Isomeric Tropane Alkaloids from the Aerial Parts of *Schizanthus tricolor*

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Investigation of the aerial parts of *Schizanthus tricolor* yielded seven isomeric tropane alkaloids: 3α-(1-methylitaconyl)-6β-senecioyloxytropane (**1**), 3α-(1-methylitaconyl)-6β-angeloyloxytropane (**2**), 3α-(1-methylmesaconyl)-6β-senecioyloxytropane (**3**), 3α-(1-methylmesaconyl)-6β-angeloyloxytropane (**4**), 3α-(1-methylmesaconyl)-6β-tigloyloxytropane (**5**), 3α-(1-methylcitraconyl)-6β-senecioyloxytropane (**6**), and 3α-(1-methylcitraconyl)-6β-angeloyloxytropane (**7**). Their structures were established by NMR including ^{1}H, ^{13}C NMR, HSQC, HMBC, COSY, and NOESY experiments, UV, IR, and mass spectrometry. Compounds **1**, **6**, and **7** are new to the literature. Alkaloids **1**, **3**, **4**, and **5** and a mixture of **3**, **4**, and **5** were evaluated for in vitro antiplasmodial and cytotoxic activity. Compounds **1**, **4**, and **5** showed marginal inhibition of *Plasmodium falciparum* strain K1 with IC_{50} values of 22.8, 24.8, and 36.0 μM and displayed no cytotoxicity on MRC-65 cells (CC_{50} > 64 μM). Alkaloid **3** was inactive (IC_{50} 63.5 μM). The alkaloid mixture exhibited slightly higher activity (IC_{50} 17.0 μM) than the pure compounds, indicating some synergy between the different isomers.

Malaria is a scourge that affects humans mainly from the developing world, killing 1−3 million and causing disease in 300−500 million people annually. The most severe form of malaria is caused by *Plasmodium falciparum* in children in sub-Saharan Africa.[1] There is a need for new active substances to treat this disease due to the increase in resistance of the parasite toward current antimalarial medicines. As part of ongoing investigations of members of the genus *Schizanthus* in our laboratory,[2−5] an alkaloid extract was prepared from the Chilean species *Schizanthus tricolor* Grau et Gronbach (Solanaceae) and fractionated with the aim to isolate and characterize compounds having antimalarial potential.

The genus *Schizanthus* R. et. P. comprises 27 species, and 12 of these are endemic to Chile.[6,7] These plants grow on western slopes of the Andes and are cultivated for ornamental purposes. The genus *Schizanthus* is characterized by the presence of numerous tropane alkaloids esterified with the monocarboxylic isomeric C_5 acids angelic, senecioic, and tiglic acids and with the dicarboxylic C_5 itaconic and mesaconic acids. Esterification between these acids and 3α,6β-dihydroxytropane (Figure 1) leads to the formation of various positional isomers, as well as dimers and trimers.[7]

This paper describes the isolation and characterization of seven isomeric tropane alkaloid derivatives, as well as their antiplasmodial and cytotoxic activity. Compounds **1**, **6**, and **7** have not been described previously in the literature.

Results and Discussion

The alkaloid extract of aerial parts of *S. tricolor* showed inhibitory activity in vitro against *P. falciparum* (IC_{50} = 9.5 μg/mL) (Table 1). In order to identify the compounds responsible for the parasite growth inhibition, a preliminary bioassay-guided fractionation was carried out by flash chromatography on a small quantity of crude extract. Fraction 8 showed significant activity (IC_{50} = 1.9 μg/mL) and contained mainly seven isomers with a mass of 365 Da (compounds **1**−**7**).

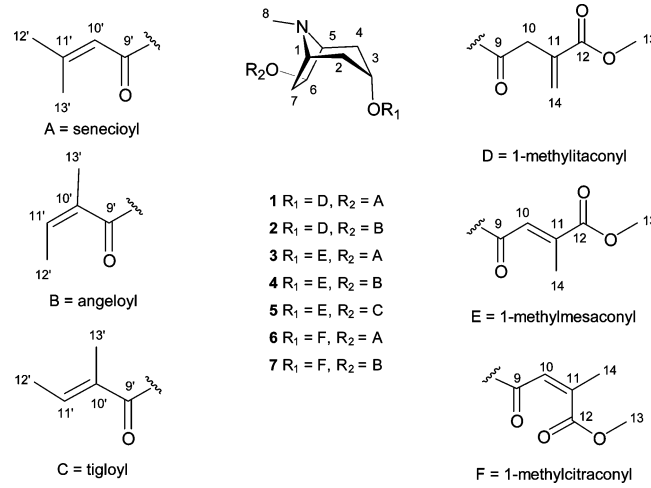

Figure 1. Structures of the seven isomers with a mass of 365 Da.

Table 1. In Vitro Activities of Crude Alkaloid Extract and Compounds **1**, **3**, **4**, and **5**

	P. falciparum K1	
	IC_{50} (μg/mL)	IC_{50} (μM)
crude alkaloid extract	9.5	
compound		
1	8.3	22.8
3	23.2	63.5
4	9.1	24.8
5	13.1	36.0
(**1**, **4**, and **5**)	6.2	17.0
amodiaquine		<0.25

Fractionation of the crude alkaloidal extract afforded two fractions containing seven isomers of 365 Da. Optimized chromatographic conditions were developed to separate the isomers at the analytical scale using ultra-high-pressure liquid chromatography (UHPLC) and then geometrically transferred to semipreparative LC.[8]

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Table 2. ^{1}H NMR Data of Compounds **1**−**7** in CD_3OD (500 MHz, *J* in Hz)[a]

position	1	2	3	4	5	6	7
1	3.32 br s	3.37 br s	3.34 br s	3.39 br s	3.35 br s	3.33 br s	3.37 br s
2_{endo}	1.63 d (15.2)	1.69 d (16.3)	1.75 d (15.4)	1.75 d (15.4)	1.74 d (15.5)	1.71 d (15.6)	1.75 d (15.2)
2_{exo}	2.11 m	2.15 m	2.19 m	2.19 m	2.18 m	2.17 m	2.16 m
3	4.98 t (5.2)	5.01 t[b]	5.07 t (5.3)	5.08 t (5.3)	5.08 t (5.2)	5.04 t[b]	5.04 t[b]
4_{endo}	1.83 d (14.6)	1.89 [c]	1.91 d (15.1)	1.93 d (18.1)	1.93 d (15.2)	1.96 [c]	1.98 [c]
4_{exo}	2.13 m	2.19 m	2.21 m	2.22 m	2.21 m	2.20 m	2.20 m
5	3.15 br s	3.23 br s	3.17 br s	3.23 br s	3.22 br s	3.23 br s	3.24 br s
6	5.37 dd (7.8, 3.2)	5.47 m [b]	5.44 dd (7.8, 3.2)	5.52 dd (7.8, 3.2)	5.49 dd (7.7, 3.2)	5.43 m [b]	5.51 m [b]
7_{endo}	2.51 m (7.1)	2.57 m	2.56 m (7.1)	2.60 m (7.1)	2.59 m (7.1)	2.57 m	2.59 m
7_{exo}	2.13 m	2.23 m	2.19 m	2.23 m	2.22 m	2.22 m	2.23 m
8	2.46 s	2.51 s	2.48 s	2.51 s	2.51 s	2.50 s	2.51 s
9							
10	3.38 d (0.8)	3.42 s	6.75 q (1.6)	6.77 q (1.6)	6.76 q (1.6)	6.09 s	6.10 s
11							
12							
13	3.75 s	3.77 s	3.80 s	3.81 s	3.80 s	3.80 s	3.81 s
14	a 5.83 d (1.0) b 6.33 d (1.0)	a 5.87 s b 6.36 s	2.27 d (1.6)	2.28 d (1.6)	2.27 d (1.6)	2.07 s	2.08 s
9′							
10′	5.65 s		5.68 s			5.70 s	
11′		6.14 m [b]		6.13 qq (7.2, 1.5)	6.87 qq (7.0, 1.5)		6.16 m [b]
12′	2.17 d (1.2)	1.99 s	2.16 d (1.2)	1.97 dq (7.2, 1.5)	1.80 dd (7.1, 1.0)	2.19 s	2.00 s
13′	1.91 d (1.2)	1.91 s	1.90 d (1.2)	1.87 m (1.5)	1.83 s	1.93 s	1.90 s

[a] Chemical shift values are in δ (ppm), and coupling constants are in parentheses. [b] No coupling constant due to low resolution for some signals recorded with capNMR probe. [c] No coupling constant due to overlapping peak problem.

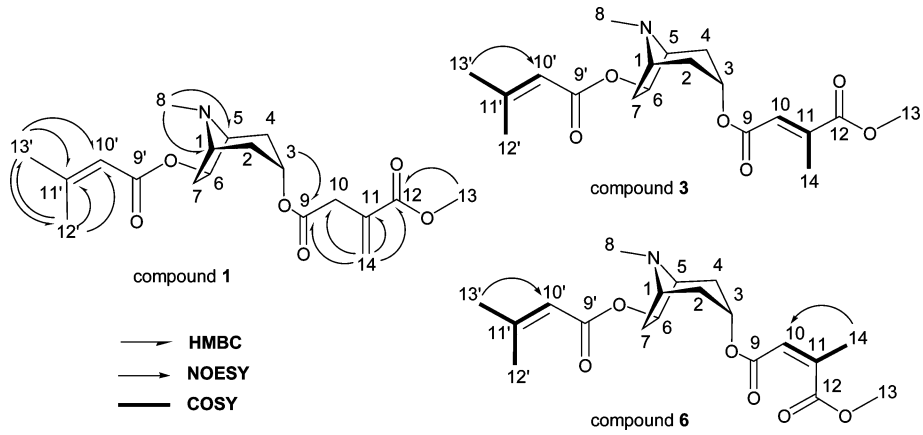

Figure 2. Important correlations for compounds **1**, **3**, and **6**.

HRMS provided the molecular formula $C_{19}H_{28}NO_6$ ($[M + H]^+$, *m/z* 366.4210−366.4236) for each compound, and infrared spectra showed an absorption band between 1715 and 1725 cm^{-1} that indicated the presence of ester function(s) in the molecule. The ^{1}H spectra (Table 2) showed proton signals characteristic of 3α,6*β*-diacyloxytropane for all the isomers with chemical shifts for H-1, H-3, H-5, and H-6 at δ 3.32−3.39 (br s), 4.98−5.08 (t, $J = 5.2-5.3$ Hz), 3.15−3.24 (br s), and 5.37−5.51 (dd, $J = 7.8, 3.2$ Hz), respectively.[9−12] Structures of the ester moieties of compound **1** were also determined from their characteristic signals in the ^{1}H spectra: δ 3.38 (2H, d, $J = 0.8$ Hz, H-10), 5.83 and 6.33 (1H each, s, H-14a and H-14b, respectively) for 1-methylitaconic ester, and δ 1.91 (3H, d, $J = 1.2$ Hz, H-13′), 2.17 (3H, d, $J = 1.2$ Hz, H-12′), and 5.65 (1H, m, H-10′) for senecioic ester.[13] The two methyl groups (H-12′ and H-13′) of the latter acid correlated in a 2D COSY experiment between them and with the vinylic proton H-10′. Similarly, the HMBC spectrum demonstrated that H-12′ and H-13′ correlated with C-10′. Another long-range HMBC correlation between H-3 and C-9 indicated attachment of the 1-methylitaconic ester on the tropane ring at C-3 (Figure 2). Thus, compound **1** was characterized as 3α-(1-methylitaconyl)-6*β*-senecioyloxytropane, a compound not described previously in the literature.

For compounds **2** to **5**, the chemical shifts observed for the esterified acids were as follows: δ 2.27−2.28 (3H, d, $J = 1.6$ Hz, H-14) and 6.75−6.77 (1H, q, $J = 1.6$ Hz, H-10) for 1-methylmesaconic esters; δ 1.87−1.91 (3H, m, H-13′), 1.97−1.99 (3H, dq, $J = 7.2, 1.5$ Hz, H-12′), and 6.13−6.14 (1H, qq, $J = 7.2, 1.5$ Hz, H-11′) for angelic esters; δ 1.80 (3H, dd, $J = 7.1, 1.0$ Hz, H-12′), 1.83 (3H, s, H-13′), and 6.88 (1H, qq, $J = 7.1, 1.0$ Hz, H-11′) for tiglic esters.[13,14] As for compound **1**, COSY and long-range HMBC correlations permitted us to identify esters and to confirm their positions on the tropane ring. In addition, these NMR data are similar to those of the literature, where compounds **2**, **4**, **5**[13] and **3**[14] were first described. However, for compounds **6** and **7**, signals

Table 3. ^{13}C NMR Data (δ) of Compounds **1**−**7** (125 MHz, in CD_3OD)

position	1	2	3	4	5	6	7
1	60.9	60.9	61.0	61.4	61.0	60.7	60.9
2	34.6	34.0	34.8	35.4	34.5	33.8	34.2
3	68.6	67.5	68.5	68.4	68.5	68.4	67.5
4	33.1	32.1	33.3	34.0	33.1	32.8	32.8
5	67.0	66.2	67.0	67.4	67.3	66.0	66.2
6	79.3	80.1	79.2	79.8	79.3	79.0	79.7
7	36.4	41.0	36.6	36.4	36.6	35.2	34.8
8	39.9	39.3	40.1	40.6	40.2	39.5	39.3
9	171.0	170.1	168.0	168.0	170.2	166.0	167.5
10	39.3	38.1	127.6	127.6	127.5	122.1	121.8
11	135.5	134.1	144.0	144.0	143.9	144.8	145.2
12	169.0	167.3	169.0	169.0	168.9	169.2	168.8
13	52.7	51.2	53.1	53.1	53.0	51.7	51.6
14	129.7	129.0	14.5	14.6	14.5	18.9	19.8
9′	[a]	170.14	[a]	169.5	169.7	[a]	170.1
10′	116.8	128.0	116.8	129.0	128.7	116.8	128.5
11′	159.0	139.2	159.0	139.5	139.0	158.5	139.2
12′	20.3	15.3	20.5	15.9	14.6	20.2	15.4
13′	27.4	19.4	27.4	20.7	12.2	27.2	19.6

[a] Signal too weak to be measured.

in the ^1H spectra at δ 6.09 and 6.10 (1H, s, H-10), respectively, were observed (Table 1) that did not match with any of the protons for the esters previously mentioned. Similarly, in the ^{13}C spectra, chemical shifts for C-14 at δ 18.9 and 19.8, respectively (Table 3), did not correspond to the chemical shift of C-14 of 1-methylmesaconic acid (δ 14.5−14.6). In the 2D COSY spectrum, H-10 correlated with H-14 at δ 2.07 and 2.08 (3H, s) for **6** and **7**, respectively. Finally, a 2D NOESY experiment revealed that H-10 was close in space to H-14 (Figure 2). This result demonstrated that H-10 and H-14 were *cis* configured in both **6** and **7** and implied the presence of 1-methylcitraconic acid. No correlation between H-10 and H-14 was observed in 2D NOESY spectra for 1-methylmesaconic acid (*trans* isomers **3**, **4**, **5**). To our knowledge, this is the first time that tropane alkaloids esterified with citraconic acid have been observed. A possible reason for the difficulty in isolating alkaloids esterified with this acid is the isomerization of the double bond between C-10 and C-11 in alkaline conditions, giving rise to esters of the *trans* isomer (1-methylmesaconic acid), which are thermodynamically more stable.[15]

Compounds **1**, **3**, **4**, and **5** showed weak activity against *P. falciparum* K1 strain (Table 1) compared to fraction 8 and to the control amodiaquine. Compounds **2**, **6**, and **7** were not tested due to insufficient quantities isolated for full investigation. A fraction containing compounds **1**, **4**, and **5** was also tested and showed slightly higher activity than the pure compounds. While synergy with compounds **2**, **6**, or **7** may be involved to explain this discrepancy, it is also possible that **2** or **6** or **7** (or another component) may have very much higher activity alone. No cytoxicity was detected for the pure compounds, the fractions, or the crude extract. Although the antiplasmodial activity was weak, this is the first time that an antiparasitic activity has been observed for tropane derivatives.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 241 polarimeter (MeOH, *c* in g/100 mL). UV spectra were recorded on a Perkin-Elmer Lambda-20 UV−vis spectrophotometer (Wellesley, MA) in MeOH. IR spectra were measured on a Perkin-Elmer Spectrum 100 instrument. ^1H and ^{13}C NMR spectra were recorded in CD_3OD on a Varian Unity Inova 500 MHz NMR instrument (Palo Alto, CA). For compounds **2**, **6**, and **7** (quantities less than 1 mg), ^1H spectra were recorded on the same instrument by direct injection of 5 μL samples in CD_3OD in a CapNMR probe from Protasis/MRM (Savoy, IL). GC-MS analyses were carried out using a Hewlett-Packard chromatograph 5890 series II coupled to a Hewlett-Packard 5972 mass spectrometer (Agilent Technologies, Palo Alto, CA). The MS transfer line was set at 280 °C, and the MS detector was used in electron ionization (EI) mode at 70 eV. Mass spectra were recorded in the range *m/z* 40−550 Da with a scan time of 1.0 s. A HP5-MS (Agilent) capillary column of 30 m × 0.25 mm i.d., 0.25 μm film thickness was used with He as carrier gas (1 mL/min). The oven temperature program was a linear gradient from 70 to 285 °C at 5 °C/min, then hold at the final temperature for 15 min. Sample volumes of 1 μL were injected in splitless mode into a laminar linear at 250 °C using a fast HP 6890 series autosampler. Retention indices were calculated using the Van Den Dool and Kratz model with a series of *n*-alkanes (C_8−C_{30}) as reference standards. HRMS spectra were obtained on a Micromass LCT Premier time-of-flight mass spectrometer (Waters, Milford, MA) using electrospray in positive mode. Capillary voltage was set at 2.8 kV, cone voltage at 40 V, source temperature at 120 °C, desolvation temperature at 250 °C, cone gas flow at 20 L/h, and desolvation gas flow at 600 L/h. UHPLC was performed on an Acquity UPLC System (Waters) with an Acquity BEH C18 column (1.7 μm; 50 × 2.1 mm i.d.; Waters). Low-pressure liquid chromatography was performed with an Ismatec pump (Glattbrugg, Switzerland) equipped with a Knauer UV detector, using a Si-60 Lichroprep (40−63 μm; 440 × 37 mm i.d.; Merck) and a RP-18 Lichroprep (40−63 μm; 310 × 25 mm i.d.; Merck) column. Flash chromatography was performed on an ARMEN Spot System (Saint-Avé, France) with a SVF D26 precolumn (RP-18, 40−63 μm, Merck) and a RP-18 Lichroprep column (15−25 μm; 400 × 30 mm i.d.). Semipreparative LC using a XTerra Prep-MS C18 ODB column (5 μm, 19 × 150 mm; Waters) was performed with a Varian 9012 pump coupled with a triple quadrupole mass spectrometer (TSQ700, Finnigan MAT, San Jose, CA) equipped with a Finnigan ESI interface. ESI conditions: capillary temperature 200 °C, source voltage 4.5 kV, sheath gas nitrogen 50 psi, acquisition in positive ion mode, full scan *m/z* 100−500 Da, scan time 0.5 s. A Quicksplit adjustable flow splitter (El Sobrante, CA) was used to split the flow to the MS detector and to manually collect samples. To ensure simultaneous MS detection and fraction collection, a tube of 3 m length (0.01 in. i.d.) was used for collecting samples, with a 25 cm length fused silica capillary (50 μm i.d.) between the splitter and the MS system.[16]

Plant Material. Aerial parts of *S. tricolor* were collected in December 2003 in Cachagua (Chile). Their identification was confirmed by Prof. Fernanda Pérez (Departamento de Botanica, Universidad de Chile). Voucher specimens were deposited at the Facultad de Ciencas Quimicas (No. 2000-3).

Extraction and Isolation. The plant material (1.3 kg) was extracted successively with hexane and MeOH at room temperature. After filtration, the alcoholic solution was evaporated to dryness. The residue (161.2 g) was taken up in 0.1 M HCl and extracted with Et_2O. The aqueous solution was basified with 4% NH_4OH to pH 12 and then extracted with CH_2Cl_2. The organic solvent was dried with anhydrous Na_2SO_4, filtered, and evaporated, yielding 3.7 g of a gummy alkaline residue. First, 2.5 g of extract was fractionated by low-pressure chromatography on a Lobar silica gel column eluted with EtOAc−MeOH−3% NH_4OH (20:2:1), giving 13 fractions (A−M). Fractions E and F were combined (270 mg) and further separated on a Lobar RP-18 column using a solvent gradient of alkaline H_2O−MeOH (10

to 100%) (pH 8), which gave 22 fractions (1−22). Fractions 4 (20 mg) and 14 (12 mg) were purified by semipreparative LC with the eluent MeCN−H_2O (1:4) each containing 0.1% NH_4OH in isocratic mode. Fraction 4 yielded 1.3 mg of 3α-(1-methylitaconyl)-6β-senecioyloxytropane (**1**), 0.3 mg of 3α-(1-methylitaconyl)-6β-angeloyloxytropane (**2**), 2.7 mg of 3α-(1-methylmesaconyl)-6β-senecioyloxytropane (**3**), and 1.5 mg of 3α-(1-methylmesaconyl)-6β-angeloyloxytropane (**4**). Fraction 14 yielded 1.0 mg of 3α-(1-methylmesaconyl)-6β-tigloyloxytropane (**5**), 0.6 mg of 3α-(1-methylcitraconyl)-6β-senecioyloxytropane (**6**), and 0.3 mg of 3α-(1-methylcitraconyl)-6β-angeloyloxytropane (**7**).

Antiplasmodial and Cytotoxicity Assays. The malaria and cytotoxicity screens were conducted as previously described.[17] Results are expressed in μg/mL for plant extracts and in μM for pure compounds. Amodiaquine was used as positive control.

In vitro *P. falciparum* Culture and Drug Assay. The K1 strain of *P. falciparum* (resistant to chloroquine and pyrimethamine) was used. Parasites were cultured in human erythrocytes A+ at 37 °C under a low oxygen atmosphere (3% O_2, 4% CO_2, and 93% N_2) in a modular incubation chamber. The culture medium was RPMI-1640, supplemented with 10% human serum. Two hundred microliters of infected human red blood cell suspension (1% parasitaemia, 2% hematocrit) was added to each well of the plates with test compounds and incubated for 72 h. After incubation, test plates were frozen at −20 °C. Parasite multiplication was measured by the Malstat method. One hundred microliters of Malstat reagent was transferred in a new plate and mixed with 20 μL of the hemolysed parasite suspension for 15 min at room temperature. After addition of 20 μL of NBT/PES solution and 2 h incubation in the dark, the absorbance was spectrophotometrically read at 655 nm (Biorad 3550-UV microplate reader). Percentage growth inhibition was calculated compared to the negative blanks.

Cytotoxicity Test on MRC-5 Cells. MRC-5 SV2 cells, human fetal lung fibroblasts, were cultivated in MEM, supplemented with L-glutamine (20 mM), 16.5 mM $NaHCO_3$, and 5% FCS at 37 °C and 5% CO_2. For the assay, 104 MRC-5 cells/well were seeded onto the test plates containing the prediluted compounds and incubated at 37 °C and 5% CO_2 for 72 h. After incubation, parasite growth was assessed fluorimetrically by adding resazurin for 24 h at 37 °C. Fluorescence was measured using a GENios Tecan fluorimeter (excitation 530 nm, emission 590 nm).

3α-(1-Methylitaconyl)-6β-senecioyloxytropane (1): colorless oil; $[\alpha]_D^{22}$ −10 (MeOH, *c* 0.1); UV (MeOH) λ_{max} (log ε) 220 nm (2.5); IR ($CHCl_3$) ν_{max} 2949, 1719, 1651, 1572, 1440, 1228, 1149, 1074 cm^{-1}; ^1H and ^{13}C NMR, see Tables 2 and 3; RI_{PT} = 2457.5; EIMS *m/z* 365 $[M]^{+\bullet}$ (10), 239 (8), 222 (36), 138 (20), 122 (42), 94 (100), 83 (25), 55 (10); HRESIMS *m/z* 366.4217 ($C_{19}H_{28}NO_6$ $[M + H]^+$, requires 366.4208).

3α-(1-Methylitaconyl)-6β-angeloyloxytropane (2): colorless oil; $[\alpha]_D^{22}$ see De la Fuente et al.;[13] UV (MeOH) λ_{max} (log ε) 220 nm (2.6); IR see De la Fuente et al.;[13] ^1H and ^{13}C NMR, see Tables 2 and 3; RI_{PT} = 2400.5; EIMS *m/z* 365 $[M]^{+\bullet}$ (10), 239 (9), 222 (25), 138 (20), 122 (55), 94 (100), 84 (23), 55 (20); HRESIMS *m/z* 366.4210 ($C_{19}H_{28}NO_6$ $[M + H]^+$, requires 366.4208).

3α-(1-Methylmesaconyl)-6β-senecioyloxytropane (3): colorless oil; $[\alpha]_D^{22}$see Muñoz et al.;[14] UV (MeOH) λ_{max} see Muñoz et al.;[14] IR see Muñoz et al.;[14] ^1H and ^{13}C NMR, see Tables 2 and 3; RI_{PT} = 2525.8; EIMS *m/z* 365 $[M]^{+\bullet}$ (9), 238 (13), 222 (11), 138 (15), 122 (22), 94 (100), 83 (20), 55 (13); HRESIMS *m/z* 366.4224 ($C_{19}H_{28}NO_6$ $[M + H]^+$, requires 366.4208).

3α-(1-Methylmesaconyl)-6β-angeloyloxytropane (4): colorless oil; $[\alpha]_D^{22}$ see De la Fuente et al.;[13] UV (MeOH) λ_{max} (log ε) 220 nm (2.3); IR see De la Fuente et al.;[13] ^1H and ^{13}C NMR, see Tables 2 and 3; RI_{PT} = 2467.5; EIMS *m/z* 365 $[M]^{+\bullet}$ (8), 238 (15), 222 (15), 138 (18), 122 (38), 94 (100), 82 (15), 55 (15); HRESIMS *m/z* 366.4219 ($C_{19}H_{28}NO_6$ $[M + H]^+$, requires 366.4208).

3α-(1-Methylmesaconyl)-6β-tigloyloxytropane (5): colorless oil; $[\alpha]_D^{22}$ see De la Fuente et al.;[13] UV (MeOH) λ_{max} (log ε) 220 nm (2.4); IR see De la Fuente et al.;[13] ^1H and ^{13}C NMR, see Tables 2 and 3; RI_{PT} = 2500.5; EIMS *m/z* 365 $[M]^{+\bullet}$ (8), 238 (15), 222 (10), 138 (15), 122 (32), 94 (100), 81 (20), 55 (15); HRESIMS *m/z* 366.4236 ($C_{19}H_{28}NO_6$ $[M + H]^+$, requires 366.4208).

3α-(1-Methylcitraconyl)-6β-senecioyloxytropane (6): colorless oil; $[\alpha]_D^{22}$ not measured due to lack of material; UV (MeOH) λ_{max} (log ε) 220 nm (2.4); IR not measured due to lack of material; ^1H and ^{13}C NMR, see Tables 2 and 3; RI_{PT} = 2487.2; EIMS *m/z* 365 $[M]^{+\bullet}$ (5), 238 (10), 222 (13), 138 (17), 122 (30), 94 (100), 84 (18), 55 (13); HRESIMS *m/z* 366.4216 ($C_{19}H_{28}NO_6$ $[M + H]^+$, requires 366.4208).

3α-(1-Methylcitraconyl)-6β-angeloyloxytropane (7): colorless oil; $[\alpha]_D^{22}$ not measured due to lack of material; UV (MeOH) λ_{max} (log ε) 220 nm (2.4); IR not measured due to lack of material; ^1H and ^{13}C NMR, see Tables 2 and 3; RI_{PT} = 2427.5; EIMS *m/z* 365 $[M]^{+\bullet}$ (8), 238 (12), 222 (11), 138 (8), 122 (45), 94 (100), 82 (25), 55 (20); HRESIMS *m/z* 366.4211 ($C_{19}H_{28}NO_6$ $[M + H]^+$, requires 366.4208).

Note Added after ASAP Publication: This paper was published on the Web on Feb 18, 2010, with one author name omitted. The corrected version was reposted on April 2, 2010.

Supporting Information Available: ^1H NMR spectra of compounds **1**−**7**. This information is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

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