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Investigación

Lewis Acid Catalyzed Transformations of *Z*-Ligustilide

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This paper is dedicated to the memory of Dr. Lydia Rodríguez-Hahn

Resumen. Se investigaron algunas reacciones de *Z*-ligustílida (**1**), un constituyente bioactivo de la planta medicinal *Ligusticum porteri*, catalizadas por ácidos de Lewis. Estas reacciones produjeron mezclas variables de *Z*-butilidenftálida (**7**), *E*-butilidenftálida (**8**), *n*-butilftálida (**13**), y ftálidos diméricos lineales novedosos (**9-12**) como productos principales. La formación de los dímeros procedió en rendimientos bajos y con *regio*- y *situ*- selectividad. La *O*- y *C*- complejación competitiva inicial del ácido de Lewis con *Z*-ligustílida promueve la formación de cationes en C(8), C(6) y C(7), los cuales son estabilizados por la adición de la olefina C(6')-C(7') de una segunda unidad de la materia prima para generar los cationes en C(6')-C(7'). Isomerizaciones subsecuentes y la eliminación del catalizador conducen a los productos diméricos **9-12**. Los rendimientos y estructuras de los productos son dependientes de las variaciones de las condiciones de reacción y del catalizador empleado.

Palabras clave. ftálidas, *Z*-ligustílida, *Ligusticum porteri*, ácidos de Lewis, dimerizaciones, catálisis ácida, ftálidos diméricos lineales, reacciones carbocatiónicas.

Abstract. Some Lewis acid mediated reactions of *Z*-ligustilide (**1**), a bioactive constituent of the medicinal species *Ligusticum porteri*, were investigated. These reactions provided varying mixtures of *Z*-butylidenephthalide (**7**), *E*-butylidenephthalide (**8**), *n*-butylphthalide (**13**), and novel linear dimeric phthalides (**9-12**) as the main products. The formation of the dimers occurred in low yields and with *regio*- and *situ*- selectivity. Initial competitive *O*- and *C*- complexation of the Lewis acid with *Z*-ligustilide promoted the formation of carbocations at C(8), C(6) and C(7), which were stabilized by the addition of the C(6')-C(7') olefin of a second unit of the starting material, to provide cations at C(6') and C(7'). Subsequent isomerizations and elimination of the catalyst afforded the dimeric products **9-12**. The yields and structure of the products are quite dependent on variations of the reaction conditions and the catalyst employed.

Key words. phthalides, *Z*-ligustilide, *Ligusticum porteri*, Lewis acids, dimerizations, acid catalysis, linear dimeric phthalides, carbocationic reactions.

Introduction

Phthalides are a relatively small group of acetogenins that have been isolated mainly from umbelliferous plants [1] used in traditional medicine in different parts of the world [2], and the variety of pharmacological properties associated with them [3,4] have stimulated interest for the synthesis of phthalide analogs [5]. *Z*-ligustilide (**1**) may be considered as the biogenetic precursor of a series of natural racemic dimeric compounds derived from [π4s + π2s] and [π2s + π2s] cycloadditions, and recent work has led to the synthesis of diligustilide (**2**) [6,7] and tokynolide B (**3**) [6] from **1**. It is interesting to note that the relatively unexpected chemical reactivity of the dimeric phthalides reflects their particular molecular architecture [7,8]. For instance, base

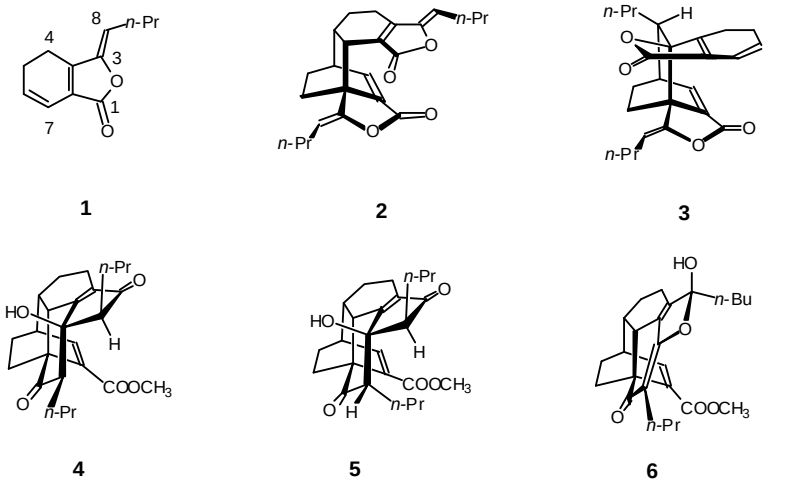

Figure 1.

treatment of **2** afforded the pentacyclic compounds **4-6** *via* intramolecular condensations and competitive equilibrations [9]. Although some Diels-Alder reactions may be promoted by Lewis acid (LA) catalysis [10], attempts to catalyze the relay synthesis of **2** using **1** as diene and dienophile were unsuccessful, as previously informed [7]. Instead, the Lewis acid catalyzed reaction of **1** afforded complex reaction mixtures, and some polymeric material. Here we report the structures of the reaction products and the proposed mechanisms for their formation.

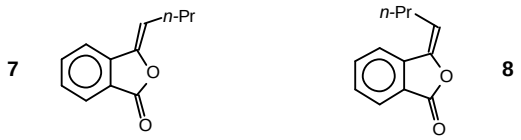

Figure 2.

Results and Discussion

Treatment of **1** with $LiClO_4$ in THF did not transform the starting material at room temperature, even at long reaction periods. When the reaction mixture was refluxed for several hours, Z-butylidenephthalide **7** [11] was obtained as the main product. Similar result was obtained with Et_2AlCl in CH_2Cl_2, which afforded a mixture of **1**, **7** and *E*-butylidenphthalide (**8**) [12].

Treatment of **1** with Et_2OBF_3 in CH_2Cl_2 gave a mixture of **7** and the dimers **9-12**. The major dimer, **9**, analyzed for $C_{24}H_{26}O_4$ and exhibited UV absorptions at λ_{max} 271, 256 and 209 nm, indicative of an α,β,γ,δ- unsaturated carbonyl group and a benzenoid ring. The IR absorption at 1771 cm^{-1} was consistent with the presence of an unsaturated γ-lactone, and the signals at δ_C 168.61 and δ_C 166.64 confirmed the presence of two γ-lactones. Compound **9** showed in its ^1H NMR spectra signals of an ABCD system corresponding for an *o*-disubstituted benzenoid ring at δ_H 7.92-7.50, and the presence of only one triplet at δ_H 5.21, assigned to H(8'), indicated the C(8)

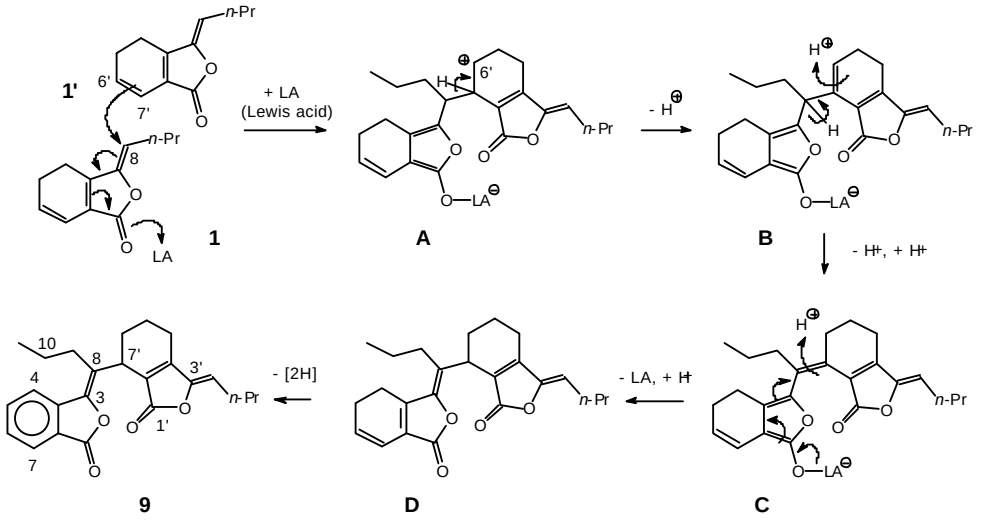

Figure 3.

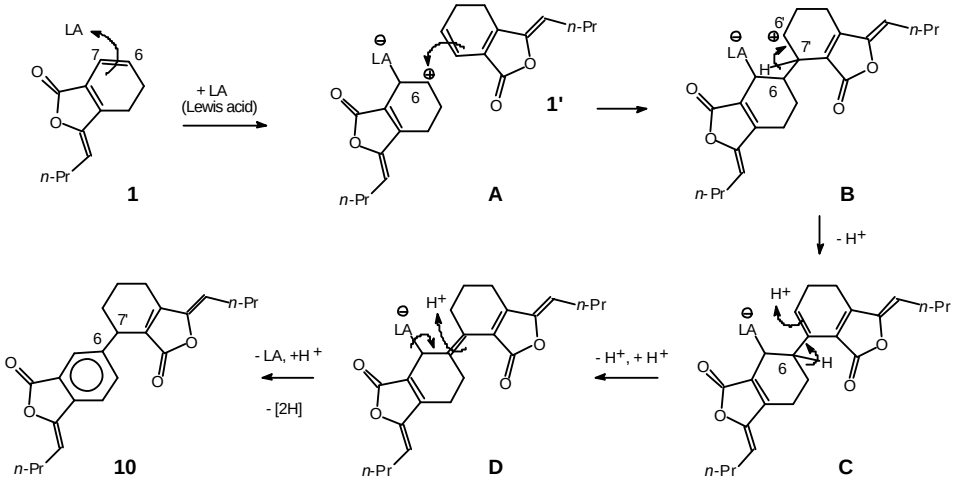

Figure 4.

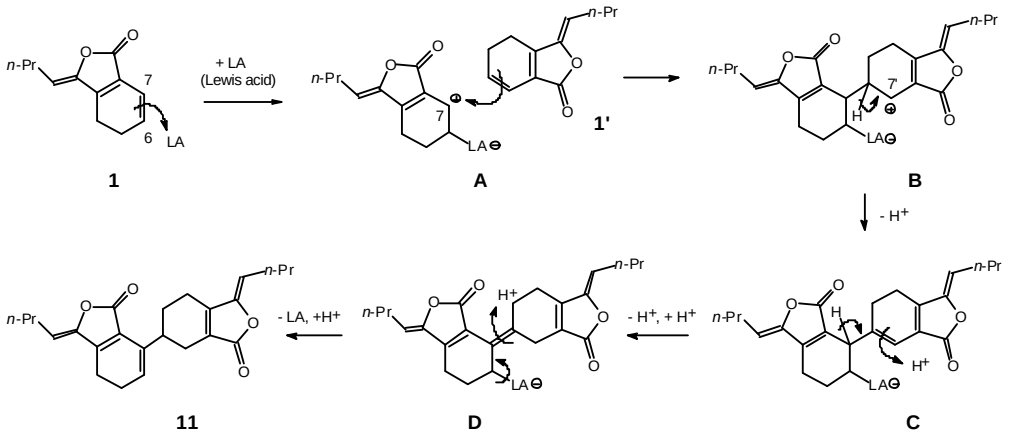

Figura 5.

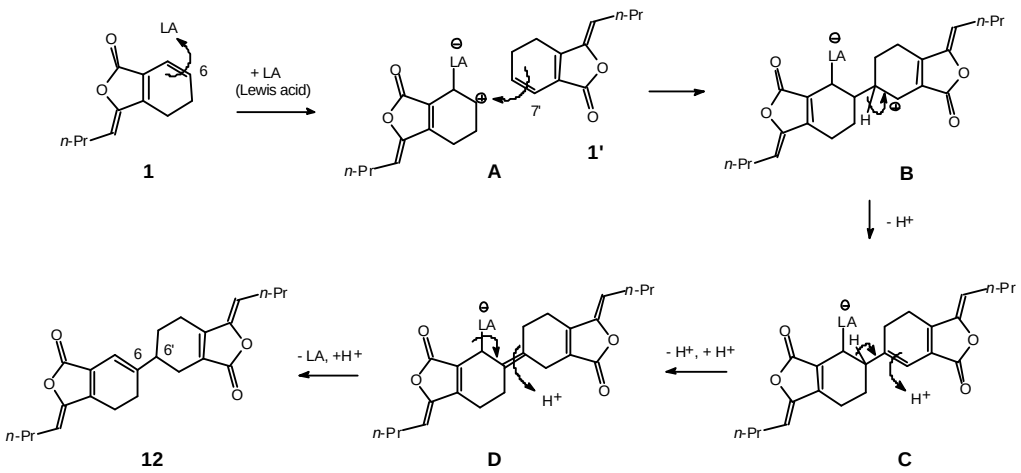

Figura 6.

connectivity with the second monomeric unit. The broad singlet at δ_H 3.99 was assigned for H-7', due to its low chemical shift, and this established the C(8)-C(7') connectivity in **9**; the amplitude of this signal ($W_{1/2}$ = 16 Hz) indicated its pseudo–*axial* orientation. In the NOESY experiment, the signal of H(4) showed crosspeaks with the signals for H(9) and H(10); hence, the olefin at C(3)-C(8) is *Z*, and the dimer can be trivially named 4,5-dehydro-6',7'-dihydro-*Z*,*Z*'-8.7'-diligustilide (**9**) [13]. The structure was confirmed by COSY, HMBC and HMQC experiments. The formation of **9** can be explained by the reaction sequence shown in Fig. 3 [14]. Complexation of the Lewis acid with the carbonyl group of **1** promotes the regiodifferentiated nucleophilic addition of the C(6')-C(7') double bond of a second unit of *Z*-ligustilide (**1'**) to C(8), to afford a cation at C(6') (intermediate **A** in Fig. 3). Isomerizations *via* a series of proton shifts (**A** ® **B** ® **C** ® **D**), followed by dehydrogenation, provided **9**.

Compound **10**, $C_{24}H_{26}O_4$, is isomeric with **9**. The UV and IR data also indicated an α,β,γ,δ- unsaturated carbonyl group and a benzenoid ring, and the presence of an ABC system for an 1,2,4-trisubstituted benzene ring in the ^{1}H NMR spectrum (δ 7.56, H-7; δ 7.55, H-4; δ 7.54, H-5) was indicative for a C(6) substitution of a *Z*-butylidenephthalide unit. The resonance at δ 3.95 was assigned to H(7') of a *Z*-ligustilide fragment; therefore, there was connectivity between C(6) and C(7'). Compound **10** could be formed as is shown in Fig. 4. Complexation of the Lewis acid to the C(6)-C(7) double bond of *Z*-ligustilide produces a cation at C(6) (intermediate **A**, Fig. 4). This promotes the addition of the C(6')-C(7') olefin of the second monomeric unit, to form a cation at C(6') (intermediate **B**). The cation is stabilized by hydrogen elimination (intermediate **C**), and the isomerization indicated (**C** ® **D**), followed by aromatization, affords 4,5-dehydro-6',7'-dihydro-*Z*,*Z*'-6.7'-diligustilide (**10**).

Compound **11** was isolated as colorless oil. The molecular formula was established as $C_{24}H_{28}O_4$ by EIMS and spectroscopic analysis. The prominent carbonyl absorptions at 1773 and 1732 cm^{-1} indicated the presence of the unsaturated γ-lactones, which were confirmed from the ^{1}H NMR spectrum, showing diagnostic signals for the *Z*-ligustilide units.

The signal for the vinylic proton at δ_H 5.42 (H(6)) vicinal to a methylene, indicated a trisubstituted doble bond, and therefore, a substituent at C(7). The broad signal at δ_H 3.26 was assigned to H(6'), since it was shifted upfield with respect to the allylic methines in **9** ($\Delta\delta$ 0.73) and **10** ($\Delta\delta$ 0.69), establishing the C(7)-C(6') connectivity. The formation of **11** can be rationalized as arising from complexation of the Lewis acid with the C(6)-C(7) olefin of *Z*-ligustilide, to form, in this case, a cation at C(7) (intermediate **A**, Fig. 5). Addition of the C(6')-C(7') olefin of another *Z*-ligustilide unit (**1'**) affords a cation, now at C(7') (intermediate **B**), which is stabilized by the sequence **B** ® **C** ® **D** as shown in Fig. 5, to form 6',7'-dihydro-7.6'-*Z*,*Z*'-diligustilide (**11**).

Compound **12** had a molecular formula $C_{24}H_{28}O_4$, determined by EIMS and spectroscopic analysis, and it is also a dimer of *Z*-ligustilide. Its ^{1}H NMR spectrum presented signals at δ_H 5.85 (s), δ_H 5.23 (t) and δ_H 5.21 (t) for the vinylic hydrogens; the last two signals corresponded to the hydrogens at C(8) and C(8'). The site of connectivity was established by the chemical shift and multiplicity of the signal at δ_H 5.85, which was assigned to H(7). This signal is shifted downfield with respect to that of H(6) of **11** ($\Delta\delta$: 5.42-5.85 = -0.43), due to the deshielding of the carbonyl group, and therefore, there is substitution at C(6) in one *Z*-ligustilide fragment. The broad signal at δ_H 3.30 was assigned to H(6') of the second unit and corresponded to an allylic methine with two flanking methylene groups, thus establishing the C(6)-C(6') connectivity for **12**. The sequence described in Fig. 6 explains the formation of **12**. Cation formation at C(6) (intermediate **A**, Fig. 6), promoted by the Lewis acid, followed by the addition of the C(6')-C(7') of a second *Z*-ligustilide unit affords a C(7') cation (intermediate **B**), which is stabilized by loss of a proton (intermediate **C**). Subsequent equilibrations gives 6',7'-dihydro-*Z*,*Z*'-6.6'-diligustilide (**12**).

Treatment of *Z*-ligustilide (**1**) with tin tetrachloride in dichloromethane afforded *Z*-butylidenephthalide (**7**) as the major product, *E*-butylidenephthalide (**8**), *n*-butylphthalide (**13**) [12], and the dimers **9** and **10**.

It is interesting to point out the different complexation sites of the Lewis acids with *Z*-ligustilide (*O*- *vs*. *C*- complexation, see Fig. 8), to form different cations (C(8), C(6) and C(7)), which are stabilized by the addition of the C(6')-C(7') olefin to the cation, following the reaction paths shown in Fig. 8. The structures and yields of the products indicate: (a) the tendency of **1** to form aromatic products, (b) the low reactivity

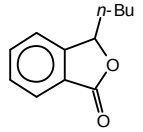

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Figure 7.

of **1** toward Lewis acid catalyzed reactions, (c) the slight preference for *O*-complexation (*vs*. *C*- complexation), and (d) the low nucleophilicity and regioselection displayed by the C(6')-C(7') double bond (to stabilize the cation at **1**). As previously noted [15], the course of these reactions is sensibly dependent on the catalysts, polarity of the solvents, and reaction conditions. Although the yields were not optimized, these acid catalyzed reactions could be considered for the preparation of some linear dimeric phthalides.

The accumulated results regarding the chemical reactivity of *Z*-ligustilide (**1**) [6,7] have demonstrated the practical difficulties to obtain natural (or semisynthetic) dimers efficiently by direct chemosynthesis [16]. Although some products derived from exposure of **1** to sunlight have been identified as previously reported natural dimers [17], the yields and variability of the dimeric phthalides in the natural sources clearly indicate that they are formed by biosynthetic pathways.

Experimental

For information on instruments and adsorbents, see reference [7]. *Z*-Ligustilide (**1**) was isolated from the organic extracts of the roots of *Ligusticum porteri* by succesive column chromatographies, as described previously [8]. The samples of **1** used for the reactions contained *ca*. 5% of **7**. All reactions were carried out under an atmosphere of nitrogen.

Treatment of *Z*-ligustilide (1) with $LiClO_4$. Three solutions of **1** (45.7 mg, 0.24 mmol; 72.7 mg, 0.38 mmol; 65.3 mg, 0.34 mmol) in dry THF (10 mL) were deoxygenated for 15 min (N_2) and stirred with $LiClO_4$ (12.8 mg, 0.12 mmol; 20.4 mg, 0.19 mmol; 18.3 mg, 0.17 mmol, respectively) at three temperatures (0°C, room temperature and reflux, respectively) for 48 h. The mixtures were filtered through Celite, diluted with water and extracted with chloroform. The extracts were

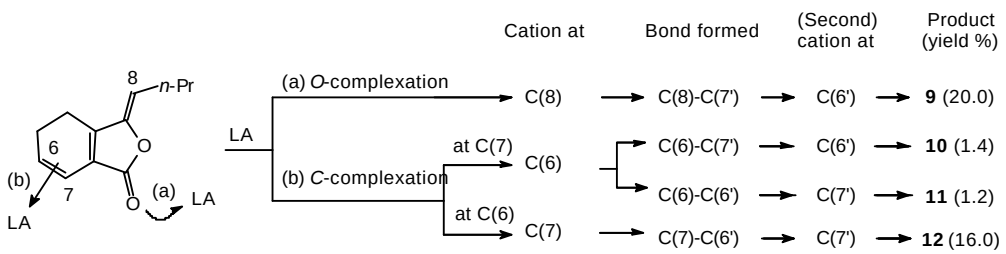

Figura 8.

washed, dried, evaporated to dryness and chromatographed (PTLC, *n*-hexane-EtOAc, 20:1), to provide a mixtures of **1** and *Z*-butylidenephthalide **7** [12]. The best transformation of the starting material was from the reaction under reflux. **1**: 64%; **7**: 25%.

Treatment of *Z*-ligustilide (1) with Et_2AlCl. A solution of Et_2AlCl (Aldrich, in CH_2Cl_2, 1.0 mL, 2.79 mmol) was added dropwise to *Z*-ligustilide (**1**, 1.06 g 5.58 mmol). The mixture was stirred at room temperature for 7 days, but the starting material remained practically unchanged (TLC analysis). An additional amount of Et_2AlCl in CH_2Cl_2 (1 mL, 2.79 mmol) was added and the mixture was refluxed for 6 h. The residue was filtered through Celite, diluted with CH_2Cl_2, washed with brine, dried, and concentrated. Purification of the residue by column chromatography (*n*-hexane-EtOAc, 20:1) provided **1** (60%), **7** (22%) and **8** [12] (9%).

Treatment of *Z*-ligustilide (1) with BF_3OEt_2. To a stirred solution of **1** (322 mg, 0.21 mmol) in dry CH_2Cl_2 (10 mL) under nitrogen, was added dropwise BF_3OEt_2 (1.5 mL, 12.9 mmol). The mixture was refluxed for 24 h, and after this time, TLC analysis indicated only a partial trasformation of the starting material. Therefore, the mixture was stirred at room temperature for 7 days. The reaction mixture was directly adsorbed over silica gel (70-230 mesh) and chromatographed in a column packed whith 60 g of the same silica-gel (elution system: *n*-hexane and *n*-hexane-EtOAc gradient). PLC of selected fractions allowed to obtain *Z*-butylidenephthalide (**7**, 133 mg, 41.7%), 4,5-dehydro-6',7'-dihydro-*Z*,*Z*'-8.7'-diligustilide (**9**, 66 mg, 20%), 4,5-dehydro-6',7'-dihydro-*Z*,*Z*'-6.7'-diligustilide. (**10**, 4.5 mg, 1.4%), 6',7'-dihydro-*Z*,*Z*'-7.6'-diligustilide (**11**, 4 mg, 1.2%) and 6',7'-dihydro-*Z*,*Z*'-6.6'-diligustilide (**12**, 51.4 mg, 16%). When the reaction mixture was refluxed for 72 h, the same mixture of products was obtained.

4,5-dehydro-6',7'-dihydro-*Z*,*Z*'-8.7'-diligustilide (9). Colorless oil. UV (MeOH) λ_{max} (ε): 271 (7247), 257 (6022), 210 (13034) nm; IR (film) ν_{max}: 3022, 2961, 2935, 2873, 1771, 1677, 1610, 1473, 1458, 1266, 1090, 1018 y 768 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, assignments by COSY, HMBC and NOESY): δ 7.92 (1H, dt, J = 8.0, 0.5 Hz, H-7), 7.70 (1H, ddd, J = 8.0, 7.0, 1.0 Hz, H-5), 7.66 (1H, d, J = 8.0, Hz, H-4), 7.50 (1H, ddd, J = 8.0 ,7.0, 1.0 Hz, H-6), 5.21 (1H, t, J = 7.5 Hz, H-8'), 3.99 (1H, br s, $W_{1/2}$ = 16 Hz, H-7' pseudo-*axial*), 2.53 (1H, m, H-9a), 2.51 (2H, m, H-4'), 2.37 (2H, q, J = 7.5 Hz, H-9'), 2.28 (1H, m, H-9b), 2.07 (2H, m, H-5'), 1.76 (2H, m, H-6'), 1.64 (2H, m, H-10), 1.51 (2H, q, J = 7.5 Hz, H-10'), 1.05 (3H, t, J = 7.5 Hz, H-11), 0.97 (3H, t, J = 7.5 Hz, H-11'); ^{13}C NMR (75 MHz, $CDCl_3$, assignments by APT and HMBC): δ 168.61 (s, C-1'), 166.64 (s, C-1), 152.60 (s, C-3'a), 148.77 (s, C-3'), 143.21 (s, C-3), 138.32 (s, C-3a), 134.33 (d, C-5), 128.78 (d, C-6), 127.16 (s, C-7'a), 127.16 (s, C-7a), 127.16 (s, C-8), 125.55 (d, C-7), 122.96 (d, C-4), 111.38 (d, C-8'), 36.19 (d, C-7'), 31.75 (t, C-9), 28.50 (t, C-6'), 27.88 (t, C-9'), 22.53 (t, C-10), 22.36 (t, C-10'), 21.40 (t, C-5'), 21.17 (t, C-4'), 14.47 (q, C-11) 13.73 (q, C-11'); EIMS *m/z* (rel. int.): 378 [M^+] (23), 349 [M^+-C_2H_5] (11), 335 [M^+-C_3H_7] (24), 319 (16), 192 (100), 190 (96), 187 (64), 186 (53), 149 (25), 148 (20), 105 (17), 91 (9), 77 (13), 59 (19), 55 (23).

4,5-Dehydro-6',7'-dihydro-*Z*,*Z*'-8.7'-diligustilide (10). Colorless oil. UV (MeOH) λ (ε): 269 (18818), 207 (5139) nm; IR ($CHCl_3$) ν_{max}: 2965, 2936, 2876, 1773, 1732, 1464, 1267, 1091, 1024 cm^{-1}; ^1H NMR (200 Mz, $CDCl_3$): δ 7.68-7.49 (3H, m, H-4, H-5 and H-7), 5.60 (3H, t, J = 7.9 Hz, H-8), 5.30 (3H, t, J = 7.9 Hz, H-8'), 3.95 (1H, br s, $W_{1/2}$ = 12 Hz, H-7' pseudo-*axial*), 2.53 (2H, m, H-4'), 2.44 (2H, dd, 15.0, 7.4 Hz, H-9), 2.40 (2H, dd, J=15.2, 7.5 Hz, H-9'), 1.77 (2H, m, H-6'), 1.60 (2H, m, H-5'), 1.54 (4H, q, J = 7.5 Hz, H-10 and H-10'), 0.99 (3H, t, J = 7.2 Hz, H-11'), 0.98 (3H, t, J = 7.2 Hz, H-11); EIMS *m/z* (rel. int.): 378 [M^+] (36), 349 [M^+-C_2H_5] (94), 338 (62), 309 (100), 296 (46), 254 (50), 192 (32), 190 (25), 187 (47), 186 (17), 149 (37), 104 (18), 97 (17), 83 (21), 71 (30), 57 (34) 55 (35), 43 (42).

6',7'-Dihydro-*Z*,*Z*'-7.6'-diligustilide (11). Colorless oil. UV (MeOH) λ (ε): 268 (2442), 207 (665) nm; IR ($CHCl_3$) ν_{max}: 2963, 2932, 2874, 1773, 1732, 1456, 1094, 1024 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, assignments by COSY): δ 5.42 (1H, m, $W_{1/2}$ = 8 Hz, H-6), 5.21 (1H, t, J = 7.9 Hz, H-8'), 5.13 (1H, t, J = 7.9 Hz, H-8), 3.26 (1H, m, $W_{1/2}$ = 13 Hz, H-6' pseudo-*axial*), 3.08 (2H, m, H-4), 2.97 (2H, d, J = H-5), 2.36 (2H, dd, J = 7.7, 7.5 Hz, H-9, H-9'), 2.35 (4H, dd, J = 7.7, 7.5 Hz, H-4', H-7'), 1.77 (2H, m, H-5'), 1.50 (4H, m, H-10, H-10'), 0.96 (3H, t, J = 7.4 Hz, H-11'), 0.94 (3H, t, J = 7.4 Hz, H-11); EIMS *m/z* (rel. int.): 380 [M^+] (44), 378 [M^+-H_2] (29), 349 [M^+-H_2 - C_2H_5] (59), 336 (16), 319 (8), 294 [M^+-H_2 - C_4H_6CO] (9), 256 (14), 192 (100), 190 (46), 189 (54), 187 (27), 186 (24), 161 (21), 149 (33), 129 (20), 104 (14), 97 (25), 83 (31), 73 (27), 71 (31), 57 (49), 55 (48), 43 (44).

6',7'-Dihydro-*Z*,*Z*'-6.6'-diligustilide (12). Colorless oil. UV (MeOH) λ nm (ε): 269 (7419), 256 (6935), 207 (17733); IR ($CHCl_3$) ν_{max}: 2963, 2934, 2874, 1771, 1734, 1464, 1267, 1092, 1036 cm^{-1}; ^1H NMR (300 Mz, $CDCl_3$): δ 5.85 (1H, s, H-7), 5.23 (1H, t, J = 7.5 Hz, H-8), 5.21 (1H, t, J = 7.5 Hz, H-8'), 3.30 (1H, brs, $W_{1/2}$ = 14.0 Hz, H-6' pseudo-*axial*), 2.65 (2H, m, H-4), 2.51 (2H, m, H-5), 2.36 (6H, m, H-4', H-9' and H-9), 1.77 (4H, m, H-5' and H-7'), 1.51 (2H, q, J = 7.5 Hz, H-10), 1.49 (2H, q, J = 4.5 Hz, H-10'), 0.97 (3H, t, J = 7.5 Hz, H-11), 0.95 (3H, t, J = 7.5 Hz, H-11'); ^{13}C NMR (75 MHz, $CDCl_3$): 168.86 (s, C-1'), 167.74 (s, C-1), 153.07 (s, C-6), 148.64 (s, C-3), 148.38 (s, C-3'), 145.86 (s, C-3a), 143.37 (s, C-3'a), 126.45 (s, C-7a), 124.68 (s, C-7'a), 113.60 (d, C-7), 112.83 (d, C-8), 111.95 (d, C-8'), 37.76 (d, C-6'), 28.10 (d, C-9), 27.88 (d, C-9'), 26.98 (d, C-7'), 26.41 (d, C-5), 22.40 (d, C-10), 22.35 (d, C-10'), 21.07 (d, C-4'), 19.49 (d, C-4), 17.94 (d, C-5'), 13.83 (q, C-11), 13.74 (q, C-11'). EIMS *m/z* (rel. int.): 380 [M^+] (22), 378 [M^+-H_2] (18), 349 [M^+-C_2H_5] (24), 335 [M^+-C_3H_7] (17), 192 (100), 190 (62), 187 (43), 186 (35), 149 (27), 105 (15), 91 (8), 77 (9), 55 (17).

Treatment of *Z*-ligustilide (1) with $SnCl_4$. A solution of $SnCl_4$ in CH_2Cl_2 (Aldrich, 1M, 0.6 mL, 3.4 mmol) was added dropwise to *Z*-ligustilide (**1**, 1.02 g, 5.37 mmol) with stirring at room temperature. After 7 days at room temperature, an additional amount of 0.5 mL of $SnCl_4/CH_2Cl_2$ (2.8 mmol) was added and the mixture was then refluxed for 8 h. The mixture was filtered through Celite, washed with NH_4Cl, diluted with chloroform, washed with brine, dried, and concentrated. Chromatography of the residue and elution with *n*-hexane-EtOAc gradient allowed to isolate **7** (35%), **9** (12%), **12** (7%), *E*-butylidenephthalide (**8**, 12%) [12] and *n*-butyl-phthalide (**13**, 10%) [12]. **8** is a colorless oil: ^{1}H NMR (300 Mz, $CDCl_3$): δ 7.94 (1H, dd, J = 7.8, 0.9 Hz, H-7), 7.72 (2H, dd, J = 8.1, 1.2 Hz, H-4 and H-5), 7.55 (1H, m, H-6), 5.88 (1H, t, J = 7.8 Hz, H-8), 2.55 (2H, dd, J = 15.3, 7.8 Hz, H-9), 1.65 (2H, q, J = 7.2 Hz, H-10), 1.04 (3H, t, J = 7.2 Hz, H-11). **13** is a colorless oil: ^{1}H NMR (300 Mz, $CDCl_3$): 7.90 (1H, d, J = 7.5 Hz, H-7), 7.67 (1H, ddd, J = 7.8, 7.8, 1.5 Hz, H-5), 7.53 (1H, dd, J = 7.5, 7.5 Hz, H-6), 7.44 (1H, dd, J = 7.5, 0.8 Hz, H-4), 5.48 (1H, dd, J=8.1, 4.5 Hz, H-3), 2.04 (2H, m, H-9), 1.78 (2H, m, H-8), 1.37 (2H, m, H-10), 0.91 (3H, t, J=7.2 Hz, H-11); ^{13}C NMR (75 MHz, $CDCl_3$): 170.68 (s, C-1), 150.10 (s, C-3a), 136.51 (s, C-7a), 133.90 (d, C-7), 129.00 (d, C-5), 125.70 (d, C-6), 121.67 (d, C-4), 81.43 (d, C-3), 34.42 (t, C-8), 26.87 (t, C-9), 22.41 (t, C-10), 13.85 (q, C-11).

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References and Notes

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