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Adulticidal Activity of Dillapiol and Semi-synthetic Derivatives of Dillapiol against *Aedes aegypti* (L.) (Culicidae)

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Abstract Phenylpropanoid dillapiol (**1**) isolated from the essential oil in leaves of *Piper aduncum* L. and thirteen semi-synthetic, C_3 side-chain modified dillapiol derivatives **2-14** were evaluated for lethality against hemorrhagic dengue fever mosquito vector *Aedes aegypti* L.. First, adult female mosquitoes were exposed to these substances in a contact bioassay carried out in glass bottles at a single surface density (0.57 μg/cm^2). Then, median lethal concentrations (LC_{50}) and LC_{90} were determined for active compounds. It was found that the structure of the C_3 side chain was important for the toxic effects of these substances against *A. aegypti* adult females. Isodillapiol (**2**) and methyl, propyl and butyl 1-(2′,3′-dimethoxy-4′,5′-methylenedioxyphenyl)propan-2-yl ethers (**3**, **5** and **6**, respectively) all exhibited greater mosquitocidal activity than dillapiol (**1**). The order of molar per surface area of mosquitocidal activities was isodillapiol (**2**) > butyl ether **6** > methyl ether **3** > propyl ether **5** > dillapiol (**1**). The potential of dillapiol and derivatives as *A. aegypti* mosquitocides was discussed.

Keywords Mosquitocidal activity; Isodillapiol; 2-methoxy dillapiol; 2-ethoxy dillapiol; 2-n-propoxy dillapiol; 2-n-butoxy dillapiol; *Aedes aegypti*

Introduction

The number of people afflicted by dengue hemorrhagic fever has risen in recent years. *Aedes aegypti* (L.) is the main vector of dengue hemorrhagic fever in the Americas. According to the World Health Organization (WHO, 2006), effective control of *A. aegypti* is attained with the use of chemical insecticides such as pyrethroids (cypermethrin, deltamethrin). However, contamination of the environments in the Amazon and other regions has occurred due to the use of pyrethroids and other long-lasting synthetic chemical insecticides for the control of *Aedes* spp.. Also, resistance of *A. aegypti* and other mosquito vectors to pyrethroids and other commercially available insecticides has increased in recent years as have the population densities of mosquitoes in many regions and urban centers (Campos and Andrade, 2001; Luna et al., 2004; Barreto, 2005; Braga and Valle, 2007).

Bioactive chemicals isolated from plants are potential alternative agents for the control of *A. aegypti* and other insects (Chapagain et al., 2008). Research on the use of plant-derived chemicals to control mosquitoes and other insects has increased in recent years. This is especially true for the use of natural products based on plant essential oils (EOs) as insecticides and repellents (Shaalan et al., 2005; Georges et al., 2008; Nerio et al., 2010; Pohlit et al., 2011a; 2011b). It is firmly established that substances which contain a methylenedioxyphenyl nucleus such as synthetic piperonyl butoxide or components of EOs such as safrole, sesamolin, sesamin, myristicin and dillapiol (**1**) (Figure 1) have insecticide synergist and other properties which are important for insect control (Cassida, 1970; Alibhai, 1999).

Journal of Mosquito Research, 2012, Vol.2, No.1, 1−7
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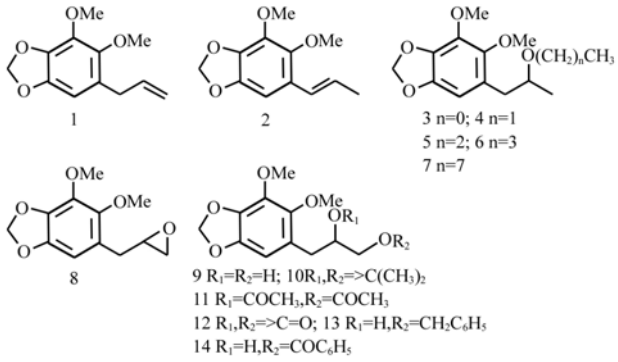


Figure 1 Chemical structures of dillapiol (**1**) and semi-synthetic derivatives (**2-14**)

Dillapiol (**1**) is the major component of the EO obtained from the leaves of *Piper aduncum* L. (Cicció and Ballestero, 1997). It has insecticidal activity against *Drosophila melanogaster* (LD_{50} 0.27 mg/jar) and *A. aegypti* larvae (LD_{50} 11.0 ppm, Lichtenstein et al., 1974). **1** is also known as an effective *in vitro* inhibitor of the epoxidase activity in larvae of the mosquito *Ostrinia nubilalis* (92% inhibition). Epoxidase is important to insect defenses because it detoxifies insecticidal agents allowing mosquitoes and other insects to survive (Bernard et al., 1989; Demetzos et al., 2000). Also, **1** is an inhibitor of cytochrome polymerase−β P450 and it inhibits the activity of the polysubstrate monooxygenases which are used by insects to metabolize toxins as well as enzyme-lyase activity (Larocque et al., 1999; Amiguet et al., 2006).

Dillapiol (**1**) exhibits synergism with several classes of substances used in insect control. For example, synergism of **1** was observed with pyrethrins (factor of synergism 2.0) against the wheat flour beetle *Tribolium castaneum* (Tomar et al., 1979a; 1979b) with α-terthienyl against larvae of *Aedes atropalpus* (LC_{50} 41.1 ng/mL) and factor of synergism 1.9 (Majerus, 1997; Alibhai, 1999; Belzile et al., 2000) with pyrethrin and carbaryl against adults of the red flour beetle *Tribolium castaneum* (Larocque et al., 1999). Also, **1** exhibits synergism with the pyrethroids deltamethrin and cypermethrin providing 70% and 100% mortality in adult *A. aegypti* in 90 min and 15 min, respectively. Furthermore, combination of **1** with α-cypermethrin led to 100% mortality against *Anopheles albitarsis* adults in 45 min (Gomes et al., 2005; 2006). **1** exhibits antifungal synergistic effects in combination with the sesquiterpene dialdehyde cinnamodial against *Alternaria alternata*, *Candida albicans* and *Wangiella dermatitides* (Amiguet et al., 2006). Also, **1** exhibits synergistic activity in combination with gedunin (79.0±5.3) % as an active antimalarial (Omar et al., 2003).

Semi-synthetic derivatives of **1** which exhibit intact methylenedioxyphenyl nuclei also exhibit synergism against insect species. For example, derivatives **2-6** (Figure 1) and other derivatives of **1** exhibited *in vitro* synergism (2.8~5.0 fold increased effects) with pyrethrin insecticides against the wheat flour beetle *Tribolium castaneum* (Tomar et al., 1979a; 1979b; Mukerjee et al., 1979) and with α-tertienyl in larvae of *Aedes atropalpus* where derivative **5** showed synergism as evidenced by 1.5 fold increased activity (Majerus, 1997; Belzile, 2000).

The general aim of this work was to identify semi-synthetic derivatives of **1** exhibiting adulticidal activity against *Aedes aegypti* found in the Brazilian Amazon. Thus, known dillapiol derivatives **2-6** and **9** and new derivatives **7-8** and **10-14** were prepared herein and evaluated for contact adulticidal activity against the hemorrhagic dengue fever vector *Aedes aegypti.* To our knowledge, this is the first time that **1** and derivatives **2-14** have been evaluated for adulticidal activity against mosquitoes.

1 Results and Discussion

Initially, adulticidal activity of dillapiol (**1**) and derivatives **2-14** was determined against *A. aegypti* adult females at a surface density of 0.57 μg/cm^2. Dillapiol (**1**) and isodillapiol (**2**) were the most active substances (100% mortality after exposure for 45 min) followed by methyl, ethyl, propyl and butyl 1-(2′,3′-dimethoxy-4′,5′-methylenedioxyphenyl)propan-2-yl ethers **3-6** which exhibited lethalities of 80%~98% to *A. aegypti* adult females after an exposure time of 90 min. Dillapiol oxide (**8**) killed about half (51%) and acetonide **10** killed 29% of mosquitoes after 90 min of exposure. Other derivatives of dillapiol

(**11-14**) were not effective (4-11% mortality) at killing *A. aegypti* adult females (Figure 2). Thus, dillapiol derivatives **8-14** exhibited lower adulticide potency than dillapiol (**1**) or isodillapiol (**2**) against *A. aegypti*. Taken together, this initial result demonstrated that functionalization of both the 2- and 3-positions on the propyl side chains with oxygen atoms or oxygen-containing moieties was associated with decreased adulticide activity compared to **1** or **2**.

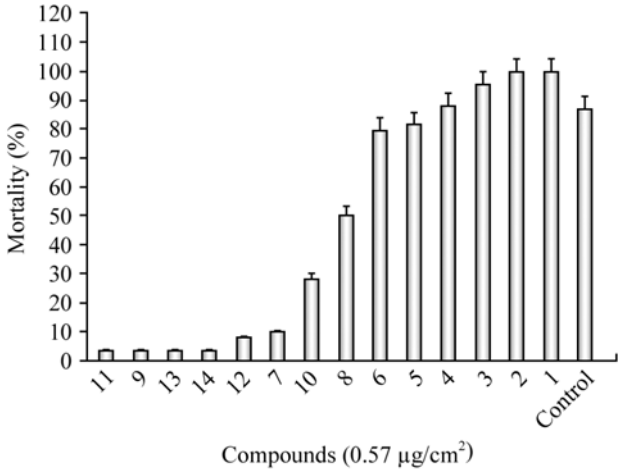


Figure 2 Percentage mortalities for dillapiol and derivatives against *Aedes aegypti* L. adult females after exposure for 90 mins to 0.57 μg/cm^2 of sample or control substance α-cypermethrin (0.59 ng/cm^2).

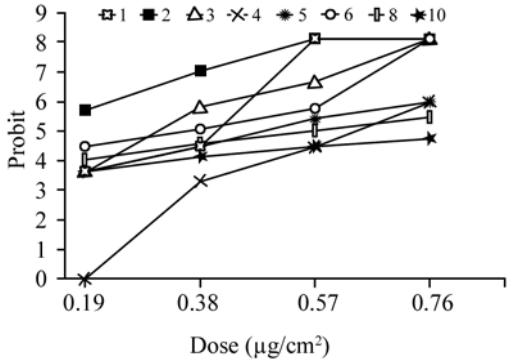


Figure 3 Probit analysis of the mortality caused by dillapiol and its derivatives against *Aedes aegypti* female adults (90 min exposure).

The more active substances found in the initial screening described above were then evaluated to establish the relationship between concentration and adulticidal activity in *A. aegypti*. The results of probit analysis are shown in Figure 3. The adulticide activity of ethyl ether **4** exhibited the greatest dependence on surface density in the range of surface densities evaluated and disappeared altogether at the lowest density tested (0.19 μg/cm^2).

Median lethal concentration (LC_{50}) and LC_{90} and other statistical parameters for dillapiol and derivatives against *A. aegypti* adult females are presented in Table 1. Interestingly, the most active mosquitocide was a structural isomer of dillapiol (**1**), isodillapiol (**2**), which was 3-fold more active than **1**. Also, several alkyl 1-(2′,3′-dimethoxy-4′,5′-methylenedioxyphenyl)propan-2-yl ethers exhibited significant adulticide activity. Given the inactivity of octyl ether **7** and the adulticidal activities of methyl, ethyl, propyl and butyl ethers **3-6**, there appeared to be an optimal alkyl chain length. On a molar basis, the order of decreasing contact adulticide activity was: isodillapiol (**2**) > butyl ether **6** > methyl ether **3** > propyl ether **5** > dillapiol (**1**) > epoxide **8** > ethyl ether **4** > acetonide **10**.

Results on the mortality of *A. aegypti* adult females reported in the present study confirmed the potential of dillapiol, isodillapiol and semi-synthetic ether derivatives as mosquitocides. Furthermore, varying the chain length/structure of the alkyl group attached to the dillapiol carbon skeleton in ether derivatives could be a means to modulate physical and chemical properties such as solubility and volatility leading to improved utility and mosquitocidal activity of these derivatives in field situations.

2 Methods

2.1 Isolation of 1

Isolation of **1** from *Piper aduncum* has been described previously (Pinto, 2008; Pohlit et al., 2008). Briefly, EO of *P. aduncum* growing in the region near Manaus, Amazonas State, Brazil was prepared on a pilot scale (600 mL, d=1.082 g/mL, 2.4% based on dry weight of plant) by steam distillation of sun-dried leaves. Then, **1** (17.7 g, 73.4% w/w based on EO and 1.70% w/w based on dry plant) was obtained by fractional vacuum distillation of EO (dillapiol fraction collected at 4 cmHg, *ca*. 157℃).

Table 1 Adulticidal activities of dillapiol (**1**) and derivatives of dillapiol against *Aedes aegypti* adult females after 90 mins of exposure.

No.	LC_{50} (CI) µg/cm^2	LC_{90} (CI) µg/cm^2	Slope ± 100	SD	Chi-square χ^2	LC_{50} (CI) nmol/cm^2	LC_{90} (CI) nmol/cm^2
1	0.381 (0.319~0.442)	0.575 (0.514~0.636)	7.2 ± 0.7	0.3	32.1	1.72 (1.437-1.991)	2.59 (1.085-1.459)
2	0.136 (0.087~0.167)	0.274 (0.241~0.324)	4.2 ± 1.0	0.6	1.3	0.61 (0.391-0.752)	1.23 (1.09-1.46)
3	0.295 (0.264~0.326)	0.457 (0.409~0.531)	6.8 ± 0.8	0.4	0.9	1.16 (1.04-1.28)	1.80 (1.61-2.09)
4	0.618 (0.546~0.709)	0.845 (0.729~1.234)	9.4 ± 1.4	0.3	2.7	2.31 (2.04-2.65)	3.15 (2.72-4.60)
5	0.438 (0.316~0.604)	1.065 (0.723~3.555)	3.3 ± 0.4	0.2	3.3	1.55 (1.12-2.14)	3.78 (2.56-12.60)
6	0.315 (0.254~0.377)	0.699 (0.638~0.761)	3.7 ± 0.5	0.2	7.8	1.06 (0.857–1.27)	2.36 (2.153–2.56)
8	0.531 (0.443~0.635)	1.855 (1.269~3.835)	2.3 ± 0.5	0.2	1.0	2.23 (1.86-2.67)	7.79 (5.33-16.11)
10	1.177 (0.822~3.038)	6.600 (2.703~88.52)	1.7 ± 0.5	0.2	0.01	3.98 (2.78-10.26)	22.30 (9.13-29.90)
***Ctrl**	0.494** (0.443~0.549)	0.876** (0.761~1.069)	5.2 ± 0.7	0.2	2.9	1.19*** (1.06~1.31)	2.10*** (1.83~2.57)

Note: LC_{50} = Lethal concentration at which 50% of mosquitoes were killed. LC_{90} = Lethal concentration at which 90% of mosquitoes were killed. CL = confidence limits at 90% probability. *Control = α-cypermethrin, **ng/cm^2, ***pmol/cm^2. Values are the mean of four replicates with ± (SEM)) standard error.

2.2 Preparation of derivatives of 1

Isomerization, oxymercuration, epoxidation, bis-hydroxylation (oxidation) and reactions using **1** as substrate yielded: isodillapiol (**2**), methyl, ethyl, propyl, butyl and octyl 1,2-dihydrodillapiol-2-yl ethers **3-7**, dillapiol epoxide (**8**) and 1,2-dihydroxy-1,2-dihydrodillapiol (**9**). Acetonide formation, carbonylation, diacetylation, benzylation and benzoylation of the hydroxyl groups in **9** provided: 1,2-dihydroxy-1,2-dihydrodillapiol acetonide **10** and carbonate **12**, *O,O*-diacetyl, 1-*O*-benzyl and 1-*O*-benzoyl derivatives of 1,2-dihydroxy-1,2-dihydrodillapiol **11**, **13** and **14**, respectively (Scheme 1) as described in Pinto (2008) and Pohlit et al. (2008).

2.3 Adulticidal activity of semi-synthetic substances against *A. aegypti*

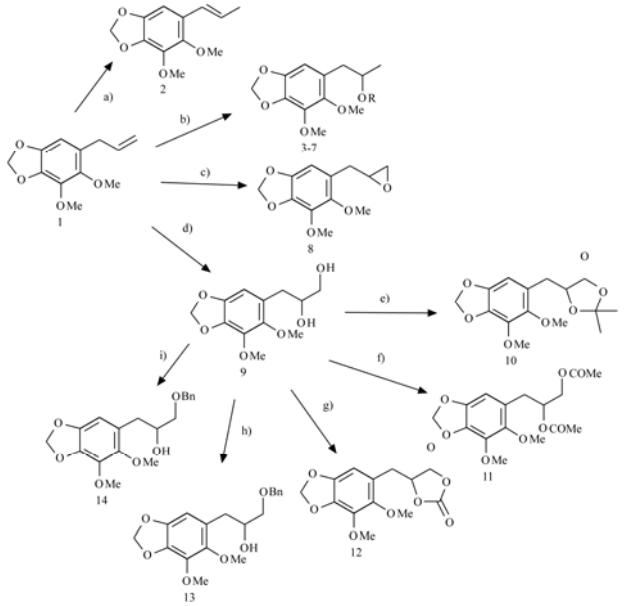
A. aegypti were maintained in the insectary of the INPA Department of Society, Environment and Health in alternating light and dark photoperiods of 12 h. They were fed periodically with the blood of rats as a source of protein used mainly for the production of eggs.

The acute activity of the above semi-synthetic derivatives was determined by contact with *A. aegypti* adult females. Substances were dissolved in HPLC grade acetone at a concentration of 10 mg/mL. Volumes of this sample solution were measured using an adjustable pipette and transferred to clear glass bottles. Sample was homogenized in each bottle and complete evaporation of the solvent was accomplished by leaving bottles open to the air overnight. The same procedure was performed for both positive controls (α-cypermethrin at a concentration of 0.59 ng/cm^2 in acetone) and negative controls (1.0 mL of acetone). Then, 15 female hematophagous *A. aegypti* aged 3 to 5 days were placed in each bottle at 25℃~27℃ and 50%~70% humidity and controlled according to WHO recommendations (WHO, 2006). The bioassay was performed in triplicate making observations every 15 min until exposure time to substances reached 90 min.

Mortality was defined as immobility and movement of mosquitoes was recorded even if immobilized mosquitoes started recovering 2 h after treatment. There was no mortality in negative control bottles.

2.4 Statistical analysis

Data on the mortality of mosquitoes (immobility, absence of movement) were analyzed using the program StatsDirect 2.6.6 (Stats Direct Limited).



Scheme 1 Synthesis of dillapiol derivatives. Reagents and conditions: a) KOH/EtOH 17%, reflux, 24 h, 81%; b) THF/$Hg(OH)_2$, alcohol, $NaBH_4$/KOH, rt, **3**: R=Me, 78%, **4**: R=Et, 62%, **5**: R= Pr, 77%, **6**: R=But, 42%, **7**: R=Oct, 17%; c) *m*-CPBA, CH_2Cl_2, -5 ℃ (2 h), rt, 240 h, 11%; d) acetone, $KMnO_4$, rt, 24h, 63%; e) $(CH_3)_2C(OCH_3)_2$, *p*-$CH_3C_6H_4SO_3H$, rt, 120 h, 82%; (6) $(CH_3CO)_2O$, pyridine, rt, 24 h, 58%; (7) $CO(OCCl_3)_2$, CH_2Cl_2, Et_3N, 0 ℃, rt, 39%; (8) C_6H_5Br, DMF, K_2CO_3, 0 ℃, rt, 12%; (9) $C_6H_5CH_2Cl$, pyridine, rt, 32%.

Significant differences were determined among treatments at 0.05 space level of significance. The average values of the absolute frequencies of mortality in those treatments with a dosage of 150 μg were analyzed for variance with free Kruskal-Wallis distribution ($p < 0.05$). Then, these data underwent a test of medium contrast at 5% level of significance using the procedure of Conover-Inman (Table 1, Conover, 1999). Data were evaluated by probit analysis (POLOPC program LeOra Software 1987) to determine the LC_{50} and LC_{90} values (in μg/cm^2) that caused 50% and 90% mortalities with 95% confidence intervals.

3 Conclusion

Isodillapiol and methyl, propyl and butyl 1,2-dihydrodillapiol-2-yl ethers were all more lethal than the isolated phenylpropanoid dillapiol to *Aedes aegypti* adult females, and they all have potential as contact mosquitocides. Remembering that the important insecticide synergist piperonyl butoxide is also a phenylpropanoid derivative, dillapiol derivatives will be further investigated for synergism with commercial pyrethroid products used presently in the Amazon and other regions of the world for mosquito vector control.

4 Experimental

^{1}H and ^{13}C NMR spectra were collected at 500MHz and 125 MHz, respectively. The derivatives have the following spectral data:

7: Colorless oil. ^{1}H NMR ($CDCl_3$): δ 6.39 (*s*, 1H), 5.88 (*s*, 2H), 4.01 (*s*, 3H), 3.76 (*s*, 3H), 3.55 (*sext*, *J*=6.0 Hz, 1H), 3.46 (*dt*, *J*=6.5, 9.3 Hz, 1H), 3.36 (*dt*, J=6.5, 9.3 Hz, 1H), 2.82 (*dd*, *J*=6.0, 13.5 Hz, 1H), 2.52 (*dd*, *J*=7.0, 13.5 Hz, 1H), 1.51 (*m*, 2H), 1.26 (*m*, 10H), 1.11 (*d*, *J*=6.0 Hz, 3H), 0.88 (*t*, *J*=6.7, Hz, 3H) ppm; ^{13}C NMR/DEPT ($CDCl_3$): δ 144.9(C); 144.5(C); 137.7(C); 136.1(C); 125.5(C); 103.9(CH); 101.2(CH_2); 76.2(CH); 69.0(CH_2); 61.3(CH_3); 60.1(CH_3); 37.2(CH_2); 32.1(CH_2); 30.3(CH_2); 29.7(CH_2); 29.5(CH_2); 26.4(CH_2); 22.9(CH_2); 19.9(CH_3); 14.3(CH_3) ppm. EI-MS: *m*/*z* 352 [M+·].

8: Yellow oil. ^{1}H NMR ($CDCl_3$): δ 6.43 (*s*, 1H), 5.89 (*s*, 2H), 4.02 (*s*, 3H), 3.77 (*s*, 3H), 3.09 (*m*, 1H), 2.78 (*m*, 3H), 2.55 (*dd*, *J*=2.6, 5.2 Hz, 1H) ppm. EI-MS: *m*/*z* 238 [M+·].

9: White solid. ^{1}H NMR ($CDCl_3$): δ 6.37 (*s*, 1H), 5.90 (*s*, 2H), 4.02 (*s*, 3H), 3.84 (*m*, 1H), 3.59 (*dd*, *J*=3.7, 11.1 Hz, 1H), 3.47 (*dd*, *J*=6.0, 11.1 Hz, 1H), 3.79 (*s*, 3H), 2.73 (*d*, *J*=6.5 Hz, 2H), 2.18 (*s*, 2H) ppm; ^{13}C NMR/DEPT ($CDCl_3$): δ 144.7(C), 144.4(C), 137.6(C), 136.3(C), 103.4(CH), 123.5(C), 101.2(CH_2), 72.7(CH), 65.7(CH_2), 61.2(CH_3), 59.9(CH_3), 34.1(CH_2) ppm. EI-MS: *m*/*z* 256 [M+·].

10: Yellow oil. ^{1}H NMR ($CDCl_3$): δ 5.91 (*d*, *J*=1.5 Hz, 1H), 5.88 (*d*, *J*=1.5 Hz, 2H), 3.99 (*s*, 3H), 3.84 (*m*, 1H), 3.77 (*dd*, *J*=3.0, 11.3 Hz, 1H), 3.75 (*s*, 3H), 3.66 (*dd*, *J*=7.0, 11.3 Hz, 1H); 2.67 (*dd*, *J*=2.8, 16.3 Hz, 1H), 2.38 (*dd*, *J*=11.0, 16.3 Hz, 1H), 1.56 (*s*, 3H), 1.51 (*s*, 3H). ppm; ^{13}C NMR/DEPT ($CDCl_3$): δ 143.9(C), 140.1(C), 136.3(C), 136.2(C), 119.9(C), 119.3(C), 101.1(CH_2), 69.6(CH), 66.1(CH_2), 60.9(CH_3), 60.3(CH_3), 73.8(CH), 28.7(CH_3), 25.8(CH_3), 25.1(CH_2) ppm. EI-MS: *m*/*z* 296 [M+·].

11: Yellow oil. ^{1}H NMR ($CDCl_3$): δ 6.34 (*s*, 1H), 5.89 (*s*, 2H), 5.24 (*dddd*, *J*=3.3, 3×6.6 Hz, 1H), 4.23 (*dd*, *J*=3.3, 12.0 Hz, 1H), 4.02 (*dd*, *J*=6.6, 12.0 Hz, 1H), 4.00 (*s*, 3H), 3.79 (*s*, 3H), 2.86 (*dd*, *J*=6.6, 14.0 Hz, 1H), 2.78 (*dd*, *J*=6.6, 14.0 Hz, 1H), 2.06 (*s*, 3H), 2.03 (*s*, 3H) ppm; ^{13}C NMR/DEPT ($CDCl_3$): δ 170.9(C), 170.6(C), 145.3(C), 144.7(C), 137.8(C), 136.7(C), 122.3(C), 103.6(CH), 101.5(CH_2), 71.9(CH), 64.8(CH_2), 61.4(CH_3), 60.2(CH_3), 31.4(CH_2), 21.3(CH_3), 21.0(CH_3) ppm. EI-MS: *m*/*z* 340 [M+·].

12: Yellow oil. ^{1}H NMR ($CDCl_3$): δ 6.36 (*s*, 1H), 5.91 (*s*, 2H), 4.89 (*m*, 1H), 4.40 (*t*, *J*=8.6 Hz, 1H), 4.18 (*dd*, *J*=7.0, 8.6 Hz, 1H), 4.03 (*s*, 3H), 3.78 (*s*, 3H), 3.05 (*dd*, *J*=6.0, 14.0 Hz, 1H), 2.89 (*dd*, *J*=7.0, 14.0 Hz, 1H) ppm; ^{13}C NMR/DEPT ($CDCl_3$): δ 155.1(C); 145.2(C); 145.0(C); 137.9(C); 137.3(C); 119.7(C); 103.6(CH); 101.7(CH_2); 76.8(CH); 68.9(CH_2); 61.4(CH_3); 60.1(CH_3); 34.2(CH_2) ppm. EI-MS *m*/*z* 282 [M+·].

13: white solid. ^{1}H NMR ($CDCl_3$): δ 7.32 (*m*, 5H), 6.39 (*s*, 1H), 5.89 (*s*, 2H), 4.55 (*s*, 2H), 4.02 (*s*, 3H), 3.99 (*m*, 1H), 3.77 (*s*, 3H), 3.49 (*dd*, J=4.0, 9.5 Hz, 1H), 3.41 (*dd*, J=7.0, 9.5 Hz, 1H), 2.74 (*d*, J= 7.0 Hz, 2H), 1.68 (*s*, 1H) ppm. ^{13}C NMR/DEPT ($CDCl_3$): δ 144.9(C), 144.8(C), 138.3(C), 137.8(C), 136.5(C), 127.9(CH), 129.0(CH), 124.1(C), 103.8(CH), 101.4(CH_2), 74.0(CH_2), 73.6(CH_2), 71.2(CH), 61.3(CH_3), 60.1(CH_3), 34.5(CH_2) ppm. EI-MS: *m*/*z* 346 [M+·].

14: white solid. ^{1}H NMR ($CDCl_3$): δ 8.03 (*dd*, *J*=1.3, 8.0 Hz, 1H), 7.61 (*t*, *J*=8.0 Hz, 2H), 7.49 (*t*, *J*= 8.0 Hz, 2H), 6.45 (*s*, 1H), 5.88 (*s*, 2H), 4.29 (*dd*, *J*=4.5, 11.0 Hz, 1H), 4.22 (*dd*, *J*=6.0, 11.0 Hz, 1H), 4.14 (*m*, 1H), 3.97 (*s*, 3H), 3.76 (*s*, 3H), 2.88 (*dd*, *J*=6.0, 13.5 Hz, 1H), 2.78 (*dd*, *J*=7.0, 13.5 Hz, 1H), 1.55 (*s*, 1H) ppm; ^{13}C NMR/DEPT ($CDCl_3$): δ 166.8(C), 144.9(C), 144.8(C), 137.7(C), 136.7(C), 133.0(CH), 132.9(CH), 129.7(C), 129.4(CH), 129.2(CH), 128.3(CH), 123.9(C), 103.6(CH), 101.4(CH_2), 69.8(CH), 68.1(CH_2), 60.4(CH_3), 59.2(CH_3), 34.6(CH_2) ppm. EI-MS: *m*/*z* 360 [M+·].

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