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Alchornoic acid derivatives from the fruits of *Alchornea cordifolia* (Schumach. & Thonn.) Muell. Arg. (Euphorbiaceae)

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ABSTRACT

Two alchornoic acid derivatives, deepoxyalchornoic acid (**1**) and bisalchornoicester (**2**), together with six known compounds, alchornoic acid (**3**), gallic acid, 4-*O*-methylgallic acid, shikimic acid, kaempferol-3-*O*-galactoside and 2,3-dihydroxypropyl octacosanoate were isolated from a dichloromethane/methanol-soluble extract of the ripe fruits of the Cameroonian medicinal plant *Alchornea cordifolia*. The structures of the new fatty acid derivatives were elucidated by interpretation of their HRESIMS, 1D and 2D NMR spectroscopic data and by comparison with those reported in the literature. Some of the isolated compounds demonstrated inhibition activity against the microbial strains *Escherichia coli, Klebsiella pneumoniae* and *Citrobacter braakii*.

1. Introduction

The genus *Alchornea* belongs to the family Euphorbiaceae and comprises 60 species (Wu, 1991). *Alchornea cordifolia* (Schumach. & Thonn.) Muell. Arg. is a shrub that grows up to 8 m tall and has a large number of branches. It is widely distributed in tropical and subtropical regions of Africa where it is extensively used in traditional medicine for the treatment of pain and inflammatory disorders, hormonal-related gynaecological disorders, infertility, urinary infections, respiratory and intestinal problems as well as malaria and fevers (Pone et al., 2016). In Ghana and Burkina Faso the leaves, root bark and fruits of *A. cordifolia* are sold in local markets from November to January and thus constitutes a source of income for the local population (Mavar-Manga et al., 2007).

The varied popular uses of different plant parts of *A. cordifolia* have led to numerous modern pharmacological investigations including antibacterial, antifungal, antiplasmodial, spasmolytic, hepatoprotective, reproductive and antiviral activities (Siwe Noundou et al., 2016; Muanza et al., 1994; Tona et al., 2000, 2007; Osadebe et al., 2012; Ajibade and Olayemi, 2015; Ayisi and Nyadedzor, 2003). Earlier phytochemical studies have described the isolation of a variety of compounds belonging to the following classes: tannins and phenolic acids (Lamikanra et al., 1990; Ogungbamila and Samuelsson, 1990; Banzouzi et al., 2002), flavonoids (Lamikanra et al., 1990; Ogungbamila and Samuelsson, 1990; Ajali, 2000), alkaloids (Mavar-Manga et al., 2004) and terpenoids (Siwe Noundou et al., 2016). In a further detailed phytochemical study of *A. cordifolia*, we report herein the isolation and structural elucidation of two new fatty acid derivatives named deepoxyalchornoic acid (**1**) and bisalchonoicester (**2**) together with six known compounds as well as their antibacterial activity.

2. Results and discussion

The dichloromethane/methanol extract of ripe fruits of *A. cordifolia* was subjected to repeated column chromatography to give several fractions which were further purified to yield eight compounds of which compounds **1** and **2** were hitherto unknowns.

Compound **1**, named deepoxyalchornoic acid (Fig. 1), was isolated as an optically active white crystals, $[\alpha]_D^{20} = +4.54$ (c = 1.10, $CHCl_3$). This observed value is in accordance with those reported for other alchornoic acid derivatives (Asilbekova et al., 1987). Its molecular formula was determined to be $C_{20}H_{38}O_4$ from the pseudomolecular ion peak $[M + H]^+$ at m/z = 343.2869 (calcd. for $C_{20}H_{39}O_4$, 343.2848), obtained by high-resolution mass spectrometry (HRESIMS) and is consistent with two degrees of unsaturation. The IR spectrum featured bands at ν_{max} 3679 cm^{-1} (free OH) and 1697 cm^{-1} (C=O). The ^1H NMR spectrum of **1** (Table 1) revealed signals indicating the presence of

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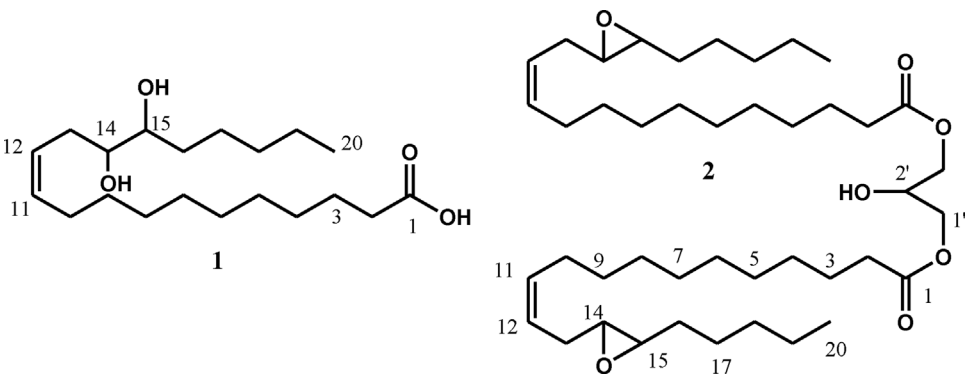

Fig. 1. Chemical structures of compounds **1** and **2**.

Table 1
^{1}H and ^{13}C NMR data for 14,15-dihydroxyeicos-11*Z*-enoic acid (**1**) and bisalchornoicester (**2**) in $CDCl_3$ (500 and 125 MHz).

Position	**1**		**2**	
	δ_H (m, J, Hz)	δ_C	δ_H (m, J, Hz)	δ_C
1		175.3		173.8
2	2.17 (t, 7.2)	34.4	2.35 (t, 7.5)	34.0
3	1.47 (m)	25.2	1.64 (m)	24.8
4	1.23 (brs)	29.3	1.35 (brs)	29.2
5–8	1.23 (brs)	29.4–29.7	1.29 (brs)	29.1–29.4
9	1.29 (brs)	29.8	1.29 (brs)	29.3
10	1.98 (m)	27.6	2.05 (m)	27.4
11	5.36 (dt, 7.2, 10.4)	131.2	5.53 (dt, 7.2, 10.5)	132.6
12	5.41 (ddd, 6.8, 7.2, 10.4)	127.7	5.41 (ddd, 7.0, 7.2, 10.5)	123.8
13	2.03 (ddd, 6.4, 6.8, 14.1) 2.20 (ddd, 6.1, 7.2, 14.1)	31.4	2.19 (ddd, 6.5, 7.0, 14.7) 2.38 (ddd, 6.2, 7.2, 14.7)	26.2
14	3.25 (m)	74.0	2.93 (m)	56.5
15	3.23 (m)	73.2	2.93 (m)	57.2
16	1.37 (m)	33.1	1.54 (m)	27.7
17	1.27 (m)	26.0	1.46 (m) 1.54 (m)	26.2
18	1.25 (m)	32.3	1.35 (m)	31.7
19	1.28 (m)	22.9	1.29 (brs)	22.5
20	0.84 (t, 6.8)	14.7	0.91 (t, 7.0)	13.9
1′			4.19 (dd, 4.3, 11.4) 4.14 (dd, 5.7, 11.4)	65.0
2′			4.09 (dd, 4.3, 5.7)	68.3

one terminal methyl group at δ_H 0.84 and a long chain of methylene protons at δ_H 1.23 − 1.98. The ^{13}C NMR spectrum of (**1**) (Table 1) displayed 20 carbon signals which were assigned in combination with DEPT and HSQC experiments to one methyl, fourteen methylenes, four methines and one quaternary carbon. Characteristic signals for a carboxylic acid group (δ_C 175.3), two olefinic carbons (δ_C 131.2 and 127.7), two oxygenated methine carbons (δ_C 74.0 and 73.2) and a terminal methyl (δ_C 14.7) were evident in the ^{13}C NMR spectrum. The fatty acid nature of (**1**) was confirmed by a set of signals at δ_C 29.4 − 29.7. In addition, the ^{1}H and ^{13}C NMR spectral data of compound **1** exhibited signals for two oxymethine protons and carbons at δ_H/δ_C 3.25/74.0 and 3.23/73.2, and two olefinic protons and carbons at δ_H/δ_C 5.36/131.2 and 5.41/127.7. Furthermore, the ^{1}H NMR spectrum had three upfield proton signals at δ_H 2.17, 2.20 and 2.03 which were assigned to two methylene groups (H-2 and H-13) adjacent to the carboxylic (C-1) and the oxymethine (C-14) carbons, respectively.

The structure of **1** was fully assigned by analyses of 2D NMR experiments. In the HMBC experiment, the proton signal at δ_H 2.17 (H-2) showed correlation peaks with carbon signals at δ_C 175.3 (C-1) and 29.3 (C-4), and cross peaks were also observed between the proton signal at δ_H 1.98 (H-10) and the carbon signals at δ_C 131.2 (C-11), 127.7 (C-12) and 29.8 (C-9). Furthermore, the methyl signal at δ_H 0.84 (H-20) showed cross peaks with two carbon signals at δ_C 22.9 (C-19) and 32.3 (C-18). The geometry of the double bond was found to be *Z* based on the coupling constant between the olefinic protons H-11 and H-12 (J = 6.8 Hz) and the chemical shifts (δ_C 27.6 and 31.4) assigned to the allylic carbons. The chemical shifts for the corresponding allylic carbons for the *E* configuration are usually more than δ_C 33.0 (Simo et al., 2008). This was confirmed in the ^{1}H NMR spectrum by the chemical shifts of allylic protons observed at δ_H 1.98, 2.03 and 2.20 (Rezanka, 2002). The NMR data of (**1**) was fully rationalized based on its comparison with those of related compounds described in the literature (Kleiman et al., 1977). Thus, the structure of **1**, named 14,15-dihydroxyeicos-11*Z*-enoic acid was assigned (Fig. 1).

Compound **2** was obtained as an optically active white crystals, $[\alpha]_D^{20}$ = + 4.48 (c = 4.68, $CHCl_3$). Its HRESIMS mass spectrum showed a pseudomolecular ion peak $[M + H]^+$ at m/z = 705.5661 (calcd. for $C_{43}H_{77}O_7$, 705.5669) corresponding to the molecular formula $C_{43}H_{76}O_7$. The IR spectrum showed absorption bands due to hydroxyl, ester carbonyls and an olefinic double bond at ν_{max} 3657, 1728, 1706 and 711 cm^{-1} respectively. Interpretation of the ^{1}H and ^{13}C NMR spectra of compound **2** (Table 1) indicated the presence of one methyl, 15 methylenes, 5 methines and one quaternary carbon. The ^{13}C NMR spectrum of **2** also indicated the presence of one characteristic ester carbonyl at δ_C 173.8, two olefinic carbons (δ_C 132.6 and 123.8), two oxymethine carbons characteristic of an epoxy group (δ_C 57.2 and 56.5), one terminal methyl (δ_C 13.9) and fourteen methylene chain carbons appearing between δ_C 34.0 − 22.5 ppm. These observations clearly indicated the presence of an alchornoic acid (**3**) moiety. Further analyses of the ^{13}C NMR spectrum displayed resonances for an oxymethine and an oxymethylene group at δ_C 68.3 and 65.0 respectively. In the ^{1}H–^{1}H COSY spectrum, cross peaks were observed between their corresponding proton signals at δ_H 4.09 (H-2′), 4.14 and 4.19 (H-1′). The ^{13}C NMR spectrum displayed only 22 carbon signals instead of 43. This lead to the conclusion that compound **2** is a dimer with alchornoic acid as a substructure. In the HMBC experiment, the oxymethine carbon signal showed a weak correlation with the methylene proton signals at δ_H 4.14 and 4.19 which in turn exhibited cross peak to the ester carbonyl signal at δ_C 173.8 (C-1). It was therefore concluded that two units of alchornoic acid have been condensed with glycerol in a symmetrical 1,3-fashion. Based on the above evidence, the structure of compound **2** was assigned and named bisalchornoicester.

The known compounds were identified as alchornoic acid (**3**) (Kleiman et al., 1977), gallic acid (**4**) (Ogungbamila and Samuelsson, 1990), 4-*O*-methylgallic acid (**5**) (Na et al., 2006), shikimic acid (**6**) (Eykman, 1885), kaempferol-3-*O*-galactoside (**7**) (Ek et al., 2006) and 2,3-dihydroxypropyl octacosanoate (**8**) (Kuigoua et al., 2010) (Fig. 2).

Compounds **1**, **4**, **5** and **6** which were obtained in sufficient quantity, were evaluated for their antibacterial activity utilizing an agar diffusion assay and compared with ciprofloxacin. The results, in terms of radius of zone of inhibition are presented in Table 2. From the table, it is evident that 4-*O*-methylgallic acid (**5**) and shikimic acid (**6**) were active against all microbial strains at our disposal (*Escherichia coli,*