AGRO-WASTE AS SOURCE OF FINE AND INDUSTRIAL CHEMICALS: SYNTHESIS OF 2-FORMYL-6-HYDROXYBENZOIC ACID AND 4-METHOXYISOBENZOFURAN-1,3-DIONE FROM CASHEW NUT SHELL LIQUID

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ABSTRACT
This paper reports on the synthesis of 2-formyl-6-hydroxybenzoic acid (8) and 4-methoxyisobenzofuran-1,3-dione (10) from a renewable natural material Cashew Nut Shell Liquid (CNSL) achieved in five and seven steps, respectively. Anacardic acid was isolated from CNSL, dimethoxylated into (E)-methyl 2-methoxy-6-(pentadec-8-enyl)benzoate which was subsequently hydrogenated into methyl 2-methoxy-6-pentadecylbenzoate. Benzylic bromination of the methoxyester, and dehydrobromination afforded (E)-methyl 2-methoxy-6-(pentadec-1-enyl)benzoate which upon ozonolysis gave methyl 2-formyl-6-methoxybenzoate. Oxidation and dehydration of 8 formed methoxyphthalic anhydride (10). The work reported in this paper has further demonstrated the resourcefulness of cashew nut shell liquid as a renewable natural resource for synthesis of fine and industrial chemicals.

Keywords: Anacardium occidentale, Cashew Nut Shell Liquid, Anacardic acid, 2-formyl-6-methoxybenzoate, methoxyphthalic anhydride

INTRODUCTION
The depletion of fossil fuels as sources of fine chemicals for various applications calls for search for alternative renewable sources. Nature is abounding with materials which when appropriately manipulated can serve as renewable supplies of fine chemicals. One such material is Cashew Nut Shell Liquid (CNSL) from the cashew plant Anacardium occidentale which is grown along the coast of Tanzania for its kernels, cashew nuts. CNSL is rich in phenolic compounds with unsaturated C₁₅ side chain meta substituents (Akinhanmi and Atasie 2008). Both the alkene, phenolic and carboxylic acid functional groups present in these natural lipids renders components of CNSL amenable to transformations into a variety of materials and fine chemicals (dos Santos and de Magalhaes 1999; Rodrigues et al. 2006; Yadavi and Srivastava 2008; Logrado et al. 2010; Vasapollo et al. 2011; Vempati et al. 2011; Reddy et al. 2012; Wisastr et al. 2012; Gandhi et al. 2014). As a continuation of efforts to add value to the abundantly available agro-waste...
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cashew nut shells (CNS) from the cashew nut industry in Tanzania (Mmongoyo et al. 2012; Mkungu et al. 2013; Mgaya et al. 2015, 2016), this paper reports on the successful conversion of anacardic acid (1) into fine chemicals methyl 2-formyl-6-methoxybenzoate (8) and 4-methoxyisobenzofuran-1,3-dione (10). Compound 10 and its precursor aldehyde 8 are versatile starting fine chemicals for a number of transformations in natural product synthesis (Dhananjeeyan et al. 2005; Singh and Geentanjali 2005; Naysmith and Brimble 2013, Schunemann et al. 2014). Hydrolysis of the ester group and demethylation of the ether group is expected to give 2-formyl-6-hydroxybenzoic acid, an equally resourceful synthetic intermediate.

MATERIALS AND METHODS
Material, Reagents, Instruments and General Procedures
Dry cashew nut shells were collected from Southern Jumbo, a small scale cashew processing factory in Dar es Salaam. All reagents and chemicals were purchased from Sigma Aldrich, South Africa. Solvents were distilled prior to use. All reactions were carried out in oven-dried glassware. Organic layers obtained following workup of reaction mixtures were dried over anhydrous MgSO₄. Column chromatographic separations were performed by using EM type 60 silica gel (230-400 mesh). Analytical Thin Layer Chromatography (TLC) was performed on Merck pre-coated silica gel (60F₂₅₄/0.2 mm) plates and spots were visualized using UV light at 254 nm and/or anisaldehyde spray reagents. A Bruker Optic GmbH 2011 FT-IR spectrophotometer was used for IR data acquisition. ¹H and ¹³C NMR spectra were recorded in deuterated chloroform (CDCl₃) at 300/500 MHz on a Bruker A.G. spectrometer and chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane (Me₄Si) as internal standard. Coupling constants were reported as J (Hz) and multiplicities with abbreviations d, doublet; dd, double doublet; t, triplet; br, broad and m, multiplet.

Isolation of Anacardic Acid
Cashew nut shells (500 g) were soaked in 1000 mL of 99% ethanol for 48 hours and then filtered to obtain 850 mL of cashew nut shell liquid extract. To the 850 mL extract, a total of 20.00 g of calcium hydroxide was added portion-wise and stirred for 3 hours while the temperature was maintained at 50 °C. The calcium anacardate (40.34 g) precipitated was collected by filtering under vacuum. Calcium anacardate (20.00 g), suspended in 80 mL of distilled water, was mixed with 13 mL of 11 M HCl and the resulting mixture was stirred for 3 hours and then extracted with ethyl acetate (2 × 100 mL). The combined ethyl acetate extract was washed with distilled water (2 × 50 mL) and dried over MgSO₄. Filtration of the drying agent followed by evaporation of the solvent gave 11.00 g (58% yields) of the crude extract of anacardic acid (5).

Preparation of methyl 2-methoxy-6-(pentadec-8-en-1-yl)benzoate (4*)
In a 250 mL round bottomed flask containing compound 5 (11.00 g, 0.030 mol), dissolved in 200 mL acetone, was added K₂CO₃ (20.00 g, 0.150 mol) followed by portion-wise addition of dimethyl sulphate (18.90 g, 0.150 mol). The reaction mixture was refluxed in an oil bath for 24 hours under a nitrogen atmosphere and then cooled to room temperature. After the evaporation of acetone, the reaction mixture was extracted with ethyl acetate (2 × 100 mL) and the combined organic extract washed with water (2 × 50 mL). The organic layer was dried over MgSO₄, filtered and the solvent evaporated in the rotary evaporator and then under high
vacuum. The crude product was then purified by column chromatography over silica gel using a mixture of hexane/ethyl acetate (95:5) to afford compound 4* (Fig.1) as a pale yellow liquid (6.00 g, 54%). ¹H NMR (300 MHz, CDCl₃): δ_H = 0.86 (t, 3H), 1.3 (m, 16H), 1.57 (m, 2H), 2.00 (m, 4H), 2.51 (t, J = 8.0 Hz, 2H), 3.8 (s, 3H), 3.9 (s, 3H), 5.32 (m, 2H), 6.73 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 7.5 Hz, 1H) and 7.20 (t, J = 7.8 Hz, 1H). FTIR (Film): 722.86 cm⁻¹, 1289.73 cm⁻¹, 1307.77 cm⁻¹, 1404.06 cm⁻¹, 1524.83 cm⁻¹, 1569.86 cm⁻¹, 1584.23 cm⁻¹, 1626.54 cm⁻¹, 2852.73 cm⁻¹, 2923.83 cm⁻¹ and 3479.50 cm⁻¹.

Preparation of methyl 2-methoxy-6-pentadecylbenzoate (5)
To a stirred solution of 4* (6.00 g, 0.020 mol) in 200 mL methanol was added 10% palladium-carbon (0.23 g) and then hydrogen gas was passed through the solution for 12 h. The reaction mass was filtered over a celite bed and washed with methanol (100 mL). The filtrate was concentrated under reduced pressure to afford product 5 (Fig. 13) as pale yellow liquid (5.70 g, 95%). ¹H NMR (300 MHz, CDCl₃): δ_H = 0.88 (t, 3H), 1.25 (m, 25H), 1.57 (m, 2H), 2.14 (m, 2H), 3.83 (s, 3H), 3.94 (s, 3H), 4.91 (t, J = 7.4 Hz, 1H), 6.85 (d, J = 8.1 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H), and 7.38 (t, J = 8.1 Hz, 1H).

Figure 1: Some Derivatives of Anacardic Acid (5); * = compound 4 is named on the basis of the predominant D8 monoenyl substituent.

Preparation of methyl 2-methoxy-6-(pentadec-1-en-1-yl)benzoate (7)
An oven dried 250 mL round bottomed flask was charged with compound 6 (4.50 g, 0.010 mol) in 150 mL of dry toluene and DBU (2.30 g, 0.015 mol) under nitrogen atmosphere. The reaction mixture was heated at 80 °C for 15 hours. The reaction mixture was cooled to room temperature, evaporated in the rotary evaporator, followed by extraction with ethyl acetate (3 × 100 mL). The organic phase was washed with water (3 × 50 mL) and dried over MgSO₄. The drying agent was filtered off and the solvent evaporated in the rotary evaporator to give a crude product, which was purified by column chromatography over silica gel using hexane/ethyl acetate mixture (95:5) to yield a yellowish liquid (4.56 g, 84%) of bromine 6. ¹H NMR (300 MHz, CDCl₃): δ_H = 0.88 (t, J = 6.5 Hz, 3H), 1.25 (m, 22H), 1.57 (m, 2H), 2.14 (m, 2H), 3.83 (s, 3H), 3.94 (s, 3H), 4.91 (t, J = 7.4 Hz, 1H), 6.85 (d, J = 8.1 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H), and 7.38 (t, J = 8.1 Hz, 1H).
MgSO\(_4\). The drying agent was filtered off and the solvent evaporated in rotary evaporator followed by high vacuum pump to give the crude product, which was purified by column chromatography (silica gel, 90:10 hexane/EtOAc) to yield the alkene 7 (Fig. 1) as a white powder (2.28 g, 60% yield). \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) = 0.88 (t, 3H), 1.26 (m, 10H), 1.44 (m, 2H), 2.17 (q, 2H), 3.83 (s, 3H), 3.92 (s, 3H), 6.25 (m, 2H), 6.78 (d, 1H), 7.11 (d, 1H) and 7.27 (t, 1H).

Preparation of methyl 2-formyl-6-methoxybenzoate (8)
To a stirred solution of methyl 2-methoxy-6-(pentadec-1-en-1-yl)benzoate (7) (2.28 g, 0.006 mol) in dry CH\(_2\)Cl\(_2\) (100 mL) was added Sodium III indicator (2 drops) while maintaining the reaction temperature at -8 °C. Ozone gas was bubbled into the reaction until the color changed from pink to colorless. Argon gas was passed into the reaction for 10 minutes and dimethyl sulfide (5.06 g, 0.081 mol) was added to the reaction at -78 °C. The reaction was then warmed to room temperature and stirred for 1 hour. The reaction mixture was then concentrated in a rotary evaporator and the residue purified by column chromatography over silica gel (15% EtOAc/hexane) to afford 1.14 g, (63% yield) of the product 8 (Fig. 1) as a white powder. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) = 3.89 (s, 3H), 3.98 (s, 3H), 7.26 (d, 1H), 7.47 (d, 1H) and 9.97 (s, 1H). \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) = 52.72 (C-9), 55.45 (C-10), 115.45 (C-4), 122.72 (C-5), 125.45 (C-2), 128.18 (C-1), 130.01 (C-6), 156.36 (C-3), 168.18 (C-8), and 169.09 (C-7). FTIR (Film): 3644.17 cm\(^{-1}\), 1043.62 cm\(^{-1}\), 1235.79 cm\(^{-1}\), 1372.78 cm\(^{-1}\), 1589.20 cm\(^{-1}\), 1736.47 cm\(^{-1}\), 2662.92 cm\(^{-1}\), 2939.57 cm\(^{-1}\), 2983.67 cm\(^{-1}\) and 3513.54 cm\(^{-1}\).

Preparation of 3-methoxy-2-(methoxycarbonyl)benzoic acid (9)
In an oven dried 50 mL round bottomed flask containing compound 8 (0.10 g, 0.520 mmol) in 10 mL tert-butanol/water (1:1 ratio) were added cyclohexene (0.10 g, 0.0012 mol), NaH\(_2\)PO\(_4\) (0.10 g, 0.830 mmol) and NaClO\(_2\) (0.07 g, 0.770 mmol). The reaction mixture was stirred for 3 hours when TLC analysis indicated no starting material. The reaction mixture was evaporated using a rotary evaporator and the residue extracted with ethyl acetate (2 \(\times\) 50 mL). The combined EtOAc extract was washed with 50 mL of water and dried over MgSO\(_4\). After filtering off the drying agent, the solvent was evaporated in rotary and in high vacuum to yield compound 9 (Fig. 1) as a needle-shaped crystalline product (0.010 g, 98% yield). \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) = 3.88 (s, 3H), 3.94 (s, 3H), 7.17 (d, \(J = 8.4\) Hz, 1H), 7.43 (t, \(J = 8.1\) Hz, 1H) and 7.70 (d, \(J = 7.8\) Hz, 1H). \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) = 52.72 (C-9), 55.45 (C-10), 115.45 (C-4), 122.72 (C-5), 125.45 (C-2), 128.18 (C-1), 130.01 (C-6), 156.36 (C-3), 168.18 (C-8), and 169.09 (C-7). FTIR (Film): 3644.17 cm\(^{-1}\), 1043.62 cm\(^{-1}\), 1235.79 cm\(^{-1}\), 1372.78 cm\(^{-1}\), 1589.20 cm\(^{-1}\), 1736.47 cm\(^{-1}\), 2662.92 cm\(^{-1}\), 2939.57 cm\(^{-1}\), 2983.67 cm\(^{-1}\) and 3513.54 cm\(^{-1}\).

Preparation of 4-methoxyisobenzofuran-1,3-dione (10)
In a 50 mL round bottomed flask containing compound 9 (0.10 g, 0.470 mmol) were added thionyl chloride (6.56 g, 0.060 mol) under a nitrogen atmosphere and mixture refluxed for 3 hours when TLC analysis indicated no starting material. The reaction mixture was evaporated using a rotary and in high vacuum to give the residue extracted with ethyl acetate (2 \(\times\) 10 mL). The combined EtOAc extract was washed with 50 mL of water and dried over MgSO\(_4\). After filtering off the drying agent, the solvent was evaporated in rotary and in high vacuum to yield compound 10 (Fig. 1) as a needle-shaped crystalline product (0.010 g, 98% yield). \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) = 7.8 Hz, 1H). \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) = 52.55 (C-9), 55.45 (C-10), 115.45 (C-4), 122.72 (C-5), 125.45 (C-2), 128.18 (C-1), 130.01 (C-6), 156.36 (C-3), 168.18 (C-8), and 169.09 (C-7). FTIR (Film): 3644.17 cm\(^{-1}\), 1043.62 cm\(^{-1}\), 1235.79 cm\(^{-1}\), 1372.78 cm\(^{-1}\), 1589.20 cm\(^{-1}\), 1736.47 cm\(^{-1}\), 2662.92 cm\(^{-1}\), 2939.57 cm\(^{-1}\), 2983.67 cm\(^{-1}\) and 3513.54 cm\(^{-1}\).
evaporator and dried under high vacuum pump to yield 0.08 g (95%) of the anhydride 10 as a needle-shaped crystalline material. $^1$H NMR (300 MHz, CDCl$_3$): $\delta_{\text{H}} = 4.08$ (s, 3H), 7.33 (d, $J = 8.5$ Hz, 1H), 7.59 (d, $J = 7.5$ Hz, 1H) and 7.85 (t, $J = 8$ Hz, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta_{\text{C}} = 56.65$ (C-9), 116.36 (C-2), 117.48 (C-4), 118.60 (C-6), 132.54 (C-1), 138.36 (C-5), 157.52 (C-3), 160.36 (C-7) and 162.59 (C-8).

RESULTS AND DISCUSSION
Extraction of CNSL from CNS and Isolation of Anacardic Acid (3)
The cashew nut shells obtained from a cashew nut processing factory in Dar es Salaam were solvent extracted with 99% ethanol for 48 hours to obtain natural cashew nut shell liquid ($n$CNSL) (Murthy et al. 2009). The yield of the CNSL was 27% of the weight of the dry shells which compares well with a 31% yield reported by Paramashivappa et al. (2001). Anacardic acid was subsequently separated from the mixture following a slight modification of Paramashivappa protocol (2001). CNSL was dissolved in 5% aqueous methanol to which calcium hydroxide was slowly added while stirring vigorously. The more acidic anacardic acid reacted with the base precipitating the acid as calcium anacardate while leaving in solution the weakly acidic phenols, cardol and cardanol (Scheme 1).

The calcium anacardate was acidified with 6 M HCl to obtain a mixture constituting monoene, diene and triene anacardic acids in 55% yield from CNSL. The yields compare well with that in literature at 60% (Gandhi et al. 2012).

Transformation of anacardic acid to 4-methoxyisobenzofuran-1,3-dione (10)
The synthetic transformation of anacardic acid to the desired phthalic anhydride 10 commenced with the protection of the phenolic and carboxylic hydroxyl groups by methylation with dimethyl sulphate in acetone under reflux to yield compound 4 (Scheme 2) in 54% yield. Although Scheme 2 depicts compound 4 as having the D8 monoenyl C$_{15}$ substituent, 4 is in reality a mixture in which the C$_{15}$ side chain occurs as a pentadecyl, D8-pentadecenyl, D8,11-pentadecadienyl and D8,11,14-pentadecatrienyl carbon chain. However, it is worth noting that the monoenyl (D8-pentadecenyl) side chain constitutes the predominant structure of the C$_{15}$ substituent in all the CNSL phenols and hence the basis for formulating compound 3 and 4 as shown in Scheme 2. The Scheme summarizes the complete synthetic transformation of anacardic acid (3) to 4-methoxyisobenzofuran-1,3-dione (10). The $^1$H NMR spectrum for compound 4 showed signals for the aromatic protons as a doublet at $\delta_{\text{H}}$ 6.73 (for H-3), doublet at 6.83 ppm (H-5) and triplet at 7.20 ppm (H-4). The methoxy protons (3H) appeared as a singlet at 3.80 ppm whereas the carbomethoxy protons (3H) appeared as a singlet at 3.9 ppm. The terminal methyl group (H-15') of the D8-pentadecenyl side chain appeared as a triplet integrating for three protons at $\delta_{\text{H}}$ 0.86 ppm. The methylene (CH$_2$) groups were observed as a multiplet at $\delta_{\text{H}}$ 1.30 ppm while the benzylic protons (H-1') appeared as a triplet at a $\delta_{\text{H}}$ 2.51 ppm. The olefinic
protons (H-8', H-9') appeared as a multiplet at 5.32 ppm.

Compound 4 was then catalytically hydrogenated using Pd/C in methanol to give compound 5 (Scheme 2, vide supra) with the saturated C_{15} side chain. The $^1$H NMR spectrum of compound 5 exhibited signals for the aromatic protons at δ_H 6.73, 6.83 and 7.20 ppm as two doublets and a triplet of one proton each for H-3, H-5 and H-4, respectively. Two singlets at δ_H 3.81 and 3.90 ppm were assigned for the methoxy (3H) and carbomethoxy (3H) protons, respectively. Logrado and co-workers (2010) reported that the signals for the two groups appeared at δ_H 3.91 and 3.92 ppm. The chemical shifts for the protons of the pentadecyl side chain of compound 5 were similar to that of compound 4 with the exception of the disappearance of the olefinic protons signal (at ca. 5 ppm). The $^{13}$C NMR spectrum fully agrees with the assigned structure. In the low field one resonance appears at δ_C 168.93 ppm, which is assigned to the quaternary carbonyl carbon of compound 5. Six signals for the aromatic carbons appeared at δ_C 156.29, 141.43, 130.22, 123.55, 121.52 and 108.40 ppm, while signals for the methoxy and the carbomethoxy carbons were observed at δ_C 55.89 and 52.09 ppm, respectively. A signal at δ_C 33.51 ppm was assigned to the benzylic carbon (C-1') while the peak at δ_C 31.17 ppm was assigned to the carbon next to the benzylic carbon (C-2'). The signal at δ_C 14.12 ppm was assigned to the terminal methyl carbon of the pentadecyl chain while the methylene carbons next to it appeared at δ_C 22.71 ppm and the other twelve methylene carbons were put together at a chemical shift range of δ_C 29.71-29.83 ppm. These δ_C values are comparable to those reported by Logrado et al. (2010).

Scheme 2: Transformation of anacardic acid (3) to 4-methoxybenzofuran-1,3-dione (10).

Benzylic bromination of 5 with NBS yielded compound 6 (Scheme 2, vide supra) in 85% as a yellowish liquid. The $^1$H NMR spectrum of bromide 6 had its aromatic protons signals appearing at δ_H 6.85, 7.22 and 7.41 ppm as two doublets and a triplet, respectively. Each of these signals represented one proton. Logrado et al. (2010) reported a slight difference in the chemical shifts of the same aromatic protons. Logrado observed that the signals for the aromatic protons appeared at δ_H 6.84, 7.21 and 7.38 ppm, respectively. A signal at δ_H 4.91 ppm (t, 1H) accounted for the proton at the benzylic position (H-1') carrying the bromine atom. The two singlets at δ_H 3.83 (3H) and 3.94 ppm (3H) were assigned to the
methoxy and carbomethoxy protons, respectively. A multiplet at δH 2.15 ppm was assigned to the H-2’ methylene protons. A multiplet of two protons resonating at a chemical shift of 1.57 ppm was assigned to H-3’ methylene protons while a multiplet at δH 1.25 ppm integrating for twenty two protons accounted for the remaining methylene groups.

Dehydrobromination of compound 6 using DBU gave the benzylic alkene 7 (Scheme 2, vide supra) in 60% yield as white crystals. Attempts to use trimethylamine as the base for the dehydrohalogenation reaction proved unsuccessful. The 1H NMR spectrum for alkene 7 had its aromatic protons appearing at δH 6.78, 7.11 and 7.30 ppm as two doublets and one triplet, respectively, each integrating for one proton. A multiplet at δH 6.25 ppm accounted for the two olefinic protons. Logrado et al. (2010) reported a δH 6.24 ppm for the same protons, which is pretty close to the present results. The two singlets at δH 3.83 and 3.92 ppm, each representing three protons, were assigned to the methoxy and carbomethoxy protons, respectively. A quartet at δH 2.13 ppm is due to the two methylene protons at the allylic position (i.e., H-3’). Next to it is a multiplet at δH 1.44 ppm assigned to the two homoallylic methylene protons. Whereas a broad multiplet at δH 1.26 was assigned to the remaining 20 methylene protons, a triplet at δH 0.86 ppm was assigned to the terminal methyl protons of the pentadeceyl side chain.

Ozonolysis of the alkene 7 in dry DCM at -78 °C resulted into aldehyde 8 (Scheme 2) as a white powder in 63% yield. In the IR spectrum of aldehyde 8 bands at 1733 and 3089 cm⁻¹ are due to the C=O and C–H stretch, respectively. The 1H NMR spectrum of aldehyde 8 showed that there was a shift in the position of the aromatic protons in the sense that these protons were more deshielded and appeared at δH range of 7.21-7.57 ppm in contrast to alkene 7 which had its aromatic protons resonating at δH 6.76-7.3 ppm. These protons, each integrated to one, appeared as two doublets at δH 7.21 and 7.47 (for H-3 and H-5, respectively) and one triplet at δH 7.57 ppm (H-4). A singlet at δH 9.97 ppm was assigned to the aldehydic proton. Tu et al. (2013) reported a slightly different δH value of 10.36 ppm for the same aldehydic proton. The signals for the methyl protons of the –OCH3 and –CO2CH3 groups appeared at δH 3.89 and 3.98 ppm, respectively. Moreover, the appearance of only 10 peaks in the 13C NMR spectrum signified the absence of the C15 side chain. The most downfield signal at δC 190.05 ppm is due to the presence of the aldehydic C=O. The signal at δC 167.46 ppm was assigned to the C=O of the ester group. The six signals at δC 116.67, 122.49, 123.61, 130.84, 134.35 and 156.27 ppm are due to the aromatic carbons. The remaining up field signals at 52.55 and 56.28 ppm were assigned to the two methyl carbons of the –CO2CH3 and –OCH3 groups, respectively.

It is worth noting that Plourde and Spaetzel (2002) have reported values ranging from 191.1 to 191.3 ppm for the groups of analogous benzaldehydes. Moreover, Daquino et al. (2009) and Seo et al. (2012) have reported 13C NMR signals appearing at δC 168 to 169.5 ppm due to benzoate ester C=O carbons. The aforementioned δC values are in close agreement to the corresponding values obtained for compound 8. Aldehyde 8 is a useful starting fine chemical for entry into synthesis of quinones and anthraquinones natural products via the Hauser-Kraus annulation chemistry (Hauser et al. 2003, Hassan et al. 2015,). Further oxidation of the aldehyde 8 with NaClO2 in NaH2PO4 buffer formed carboxylic acid 9 (Scheme 2, vide supra) as white needle-shaped crystals in 98% yield. In the IR spectrum of 9, a broad peak was observed around 3513.54 cm⁻¹ due to the carboxylic O–H
stretch. The bands observed at 1736 cm\(^{-1}\) and 1235 cm\(^{-1}\) were due to the C=O and C–O stretch, respectively. Inspection of the \(^1\)H NMR spectrum of compound 9 indicated that the aldehydic proton had disappeared. The aromatic protons appeared as two doublets at \(\delta_H\) 7.15 and 7.70 and a triplet at \(\delta_H\) 7.49 ppm for H-4, H-5 and H-6, respectively. The methyl protons for –OCH\(_3\) and –CO\(_2\)CH\(_3\) groups appeared at \(\delta_H\) 3.88 and 3.94 ppm, respectively. These \(\delta_H\) are similar to those reported by Gupta et al. (1987) for the same compound. In the case of aldehyde 8, it was noted that the aromatic proton appearing as a triplet (H-5) was more deshielded (\(\delta_H = 7.57\) ppm). However, the same proton (H-5) in compound 9 was less deshielded and appeared as triplet at \(\delta_H\) 7.49 ppm. Conversely, H-4 was more deshielded in compound 9 (\(\delta_H = 7.70\) ppm) than it was the case in compound 8 (\(\delta_H = 7.47\) ppm), which is probably due to the increase in partial positive charge on the carbonyl carbon of the carboxyl group.

The \(^13\)C NMR spectrum displayed signals at \(\delta_C\) 168.18 and 169.94 ppm due to the two carbonyl carbons of the carboxyl and ester (benzoate) groups, respectively. Daquino et al. (2009) and Kiran et al. (2013) reported \(^13\)C NMR signals appearing at \(\delta_C\) 172.3 and 164.1-166.9 ppm due to carboxyl and benzoate C=O carbons, respectively, values which are in close agreement to the corresponding values obtained for compound 9. Six signals due to the aromatic carbons were observed at \(\delta_C\) 115.45, 122.72, 125.45, 128.18, 130.01 and 156.36 ppm. The more up field signals due to the methoxy carbons for –OCH\(_3\) and –CO\(_2\)CH\(_3\) groups appeared at \(\delta_H\) 52.72 and 55.45 ppm, respectively.

Several methods were attempted to convert compound 9 to phthalic anhydride 10 including heating compound 9 under high vacuum, heating at 70 °C in the presence of dilute H\(_2\)SO\(_4\) and treatment of 9 with thionyl chloride at 70 °C. Unreacted starting material was recovered in the first two attempts. However, treatment of compound 9 with thionyl chloride gave the desired anhydride 10 in near quantitative yield. The foregoing observation suggests that successful cyclization of 9 upon treatment with SOCl\(_2\) is facilitated by formation of the acid chloride with a very good leaving group which is easily attacked by the methoxy group of the ester as indicated in Scheme 3.

The \(^1\)H NMR spectrum of compound 10 displayed a singlet at \(\delta_H\) 4.08 ppm (3H) due the methoxy group. Gupta et al. (1987) and Liu (2004) also observed that protons for the same methoxy group appeared at the same chemical shift, i.e., \(\delta_H\) 4.08 ppm. The signals due the aromatic protons appeared as two doublets at \(\delta_H\) 7.33 and 7.59 ppm and a triplet at \(\delta_H\) 7.85 ppm, which are assigned to H-5, H-6 and H-7, respectively. Liu (2004) reported that the
aromatic protons for 3-methoxyphthalic anhydride appeared at δ_H range of 7.3-7.8 ppm. The signal due to H-6, which is a triplet, appeared in the low field (δ_H = 7.85 ppm) in compound 10 compared to its position (δ_H = 7.49 ppm) in compound 9. The 13C NMR spectrum of the anhydride 10 displayed nine peaks; with peaks at δ_C 160.36 and 162.59 ppm being due to the two quaternary carbonyl carbons. The six aromatic carbon atoms had their signals appearing at δ_C 116.36, 117.48, 118.60, 132.54, 138.36, and 157.52 ppm. The signal for the methoxy carbon appeared at δ_C 56.65 ppm.

CONCLUSIONS
The authors have reported previously on the utilization of anacardic acid and cardanol components of nCNSL in the synthesis of dyes, a detergent, a kairomone component and other useful chemicals. The chemistry reported in this paper has demonstrated once again the versatility of cashew nut shell liquid as a renewable natural resource for synthesis of fine and industrial chemicals. Accordingly, further synthetic work on the use of cardanol and cardol, the other major components of CNSL, as starting material for synthesis of fine chemicals and natural products is in progress and will be reported in due course.

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