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# Polyisoprenylated benzophenone derivatives from *Clusia obdeltifolia*

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**Abstract**—Two new polyisoprenylated benzophenones along with the known compound 28,29-Epoxyplukenetione A were isolated from the hexane extract of *Clusia obdeltifolia* after extensive chromatographic procedures. One of the new benzophenone presented a novel 9-oxa-tetracyclic [11.3.1.0$^{1,10}$.0$^{3,8}$]heptadec-10-ene-12,17-dione moiety arising from complex cyclizations of isopentenyl and lavandulyl substituents. The other presented an adamantyl skeleton.


The searches for bioactive compounds from Clusiaceae have led to the isolation of structurally complex polyprenylated benzophenone derivatives. Several of them showed anti-HIV, anti-bacterial and anti-microbial activity.[1] *Clusia obdeltifolia* is a wild shrub that occurs in campo rupestre areas (rocky fields) at Chapada Diamantina, Bahia, Brazil. In a previous paper we related the isolation of five polyprenylated benzophenones, which exhibited a complex tricyclo [4.3.1.1$^{3,8}$] undecane skeleton from the hexane extract of *C. obdeltifolia*.[2] Further studies with the hexane extract allowed the isolation of two new benzophenones, 13-benzoyl-6,6,8,14,14-pentamethyl-11,15-di(3-methyl-2-butenyl)-9-oxatetracyclo[11.3.1.0$^{1,10}$.0$^{3,8}$]heptadec-10-ene-12,17-dione and 1-benzoyl-5-(1-hydroxy-1-methylethyl)-6,6,13,13-tetramethyltetracyclo[7.3.1$^{3,11}$.0$^{3,8}$]tetradecane-2,12,14-trione, along with a known compound 28,29-Epoxyplukenetione A.[3] One of the new benzophenone presented a novel 9-oxa-tetracyclic [11.3.1.0$^{1,10}$.0$^{3,8}$]heptadec-10-ene-12,17-dione moiety arising from complex cyclizations of isopentenyl and lavandulyl substituents. The other presented an adamantyl skeleton.

Dried powdered trunk was extracted with hexane and fractionated as previously described.[2] Successively chromatography on silica gel column and preparative TLC (silica gel; hexane–EtOAc 9:1) provide **1** (18 mg), **2** (8 mg) and **3** (10 mg).

Compound **1** was obtained as a yellow amorphous solid $[\alpha]_D^{25}$ +30.9 (*c* 0.25, $CHCl_3$). Its molecular formula, $C_{38}H_{50}O_4$, was deduced from HREIMS (found: 570.7998; calcd: 570.7992). The base peak at *m/z* 105 indicated the presence of a benzoyl moiety and suggested that **1** was a benzophenone derivative. $^1H$ and $^{13}C$ NMR data (Table 1) showed the presence of two isopentenyl groups and confirmed the presence of benzoyl group. Three signals at $\delta$ 208.3, $\delta$ 193.8 and $\delta$ 193.6 indicated the presence of one nonconjugated and two conjugated carbonyls. In addition to the signals of two double bonds from isopentenyl groups, two other signals at $\delta$ 126.9 and $\delta$ 169.0 indicated the presence of an enol endocyclic double bond conjugated with a carbonyl. The comparison of NMR data of **1** with those reported in the literature to polyprenylated benzophenones revealed a structural similarity of **1** with plukenetione E acetate isolated from *C.* plukenetii.[4]

$^1H$ NMR presented complex signals overlap between $\delta$ 1.47 and $\delta$ 1.53 that were resolved after extensive analysis of HMQC and HMBC data. These signals were assigned to H-27a, H-27b, H-28a, H-35 and H-7, which showed cross-peaks with carbons at $\delta$ 38.5, $\delta$ 26.4, $\delta$ 18.0 and $\delta$ 47.7, respectively (Table 1).

The bicyclo[3.3.1]nonane skeleton with isopentenyl substituents at C-3 and C-7 was established by the HMBC cross-peaks analysis. The methyl groups Me-38 ($\delta$ 1.34) and Me-37 ($\delta$ 1.42) showed correlations with each other,

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**Table 1.** NMR data of compounds **1** (500 and 125 MHz, $CDCl_3$) and **2** (300 and 75 MHz, $CDCl_3$)

| H/C | $^{13}C$ | $^{1}H$ | HMBC | H/C | $^{1}H$ | $^{13}C$ | COLOC |
|---|---|---|---|---|---|---|---|
| 1 | 77.7 | | | 1 | | 81.6 | H-25 |
| 2 | 193.6 | | | 2 | | 205.8 | H-9 |
| 3 | 126.9 | | | 3 | | 69.6 | H-7, H-9 |
| 4 | 169.0 | | | 4 | | 206.8 | H-11 |
| 5 | 49.0 | | | 5 | | 73.8 | H-11 |
| 6 | 41.8 | 2.73 d (14.4) | C-4, C-5, C-9, C-22, C-32 | 6 | 2.33 dd (5.1; 14.2) | 58.4 | H-11 |
| | | 1.98 dd (14.4; 7.5) | C-4, C-5, C-7, C-9, C-32 | | | | |
| 7 | 47.7 | 1.47 m | C-1, C-37 | 7 | 2.14 | 44.0 | H-25 |
| 8 | 48.6 | | | 8 | | 51.4 | H-26, H-7 |
| 9 | 208.3 | | | 9 | 2.65 dd (6.6; 14.3) | 43.4 | H-6 |
| | | | | | 2.04 d (14.3) | | |
| 10 | 193.8 | | | 10 | | 205.1 | H-11 |
| 11 | 137.0 | | | 11 | 3.06 t (12.3) | 34.0 | H-12 |
| | | | | | 2.54 dd (7.4; 12.3) | | |
| 12–16 | 128.3 | 7.52 d | C-10, C-13, C-14, C-15 | 12 | 2.87 dd (7.2; 12.3) | 58.4 | H-17, H-18, H-16 |
| 13–15 | 127.8 | 7.18 t | C-11, C-12, C-14, C-16 | 13 | | 45.3 | H-18, H-19 |
| 14 | 131.7 | 7.35 t | C-13, C-15 | 14 | 2.23; 1.69 | 28.8 | |
| 17 | 22.4 | 2.99 dd (13.5; 6.5) | C-2, C-3, C-4, C-18, C-19 | 15 | | 72.2 | H-11, H-17 |
| | | 3.09 dd (13.5; 8.1) | C-2, C-3, C-4, C-18, C-19 | | | | |
| 18 | 120.4 | 4.95 br t | C-17, C-20, C-21 | 16 | 1.39 s | 30.3 | |
| 19 | 131.8 | | | 17 | 1.49 s | 30.8 | |
| 20 | 18.0 | 1.64 s | C-18, C-19, C-21 | 18 | 1.08 s | 28.9 | |
| 21 | 25.7 | 1.57 s | C-18, C-19, C-20 | 19 | 1.44 s | 27.6 | |
| 22 | 29.8 | 1.30 dd (15.1; 2.6) | C-4, C-24 | 20 | 2.82 dd (7.2; 13.8) | 30.2 | |
| | | 2.88 dd (15.1; 6.0) | C-4, C-5, C-6, C-9, C-23, C-28 | | | | |
| 23 | 37.3 | 1.67 m | C-28 | 21 | 5.44 t (6.8) | 120.4 | H-24 |
| 24 | 82.6 | | | 22 | | 134.3 | H-24 |
| 25 | 49.8 | 1.87 dd (14.7; 1.6) | C-24, C-26, C-27, C-30 | 23 | 1.65 s | 26.1 | |
| | | 1.39 dd (14.7; 2.1) | C-24, C-26, C-31 | | | | |
| 26 | 30.7 | | | 24 | 1.70 s | 18.1 | |
| 27 | 38.5 | 1.53 m | | 25 | 1.60 s | 25.2 | H-26 |
| | | 1.46 m | | | | | |
| 28 | 26.4 | 1.52 m | C-24 | 26 | 1.55 s | 22.8 | H-25 |
| | | 1.93 m | C-24, C-26, C-27 | | | | |
| 29 | 28.4 | 1.20 | C-23, C-24, C-25 | 27 | | 193.5 | H-29, H-33 |
| 30 | 26.8 | 1.07 s | C-25, C-26, C-27, C-31 | 28 | | 135.7 | |
| 31 | 32.8 | 0.95 s | C-25, C-26, C-27 | 29 | 7.55 | 129.6 | H-30, H-31 |
| 32 | 29.6 | 2.10 m | C-7, C-33, C-34 | 30 | 7.37 | 128.5 | |
| | | 2.07 m | C-6, C-7 | | | | |
| 33 | 124.6 | 4.89 br t | C-7, C-35, C-36 | 31 | 7.37 | 132.5 | H-29, H-33 |
| 34 | 132.6 | | | 32 | 7.37 | 128.5 | |
| 35 | 18.0 | 1.50 s | C-33, C-34, C-36 | 33 | 7.55 | 129.6 | |
| 36 | 25.7 | 1.65 s | C-33, C-34, C-35 | | | | |
| 37 | 22.1 | 1.42 s | C-1, C-8, C-38 | | | | |
| 38 | 26.9 | 1.34 s | C-1, C-8, C-37 | | | | |

*J* values (in hertz) are presented in parenthesis.

with C-1 ($\delta$ 77.7) and C-8 ($\delta$ 48.6). The methine proton H-7 ($\delta$ 1.47) showed cross-peaks with C-37 ($\delta$ 22.1) and C-1. The methylene protons H-6a ($\delta$ 2.73) and H-6b ($\delta$ 1.98) showed correlations with C-9 ($\delta$ 208.3), C-4 ($\delta$ 169.0), C-5 ($\delta$ 49.0), C-7 ($\delta$ 47.7) C-32 ($\delta$ 29.6) and C-22 ($\delta$ 29.8). H-32a ($\delta$ 2.10) and H-32b ($\delta$ 2.07) showed correlations with C-34 ($\delta$ 132.6), C-33 ($\delta$ 124.6), C-7 ($\delta$ 47.7) and C-6 ($\delta$ 41.8). The hydrogens H-17a ($\delta$ 2.99) and H-17b ($\delta$ 3.09) showed correlations with C-2 ($\delta$ 193.6), C-4, C-3 ($\delta$ 126.9), C-18 ($\delta$ 120.4) and C-19 ($\delta$ 131.8). The connectivities observed among H-22b ($\delta$ 2.88) with C-4, C-5, C-6, C-9, C-23 ($\delta$ 37.3) and C-28 ($\delta$ 26.4); H-22a ($\delta$ 1.30) with C-4 and C-24 ($\delta$ 82.6); H-29 ($\delta$ 1.20) with C-23 ($\delta$ 37.3), C-24 and C-25 ($\delta$ 49.8); H-25a ($\delta$ 1.87) and H-25b ($\delta$ 1.39) with C-24, C-26 ($\delta$ 30.7), C-27 ($\delta$ 38.5), C-30 ($\delta$ 26.8) and C-31 ($\delta$ 32.8); and H-28a ($\delta$ 1.93) with C-24, C-26 and C-27, allowed to establish the carbon skeleton of trimethylperhydrochromene system and to link it to carbons C-4 and C-5.

The stereochemistry assignments were not straightforward, however, careful NOE difference studies supported the stereochemistry delineated in structure **1** (Fig. 1). The irradiation of Me-29 provoked increments at the signals of H-12,16 (phenyl group), Me-31 and H-22b. Therefore, these groups are located in the same face ($\alpha$-face) of molecule as depicted in Figure 1. A molecular model examination demonstrated that H-22b occupied, approximately, the same plane that C-9 carbonyl, explaining the deshielded observed to its $^{1}H$ NMR signal in relation to H-22a. The subsequent irradiation of H-22b showed an enhancement of Me-38 signal, which

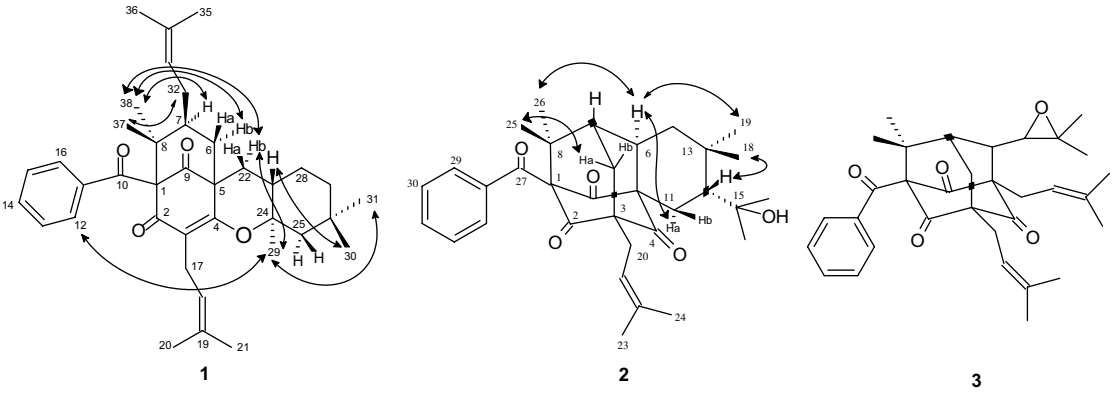


**Figure 1.** Structures of compounds **1**, **2** and **3** and selected NOE.

permitted to assign the relative position of *gem*-dimethyl Me-37 and Me-38. The increment observed at the signal of Me-38 when H-6b was irradiated corroborated with the spatial arrangement proposed. The irradiation of H-7 ($\delta$ 1.47) affected the same protons that the irradiation of Me-35 ($\delta$ 1.50) and due to proximity of these proton signals, the increments observed, especially at Me-38 and H-6b, did not permit any conclusion about C-7 stereochemistry. On the other hand, the irradiation of Me-37 produced an increment in H-32b and none in H-7 suggesting that H-7 occupied a α-position. A careful comparison of NMR data of **1** with those of similar compounds with both α-H-7 and β-H-7,[5] permitted to conclude that H-7 occupied a α-position. In this situation, the six-membered ring formed by carbons C-1, C-8, C-7, C-6, C-5 and C-9 adopted a boat conformation to minimize the repulsions that an isopentenyl axial group would have in the chair conformation.[6,7] Finally, the irradiation of Me-30 causes an increment at H-23, which defined the *trans*-junction of pyrane and cyclohexane rings, this statement is in agreement with the magnitude of coupling constant observed between H-22b and H-23 ($J$ = 6.0 Hz).

The trimethylperhydrochromene system was presumably biosynthesized from a lavandulyl side chain cyclization. Several *Clusia* species present compounds with lavandulyl side chain[8–11] and it could be imagined as a precursor of **1** a compound similar to chamone I, isolated from *C. grandiflora*.[11] The substitution pattern of trimethylperhydrochromene system of **1** can be observed in hilarianone, a compound isolated from *C. hilariana* floral resin.[10]

Compound **2** was obtained as a yellow amorphous solid $[\alpha]_D^{25}$ +10.0 (*c* 0.4, $CHCl_3$). Its molecular formula, $C_{33}H_{42}O_5$, was deduced from HREIMS (found: 518.6826; calcd: 518,6819). The base peak at *m/z* 105 indicated the presence of a benzoyl moiety and suggested that **2** was a benzophenone derivative. The $^1H$ and $^{13}C$ NMR spectra (Table 1) indicated, in addition to benzoyl moiety, the presence of an isopentenyl, a 2-hydroxyisopropyl and two *gem*-dimethyl groups. Four signals at $\delta$ 206.8, $\delta$ 205.8, $\delta$ 205.1 and $\delta$ 193.5 indicated the presence of three nonconjugated and one conjugated carbonyls. It must be emphasized the presence of three deshielded signals of quaternary carbons at $\delta$ 81.6, $\delta$ 73.8 and $\delta$ 69.6. The former (C-1) was more deshielded due to be linked to three carbonyl groups. The comparison with literature data[3,12] allowed to propose for compound **2** an adamantyl-type carbon skeleton.

The correlations observed in the COLOC spectrum permitted to trace the complete carbon skeleton of the molecule (Table 1). The six-membered ring condensed to adamantyl core adopts preferentially the chair conformation. In this conformation H-11a is axial and it is in the same plane that C-10 carbonyl, which explained its deshielding in relation to H-11b. H-12 is a β-axial hydrogen and the diaxial relation to H-11a was demonstrated by the large coupling constant between them (12.3 Hz). The α-position of H-6, H-11a, H-19, H-26 was deduced from the observation of signal enhancement of H-11a, H-19 and H-26 when H-6 was irradiated in the NOE difference experiment (Fig. 1). The irradiation of H-9a caused an enhancement of Me-25 signal becoming evident the spatial arrangements of Me-25, Me-26, H-9a and H-9b. Thus, on the basis of these spectral data, we propose the structure **2** to this compound.

Compound **3** showed all spectroscopic data (NMR, IR and EIMS) identical to those described to 28,29-Epoxyplukenetione A isolated from *C. haveotides* var. Stenocarpa.[3]

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## References and notes


1. Gustafson, K. R.; Blunt, J. W.; Munro, M. H. G.; Fuller, R. W.; McKee, T. C.; Cardelina, J. H.; McMahon, J. B.; Gragg, G. M.; Boyd, M. R. *Tetrahedron* **1992**, *48*, 10093–10102.
2. Cruz, F. G.; Teixeira, J. S. R. *J. Braz. Chem. Soc.* **2004**, *15*, 504–508.
3. Christian, O. E.; Henry, G. E.; Jacobs, H.; McLean, S.; Reinolds, W. F. *J. Nat. Prod.* **2001**, *64*, 23–25.
4. Henry, G. E.; Jacobs, H.; Carrington, C. M. S.; McLean, S.; Reynolds, W. F. *Tetrahedron* **1999**, *55*, 1581–1596.
5. Grossman, R. B.; Jacobs, H. *Tetrahedron Lett.* **2000**, 1–5.
6. de Oliveira, C. M. A.; Porto, A. L. M.; Bittrich, V.; Marsaioli, A. J. *Phytochemistry* **1999**, *50*, 1073–1079.
7. Rubio, O. C.; Cuellar, A. C.; Rojas, N.; Castro, H. V.; Rastrelli, L.; Aquino, R. *J. Nat. Prod.* **1999**, *62*, 1013–1015.
8. Gustafson, K.; Blunt, J. W.; Munro, M. H. G.; Fuller, R. W.; McKee, T. C.; Cardelina, J. H.; McMahon, J. B.; Cragg, G. M.; Boyd, M. R. *Tetrahedron* **1992**, *48*, 10093–10102.
9. Delle Monache, F.; Delle Monache, G.; Gács-Baitz, E. *Phytochemistry* **1991**, *30*, 703–705.
10. Porto, A. L. M.; Machado, S. M. F.; de Oliveira, C. M. A.; Bittrich, V.; Amaral, M. C. E.; Marsaioli, A. J. *Phytochemistry* **2000**, *55*, 755–768.
11. Lokvam, J.; Braddock, J. F.; Reichardt, P. B.; Clausen, T. P. *Phytochemistry* **2000**, *55*, 29–34.
12. Hu, L. H.; Sim, K. Y. *Org. Lett.* **1999**, *1*, 879–882.