3.88 (s, 3H, OMe), 5.10 (br s, 1H, H-4), 5.16 (d, 1H, J = 14.5 Hz, ArC*H*$_2$O), 5.64 (d, 1H, J = 14.5 Hz, ArC*H*$_2$O), 6.98 (d, 1H, J = 8.4 Hz, H-6), and 7.30 (d, 1H, J = 8.4 Hz, H-5); ^{13}C NMR (δ) 55.86 (OMe-7), 61.04 (OMe-8), 64.06 (C-1), 67.24 (C-4), 113.01 (C-6), 118.92 (C-7a), 122.90 (C-5), 126.59 (C-4a), 144.40 (C-7), 151.66 (C-8) and 173.76 (C-3). HRMS for $C_{11}H_{12}O_5$: calcd, 224.06847; found, 224.06823.

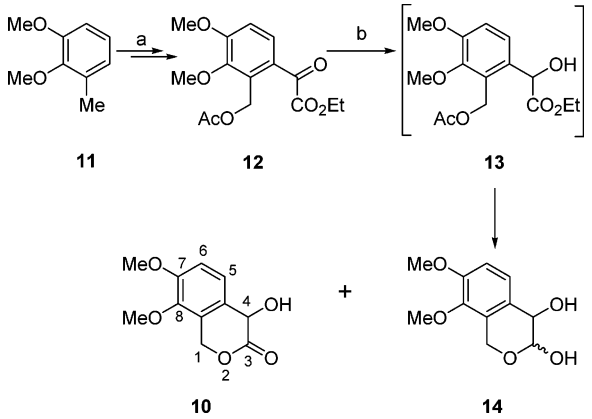
4-Hydroxy-7,8-dimethoxyisochroman-3-one (10) and 7,8-Dimethoxyisochroman-3,4-diol (14) from Glyoxylate 12. To a stirred solution of glyoxylate **12** (1000 mg, 3.22 mmol) in anhydrous MeOH (20 mL) were successively added $NaBH_4$ (243.6 mg, 6.45 mmol), K_2CO_3 (568 mg, 4.12 mmol), and NaOH (1.5 mL, 1.5 mmol), and the reaction was stirred overnight at room temperature. Diluted HCl was added until pH = 2, and after stirring for 15 min, the reaction was diluted with brine (20 mL) and extracted with EtOAc (4 × 30 mL). The combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Chromatographic purification of the residue furnished α-hydroxyketone **10** (268 mg, 37%), whose spectral data were in agreement with those of the compound obtained by lactonization of **l3** (vide supra). Increasing solvent polarity provided α-hydroxylactol **14** (175 mg, 24%) as a solid consisting in a 1:1 mixture of diastereomers; R_f = 0.35 (hexanes−EtOAc 3:7). IR (KBr, v) 3392, 3262, 2953, 2929, 1495, 1448, 1281, 1230, 1128, 1087, 1020, and 997 cm^{-1}. Major diastereomer: ^{1}H NMR (δ) 2.04 (d, 1H, J = 9.8 Hz, OH-3), 3.00 (d, 1H, J = 4.4 Hz, OH-4), 3.82 (s, 3H, OMe), 3.88 (s, 3H, OMe), 4.44 (br dd, 1H, J = 4.4 and 9.8 Hz, H-3), 4.74 (d, 1H, J = 16.1 Hz, H-1), 5.15 (d, 1H, J = 16.1 Hz, H-1), 5.20 (t, 1H, J = 4.4 Hz, H-4), 6.90 (d, 1H, J = 8.5 Hz, H-5), and 7.19 (d, 1H, J = 8.5 Hz, H-6); ^{13}C NMR (δ) 55.70 (OMe-7), 60.03 (OMe-8), 62.50 (C-1), 66.41 (C-4), 93.27 (C-3), 111.88 (C-5), 125.37 (C-8a), 127.01 (C-6), 128.16 (C-4a), 143.72 (C-7), and 152.00 (C-8). Minor diastereomer: ^{1}H NMR (δ) 2.16 (d, 1H, J = 7.7 Hz, OH-3), 3.48 (d, 1H, J = 3.0 Hz, OH-4), 3.86 (s, 3H, OMe), 3.98 (s, 3H, OMe), 4.44 (br dd, 1H, J = 2.0 and 7.7 Hz, H-3), 4.84 (d, 1H, J = 15.9 Hz, H-1), 4.97 (dd, 1H, J = 2.0 and 3.0 Hz, H-4), 4.98 (d, 1H, J = 15.9 Hz, H-1), 6.90 (d, 1H, J = 8.5 Hz, H-5), and 7.19 (d, 1H, J = 8.5 Hz, H-6); ^{13}C NMR (δ) 55.70 (OMe-7), 59.58 (C-1), 60.03 (OMe-8), 67.91 (C-4), 95.12 (C-3), 111.79 (C-5), 124.48 (C-8a), 126.27 (C-6), 127.37 (C-4a), 143.64 (C-7), and 151.65 (C-8). HRMS for $C_{11}H_{14}O_5$: calcd, 226.08413; found, 226.08383.

Effect of Compound 10 on the Germination of Tobacco Seeds. The seeds were sterilized by exposure to sodium hypochlorite (1 mL of a 1.6% solution) containing Tween 80 (0.05%) during 15 min, followed by four washings with sterilized distilled water; subsequent manipulations were carried out under a horizontal laminar flow. The seeds were germinated in an environment-controlled growth room at 25 °C in Petri dishes (36 seeds/dish) containing 15 mL of MS0 agar (*22*) and different concentrations of **10** and a control, employing a 16 h/8 h photoperiod. Fresh weight and percentage of germinated seeds were measured after 30 days.

Effect of Compound 10 on Vegetative Growth of Tobacco Plants. Two-week-old plants grown in MS0 medium were transferred to Magenta boxes (4 seedlings/box) and exposed to different concentrations of **10** (10^{-3}−10^{-7} M). After 1 month, three plants of each box were taken for analyses. Shoots and roots were homogenized to a fine powder by treatment with liquid nitrogen, and the powders were suspended in 1.5 volumes of homogenization solution [50 mM Tris-HCl, pH 7.8, 5 mM $MgCl_2$, 5 mM dithiotreitol, 5 mM ethylenediaminetetraacetic acid (EDTA), and 1 mM phenylmethanesulfonyl fluoride (PMSF)]. Protein levels were quantitated according to the spectrophotometric procedure of Bradford against a standard of bovine serum albumin ($E_{1\%,1cm}$ = 6.67 at 279 nm) (*23*), while the protein profile was determined (25 μg of protein/lane) by sodium dodecyl sulfate−polyacrylamide gel electrophoresis (SDS−PAGE) (12% polyacrylamide), followed by staining with Coomassie Brilliant Blue (*24*). Proteins were denatured by incubation during 10 min at 85 °C with a solution containing 60 mM Tris-HCl, pH 6.8, 1.25% (v/v) 2-mercaptoethanol, 10% (v/v) glycerin, 2% (w/v) sodium dodecyl sulfate, and 0.15 mg/mL Bromophenol Blue.

Pigment levels (carotenes, chlorophyll a, and chlorophyll b) were determined in ethanolic extracts according to Lichtenthaler (*25*).

Scheme 1[a]



[a] Reagents and conditions: (a) (1) EtO_2CCOCl, $AlCl_3$, CH_2Cl_2, 0 °C (94%); (2) NBS, CCl_4, reflux, 90 min (91%); (3) NaOAc, Ac_2O, HMPA–PhMe (1:3), RT, overnight (90%), see ref 21; (b) (1) $NaBH_4$, MeOH, K_2CO_3, NaOH; (2) dil HCl, pH = 2 (**14**, 24%; **10**, 37%).

Optical Microscopic Observation of the Leaves. The anatomical study was performed on leaves that were fixed in formaldehyde−acetic acid−50% ethanol (1:1:18 v/v/v) solution, dehydrated through a graded *n*-butanol series (50%, 70%, 85%, 95%, 100%), and embedded in paraffin wax, according to standard methods. Transversal sections, 6−8 μm thick, of the leaf were then cut, stained with Cresyl Violet, and mounted in Canada balsam (*26*, *27*). The photomicrographs were taken with the aid of a Zeiss Axiolab microscope fitted with an MC 80 camera.

RESULTS AND DISCUSSION

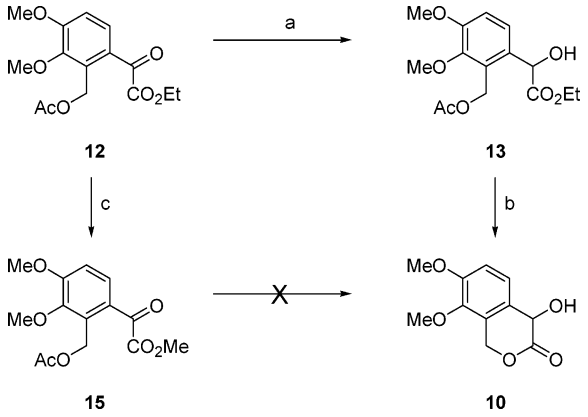
Numerous synthetic strategies have been put in practice for the elaboration of molecules carrying the isochroman skeleton (*28*); however, few of them allow the direct synthesis of isochroman-3-ones (*29*, *30*) and only scattered procedures yield 4-hydroxyisochroman derivatives (*31*−*35*). Furthermore, oxidation of the C-4 position of the isochroman skeleton is a difficult task due to the ease with which C-1 undergoes oxidation (*36*, *37*).

We decided to develop a strategy in which the 4-hydroxy substituent is introduced early in the synthesis and the heterocyclic ring containing the lactone moiety is accessed by acid-catalyzed lactonization of an appropriate precursor. This provided an extremely simple and straightforward synthesis of the desired compound **10**. In a first approach depicted in Scheme 1, submission of the easily accessible glyoxylate **12** (*21*) to reduction with sodium borohydride in dry methanol, to which 1.3 equiv of potassium carbonate and 0.45 equiv of NaOH had been added, directly furnished the desired α-hydroxylactone **10**, presumably through the intermediacy of mandelate **13**. However, the isolated yield was only 37% and the expected α-hydroxylactone required separation from more polar overreduction products, such as the α-hydroxylactol **14**, produced in 24% yield.

Therefore, a two-step synthesis was devised. Initially, and in order to avoid overreduction, glyoxylate **12** was selectively converted into mandelate **13** in 91% yield with sodium cyanoborohydride in absolute EtOH to which acetic acid was added, as shown in Scheme 2; then, compound **13** was submitted to a camphorsulfonic acid-promoted lactonization in dry MeOH, smoothly affording α-hydroxylactone **10** as the sole product in 89% isolated yield.

It was observed that reduction of starting glyoxylate **12** to mandelate **13** must be carried out before the cyclization step, since attempts to lactonize **12** in MeOH under camphorsulfonic acid promotion resulted exclusively in transesterification of the starting material to the related methyl ester **15**, which was unable to cyclize under the acidic conditions tested. On the other hand, basic hydrolysis of both ester groups of **12** followed by acidic workup also failed to give the expected cyclized product. Therefore, the route shown in Scheme 2 can be considered as the simplest and most efficient one to access **10**.

Scheme 2[a]



[a] Reagents and conditions: (a) $NaCNBH_3$, $AcOH_{gl}$, EtOH, RT, overnight (91%); (b) camphorsulfonic acid (5 mol %), MeOH, 40 °C, 6 h (89%); (c) camphorsulfonic acid (5 mol %), MeOH, 40 °C, 6 h (100%).

Table 1. Effect of **10** on the Germination of Tobacco Seeds

concn of **10**[a] (M)	fresh wt[b] (mg)	% germination[c]
control	81.1 ± 5.8	83 ± 5
1×10^{-5}	20.6 ± 8.3	82 ± 10
1×10^{-3}	25.0 ± 17.0	76 ± 11

[a] Tobacco seeds were germinated in Murashige–Skoog (MS0) agar (*22*) supplemented or not with the indicated concentrations of **10**. Experiments were carried out in duplicate. [b] Seedlings (shoots and roots) were withdrawn at 4 weeks after the seeds were planted, extensively rinsed to remove agar debris, and weighed. Means and standard deviations are expressed per Petri dish. [c] With reference to 36 ± 5 seeds per Petri dish.

Table 2. Number of Leaves, Fresh Weight, and Total Foliar Area of Tobacco Plants Grown in MS0 Medium Containing Different Concentrations of **10**[a]

concn of **10**[b] (M)	no. of leaves	fresh wt[c] (g)	total foliar area (cm^2)
control	9	0.83 ± 0.04	111.3
1×10^{-7}	9	0.74 ± 0.00	102.4
1×10^{-5}	9	0.44 ± 0.18	45.8
1×10^{-3}	8	0.24 ± 0.10	23.7

[a] Two-week-old plants were treated during 1 month. [b] Experiments were run in duplicate. [c] Fresh weight corresponds to the whole plant.

To study the activity of compound **10**, its effect on the germination of tobacco seeds was next evaluated. Analysis of the results collected in Table 1 evidenced that although **10** had no statistically significant effect on the percentage of germinating seeds (76% ± 11% in the presence of 10^{-3} M **10** vs 83% ± 5% in the control lot), a clear growth inhibition effect was observed after germination. At 30 days, the fresh weight of the plants exposed to 10^{-5} or 10^{-3} M **10** was 70−75% lower than that of the corresponding controls.

In a second series of experiments, vegetative development was studied in 2-week-old plants, grown in MS0 agar devoid of **10**. After exposure of the plants to the α-hydroxylactone at concentrations ranging from 10^{-3} to 10^{-7} M during 1 month, analysis of morphologic variables indicated important differences in fresh weight and total foliar area, as shown in Table 2.

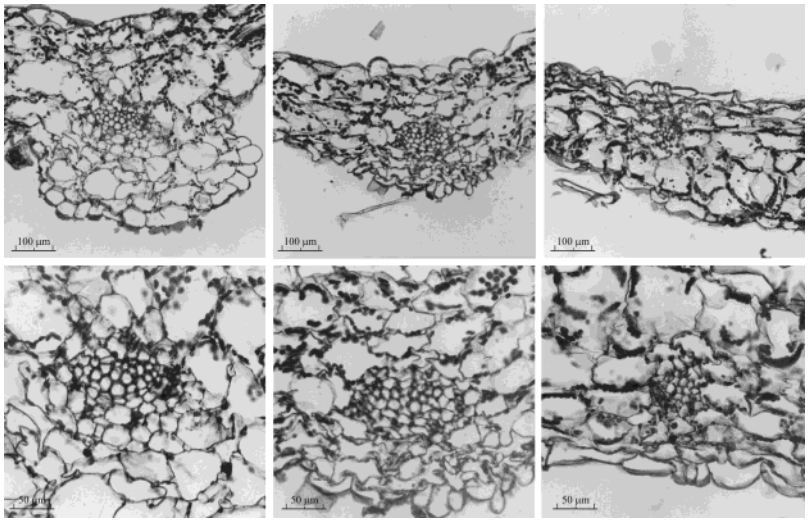


Figure 1. Morphological changes in leaves of tobacco plants (top) exposed to different concentrations of compound **10** and detailed views of the primary veins of the above samples (bottom). Left, control specimen; center, leaf of a plant exposed to **10** at a concentration of 10^{-5} M; right, leaf of a plant exposed to compound **10** at a concentration of 10^{-3} M.

Table 3. Determination of Pigment Levels of Plants Exposed to Different Concentrations of **10**

concn of **10** (M)	chlorophyll a (μg/mg of fresh weight)	chlorophyll b (μg/mg of fresh weight)	carotenes (μg/mg of fresh weight)	proteins (μg/mg of fresh weight)
control	1.05 ± 0.25	0.34 ± 0.11	0.21 ± 0.04	2.44 ± 0.25
10^{-7}	1.23 ± 0.01	0.37 ± 0.02	0.25 ± 0.01	2.78 ± 0.00
10^{-5}	1.21 ± 0.11	0.39 ± 0.02	0.25 ± 0.04	2.72 ± 0.20
10^{-3}	0.84 ± 0.13	0.26 ± 0.06	0.20 ± 0.04	2.22 ± 0.82

Values of 0.44 ± 0.18 and 0.24 ± 0.10 g were recorded for the fresh weight of plants exposed to concentrations of the test compound of 10^{-5} and 10^{-3} M, respectively, compared to 0.83 ± 0.04 g in the control plants, while the foliar area measured for plants grown in media containing 10^{-5} and 10^{-3} M α-hydroxylactone **10** were 45.8 and 23.7 cm^2, respectively; this represents 41% and 21.3% of the foliar area of the control plants.

On the other hand, the protein profiles, as well as the levels of total proteins (*23*), carotenes, and chlorophylls (a and b) (*24*) were also determined (Table 3), and no statistically significant differences were observed between the seedlings grown in media containing compound **10**, at a concentration of 10^{-3} M, and the corresponding controls.

Then, it can be concluded that treatments did not affect important metabolic pathways such as the synthesis of the major proteins and pigments, even at the highest concentration of the compound. The lack of effect on germination (Table 1) or in the number of leaves per plant (Table 2) also suggest that the developmental pattern was not affected, with the toxicity being limited to a significant inhibition of vegetative growth (cell division and/or expansion) that prevented plants from entering the flowering stage.

When the leaves were microscopically examined, morphological changes were clearly distinguished, as shown in the Figure 1. In the control specimen (left), the cross-sections of the leaves displayed their normal structure; dorsiventrally compressed, with a unistratified adaxial epidermis with well-developed cells. They also showed a smooth cuticle with stomata, the mesophyll was dorsiventral, and only one layer of palisade parenchyma was observable, with cells rich in chloroplasts, firmly pressed against the plasmalemma and the wall by a central vacuole. It was also detected that the spongy mesophyll contains laxly arranged cells widely separated by intercellular spaces and the abaxial epidermis also presents stomata; in addition, the primary vein, with a mean diameter of 100−110 μm, is well-developed in the abaxial face, having mature vessels of 10−12 μm in diameter.

When leaves of plants exposed to 10^{-5} M compound **10** were examined (center), images of the same zone revealed distinct cell deterioration and abnormal features, including disorganization of the parenchymatous structure and distortion of the cell wall. In addition, the primary vein size showed a slightly reduced size, with a mean diameter of 80−85 μm, and presented scanty vessels, transversed by a narrow ray of parenchyma. The mature vessel size was also reduced to a mean diameter of 7−8 μm.

Furthermore, when leaves from plants exposed to 10^{-3} M **10** were evaluated, it was observed that the cross-sections of the leaves showed a large parenchymatous mesophyll, with chloroplasts firmly pressed against the plasmalemma and the wall by a notoriously large central vacuole. A slight decline in the number and pigmentation of the chloroplasts was also detected. In addition, it was observed that the primary vein was composed of minute groups of vessels of small size, having a mean diameter of 50 μm, with the mature vessel size of only 5−6 μm in diameter.

It has been reported that certain isochroman derivatives behave as auxin transport inhibitors (*5*−*8*, *12*−*14*), producing similar effects on different model systems; therefore, the observed growth changes may be a result of the auxin transport inhibiting activity of α-hydroxylactone **10**, which, despite lacking a C-1 substituent, was active at lower doses than 1-substituted isochroman-3-ones (*12*).

In conclusion, a short and efficient synthesis of α-hydroxylactone **10** from the commercially available 2,3-dimethoxytoluene was described. Compound **10** inhibited the vegetative growth of tobacco seedlings, leading to lower fresh weight of the treated plants but without affecting protein and pigment levels. Changes observed are compatible with inhibition of cellular division, resulting in severe limitations in the enlargement of the meristematic tissue. The collected results suggest that compound **10** may act as an auxin transport inhibitor.

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