Research Article

Synthesis of a kairomone and other chemicals from cardanol, a renewable resource[†]

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Synthesis of a tsetse fly kairomone component (3-propylphenol), a detergent [sodium 2-(dec-8-enyl)-6-hydroxybenzenesulfonate], a polymer additive (1-octene), and a detergent precursor [3-(non-8-enyl)phenol] using cardanol [3-(pentadec-8-enyl)phenol], has been accomplished. Both carbon–carbon double bond isomerization and metathesis methodologies were employed in the syntheses of these target molecules. The kairomone component was obtained, albeit in low yield, in three steps starting with cardanol. Synthesis of a new detergent, sodium 2-(dec-8-enyl)-6-hydroxybenzenesulfonate, was achieved by direct metathesis of cardanol with *cis*-2-butene followed by sulfonation and basification. Finally, synthesis of 1-octene and 3-(non-8-enyl)phenol was accomplished in one pot by direct metathesis of cardanol with ethylene. These products have been characterized spectroscopically, especially using ^{1}H and ^{13}C NMR.

Keywords: Cardanol / Detergent / Double bond isomerization / Kairomone component / Metathesis

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1 Introduction

Syntheses using biodegradable and renewable natural resources must be developed to replace those from the petrochemical industry since oil based resources are depleting at an alarming rate. It would be especially attractive to use feedstocks that are waste byproducts of food production, since no issue regarding the competition between food and chemicals for land use would arise. Cashew nut shell liquid (CNSL) is a biodegradable and renewable natural resource, which is a byproduct of the cashew nut processing industry available at about 300 000 tonnes/year worldwide [1] and has few uses so is generally considered to be a waste stream. It consists predominantly of four phenolic compounds, the proportion of which depends on the method by which it is extracted from the shells. Solvent extraction gives mainly anacardic acid, whilst roasting gives predominantly cardanol because anacardic acid decarboxylates on heating [2] (Table 1).

Anacardic acid can be isolated from the other phenolic components by precipitation of its calcium salt using calcium hydroxide followed by acidification [4]. On heating to about 200°C the acids loses CO_2 without alteration of the side chain to give predominantly cardanol [2]. The 15-carbon side chain is located *meta* to the phenolic group and it varies in the degree of unsaturation as shown in Fig. 1, making cardanol a potentially valuable starting material for chemical manipulation. The degree of unsaturation seems to depend upon the area of origin of the cashew nuts and is somewhat variable.

The versatility of cardanol as a starting material in synthesis arises from its structure. The presence of an aromatic system and a 15 carbon unsaturated side chain *meta* to a hydroxyl function renders it amenable to a variety of chemical modifications. The design of this study related the structure of target molecules to that of cardanol (Fig. 2). The use of cardanol in synthesis is not a new concept. For instance, the

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Abbreviations: CNSL, cashew nut shell liquid; **DTBPMB,** *bis*(ditertiarybutylphosphinomethyl)benzene; **FTIR,** Fourier-transformed infrared; **GC-MS,** gas chromatography-mass spectroscopy; **HG2,** Hoveyda–Grubbs catalyst; **NMR,** nuclear magnetic resonance; **RT,** room temperature

[†] In celebration of the 60th Birthday of Christian Bruneau, Université Rennes I; a fine scientist and a good friend.

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Table 1. Typical composition of cashew nut shell liquid obtained by solvent extraction or by roasting [2] [a)]

Component	Anacardic acid **1**	Cardanol **2**	Cardol **3**	2-Methylcardol **4**
Solvent extraction	65	10	15	tr
Roasting	10	85		2

[a)] R is a C_{15} chain with 1–3 double bonds, see Fig. 1. Some polymer is formed on roasting.

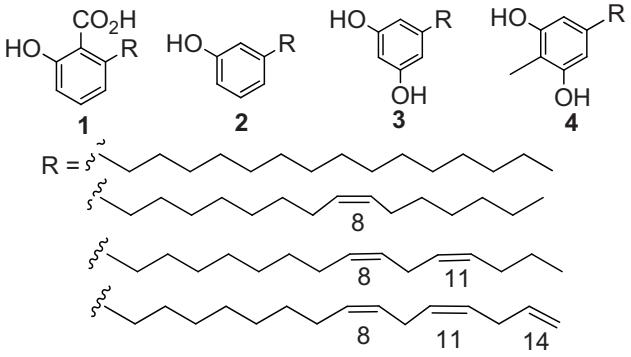


Figure 1. Phenolic compounds contained in CNSL.

synthesis of biscardanol derivatives for application as resins, surface coating and friction lining materials [5] and the synthesis of a detergent, sodium cardanol sulfate [6], from cardanol have been reported. In addition, synthesis of novel cardanol based fulleropyrrolidines has also recently been reported [7]. Cardanol [8] or sulfonated cardanol [9–11] can be functionalized to form phenolic ethers, which are used as polymer additives [9–11] or in nanofibers [8]. Although cardanol has been exploited as a starting material, the application of homogeneous catalysis to its modification to more valuable compounds has rarely been described. The one exception is metathesis [12, 13], which has been used to make alkyl chain separated biphenols (self-metathesis) and phenol esters of varying chain length (cross metathesis with, e.g., diethyl fumarate) [12] in addition to being applied to cardanol porphyrins [5, 14] and cardanol fullerenes [7]. We now report homogeneous catalytic modification of cardanol to lead to a natural tsetse fly attractant, **5**, a new detergent, **6**, 1-octene, a polymer additive, **7**, and a detergent precursor, **8** (Fig. 2).

Target compound **5** is a natural tsetse fly attractant (a kairomone component) found in excretory products like the urine of cattle and buffaloes [15, 16]. It is one of the phenolic components of the kairomone blend responsible for the characteristic smell of the urine of the cattle and the buffaloes [17, 18]. Kairomones are widely applied as baits to attract tsetse flies to traps (fake cows) treated in advance with broad spectrum insecticides to kill these known vectors of the deadly African sleeping sickness, trypanosomiasis [19, 20]. Detergent **6** may have both domestic and industrial applications. Its synthesis from cardanol may boost the value of the cashew crop. 1-Octene, **7**, is used as a plasticizer in the industrial production of linear low density polyethylene and it is also used for the synthesis of linear and branched aldehydes by hydroformylation [21]. Annual production of 1-octene is around 600 000 tonnes with a market value of $1 bn. It is mainly extracted during oil distillation or from Fischer Tropsch streams, although a new route from ethene tetramerization [22], also petroleum based, will soon be commercialized. 3-Nonylphenol, obtainable from compound **8** by hydrogenation is a detergent precursor. We think it might be a suitable replacement for 4-nonylphenol, which has been produced on a 100 000 tonnes/year scale for ethoxylaton and use as a detergent. However, 4-nonylphenol has been banned from use in European community because it has endocrine disrupting properties [23, 24]. These properties arise because the branched C_9 chain can adopt a configuration which has a similar structure to that of estrogens (Fig. 3) [25]. By having a straight chain in the 3, rather than 4 position, it is probable that the detergent properties will remain good after ethoxylation, but it should not be able to act as an estrogen mimic. It is known that 2-alkylphenols

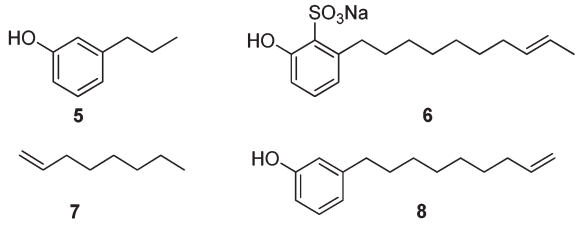


Figure 2. Structures of target molecules.

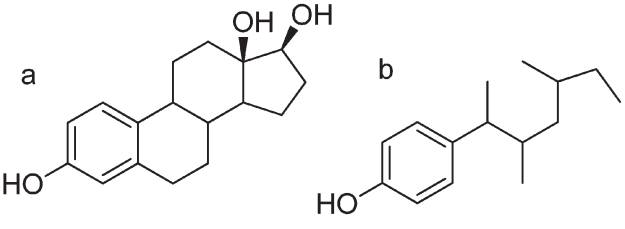


Figure 3. Comparison of the structure of (a) 17β-estradiol with (b) one isomer of 4-nonylphenol [25].

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are not endocrine disrupters [24], but the 3-isomers do not appear to have been tested. Linear chains are preferred in alkylbenzene sulfonate detergents because they cause less foaming than their branched chain analogues so linear chains may also be effective here [26].

2 Materials and methods

2.1 General

All reagents were purchased from Sigma–Aldrich and used as received. All solvents were purchased from Sigma–Aldrich and were purified, dried and stored under nitrogen atmosphere in Schlenk tubes prior to being used. Tris(dibenzylideneacetone)dipalladium(0) ($Pd_2(dba)_3$, 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro-(*o*-isopropoxyphenylmethylene) ruthenium and the ligand DTBPMB were stored in a glove box. CNSL was extracted from shells collected from Naliendele in Mtwara, Tanzania. Anacardic acid was obtained from the oil by a literature method [4] and cardanol was obtained by decarboxylation of anacardic acid. Cardanol was vacuum dried before it was subjected to reactions. The double bond composition in cardanol was determined by running single ion scans in the GC–MS for the parent ions of 3-pentadecylphenol (304), 3-pentadecenylphenol (302), 3-pentadecadienylphenol (300), and 3-pentadecatrienylphenol (298). The areas under these peaks were compared to obtain the percentage composition of each degree of unsaturation. This analysis assumes that the mass spectrometer is equally sensitive to all the parent ions.

2.2 Instruments

All weighing manipulations of air- and moisture-sensitive chemicals were carried out in the glove box of model type FF100 Recirc 13649 series purged for 30 min and flooded with nitrogen gas before use. All reactions which used air sensitive chemicals were carried out under nitrogen atmosphere using Schlenk tubes, flasks and autoclaves; gassing and degassing system and catheter tubing techniques. GC–MS analyses were carried out using a Hewlett-Packard 6890 series gas chromatograph instrument equipped with a flame ionization detector for quantitative analysis and a Hewlett-Packard 5973 series mass selective detector fitted with hp1 film for mass spectral identification of products. The temperature program used was 50°C (4 min), 20°C/min to 130°C (2 min), 20°C/min to 220°C (15.5 min). Helium was used as the carrier gas with initial flow of 1 mL/min. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 400 NMR spectrometer at 400 and 100 MHz or a Bruker AM 300 spectrometer at 300 and 75 MHz, respectively. Samples were dissolved in deuterated solvents which were referenced internally relative to tetramethylsilane (TMS) at $\delta = 0$ ppm. Chemical shifts, δ, are reported in ppm relative to TMS. All ^{13}C NMR spectra were proton-decoupled. IR spectra were recorded on a Perkin-Elmer 51107 series spectrometer using KBr pellets for solid samples and NaCl plates for liquid samples and are reported in wave numbers (cm^{-1}). Absorption peaks are shown as (*s*) = strong, (*m*) = medium, and (*w*) = weak.

2.3 Preparation of cardanol (2)

Anacardic acid (8.06 g, 23.3 mmol) was heated to 200°C for 3 h using a graphite bath. White fumes evolved to give a viscous brownish oil of cardanol (7.02 g, 23.2 mmol, 99.7%). FTIR (film): 1211.12 cm^{-1} (*m*), 1246.03 cm^{-1} (*m*), 1450.40 cm^{-1} (*m*), 1607.58 cm^{-1} (*m*), 1646.28 cm^{-1} (*m*), 2854.37 cm^{-1} (*s*), 2928.82 cm^{-1} (*s*), 3009.90 cm^{-1} (*s*), 3340.01 cm^{-1} (*s*, br). ^{1}H NMR (400 MHz, CD_2Cl_2, 297.2 K) δ: 0.78 (t, $\mathcal{J}_{HH} = 7.76$ Hz, 3H, –CH_3), 1.18 (m, 16H, $H_{3,4,6,7,11,12,13\&14}$), 1.61 (m, 2H, H_3), 1.92 (q, $\mathcal{J}_{HH} = 7.76$ Hz, $H_{7\&10}$), 2.41 (t, $\mathcal{J}_{HH} = 7.76$ Hz, 2H, H_1), 5.12 (br, s, 1H, O*H*), 5.25 (q, $\mathcal{J}_{HH} = 4.24$ Hz, 2H, $H_{8\&9}$), 6.51 (d, $\mathcal{J}_{HH} = 8.56$ Hz, 1H, Ar-$H_{6'}$), 6.53 (s, 1H, Ar-$H_{2'}$), 6.61 (d, $\mathcal{J}_{HH} = 7.44$ Hz, 1H, Ar-$H_{4'}$), 6.98 (t, $\mathcal{J}_{HH} = 8.00$ Hz, 1H, Ar-$H_{5'}$). ^{13}C NMR (100 MHz, CD_2Cl_2, 297.2 K) δ: 14.43 (C_{15}), 23.15 (C_{14}), 30.24 ($C_{4,5,6\&11}$), 31.85 (C_{13}), 34.88 ($C_{7\&10}$), 36.28 (C_1), 113.01 ($C_{6'}$), 115.72 ($C_{2'}$), 121.23 ($C_{4'}$), 129.71 ($C_{8\&9}$), 130.32 ($C_{5'}$) 145.37 ($C_{3'}$), 156.09 ($C_{1'}$). MS [*m*/*z*, relative intensity (%)]: 41 (20), 55 (20), 67 (22), 79 (21), 108 (100), 120 (30), 133 (16), 147 (19), 302 (M^+, 0.7).

2.4 Synthesis of 3-(pentadec-2-enyl)phenol (9)

An autoclave was cleaned with acetone and dried in an oven overnight. It was then charged with a magnetic stirrer and brought into a glove box. The catalyst [$Pd_2(dba)_3$] (0.28 g, 0.31 mmol) and the ligand DTBPMB (1.23 g, 3.11 mmol) were weighed and introduced into the autoclave in the glove box. The autoclave was closed before removing it from the glove box. It was then connected to a Schlenk line using rubber tubes in the fume cupboard. Cardanol (1.50 g, 5.00 mmol) was introduced into a Schlenk tube closed with a suba seal. Toluene (10 mL), methanol (2 mL) and methanesulfonic acid (65 μL) were added to the tube by syringes to make a solution. The substrate solution in the Schlenk tube was degassed three times to ensure an air-free solution. Under a nitrogen atmosphere the solution was then transferred by means of a syringe (20 mL) into the autoclave. The mixture was heated while stirring at 80°C for 96 h. A yellowish-brown oily liquid (0.55 g, 40%) was separated by chromatography on a silica gel column using a mixture of hexane:ethanol (80:20) as eluant. The remaining 60% of the product, which contained isomers with the double bond in other positions of the chain was discarded.

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^{1}H NMR (400 MHz, CD_2Cl_2, δ = ppm, 295.7 K) δ: 0.79 (t, $\mathcal{J}_{HH}$ = 6.84 Hz, 3H, CH_3), 1.18 (m, 20H, $H_{4\text{-}14}$), 1.90 (q, $\mathcal{J}_{HH}$ = 13.94 Hz, 2H, H_3), 5.01 (s, 1H, OH), 5.89 (q, $\mathcal{J}_{HH}$ = 8.00 Hz, 1H, H_2), 6.22 (d, $\mathcal{J}_{HH}$ = 2.84 Hz, 1H, H_1), 6.61 (d, $\mathcal{J}_{HH}$ = 7.21 Hz, 1H, Ar-$H_{6'}$), 6.68 (s, 1H, Ar-$H_{2'}$), 6.77(d, $\mathcal{J}_{HH}$ = 8.40 Hz, 1H, Ar-$H_{4'}$) 7.15 (t, $\mathcal{J}_{HH}$ = 7.20 Hz, 1H, Ar-$H_{5'}$). ^{13}C NMR (100 MHz, CD_2Cl_2, δ = ppm, 296.5 K) δ: 14.21 (C_3), 23.05 (C_4), 31.02 ($C_{5\text{-}12}$), 32.40 (C_{13}), 33.27 (C_3), 113.09 ($C_{2'}$), 115.58 ($C_{6'}$), 118.70 ($C_{4'}$), 125.64 (C_2), 129.62 (C_1), 131.35 ($C_{5'}$), 136.55 ($C_{3'}$), 147.47 ($C_{1'}$). MS [*m*/*z*, relative intensity (%)]: 43 (23), 77 (11), 91 (9), 108 (84), 120 (100), 133 (68), 147 (14), 161 (8), 175 (1), 302 (M^+, 15).

2.5 Synthesis of 3-(prop-2-enyl)phenol (10)

In a glove box, the catalyst 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(*o*-isopropoxyphenylmethylene)ruthenium (**HG$_2$**, 0.02 g, 0.03 mmol) was weighed and added to a glass pressure bottle charged with a magnetic stirrer. The bottle was well tightened before removing it from the box and was placed in a cold-bath (−60°C). To the bottle *cis*-2-butene (ca. 6 mL) was added under nitrogen atmosphere. Then using a syringe (15 mL), a crude solution containing a mixture of isocardanols (1.50 g) dissolved in dry DCM (10 mL) in a separate Schlenk tube was transferred into the glass pressure bottle to start the reaction under nitrogen atmosphere. While stirring the reaction was carried out for 24 h at room temperature (RT). The reaction mixture was quenched by addition of ethylvinylether (0.5 mL) [34]. The solvents were evaporated using a rotary evaporator. Column chromatography on silica gel using hexane:ethanol (80:20) mixture as eluant afforded isolation of 3-(prop-2-enyl)phenol (29.2 mg, 0.22 mmol, 11%). FTIR (film): 966.39 cm^{-1} (*w*), 1044.00 cm^{-1} (*w*), 1078.27 cm^{-1} (*w*), 1198.54 cm^{-1} (*s*), 1463.73 cm^{-1} (*m*), 1600.27 cm^{-1} (*m*), 1690.81 cm^{-1} (*m*), 2854.05 cm^{-1} (*s*), 2925.56 cm^{-1} (*s*), 3420.27 cm^{-1} (*s*). ^{1}H NMR (400 MHz, CD_2Cl_2, δ = ppm, ppm, 298.7 K) δ: 1.86 (d, $\mathcal{J}_{HH}$ = 2.4 Hz, 3H, CH_3), 5.03 (br, s, 1H, Ar-OH), 5.99 (m, 1H, =CH–), 7.03 (d, $\mathcal{J}_{HH}$ = 7.68 Hz, 1H, Ar-$H_{6'}$), 7.06 (s, 1H, Ar-$H_{2'}$), 7.07 (d, $\mathcal{J}_{HH}$ = 7.08 Hz, 1H, Ar-$H_{4'}$), 7.15 (t, $\mathcal{J}_{HH}$ = 8.36 Hz, Ar-$H_{5'}$). ^{13}C NMR (100 MHz, CD_2Cl_2, δ = ppm, 298.7 K) δ: 18.05 (C_3), 113.31 ($C_{2'}$), 114.50 ($C_{6'}$), 119.67 ($C_{4'}$), 124.66 (C_2), 128.79 ($C_{5'}$ &C_1), 137.73 ($C_{3'}$), 157.85 ($C_{1'}$). MS [*m*/*z*, relative intensity (%)]: 77 (20), 91 (30), 107 (20), 119 (31), 134 (M^+, 100).

2.6 Synthesis of 3-propylphenol (5)

To a solution of 3-(prop-2-enyl)phenol (29.2 mg, 0.22 mmol) dissolved in MeOH (10 mL), was added 5% Pd–C (0.001 g) and the mixture was transferred into an autoclave previously equipped with a magnetic stirrer. Hydrogen gas (25 bar) was introduced into the autoclave and the contents stirred at RT for 3 h. The resultant solution was filtered through celite to obtain catalyst free solution which was then concentrated and a greenish liquid (28.2 mg, 0.21 mmol, 94%) was obtained. FTIR (film): 784.02 cm^{-1} (*w*), 1049.40 cm^{-1} (*s*), 1183.23 cm^{-1} (*s*), 1646.34 cm^{-1} (*m*), 2927.48 cm^{-1} (*s*), 3423.95 cm^{-1} (*s*, br). ^{1}H NMR (400 MHz, CD_2Cl_2, δ = ppm, 295.8 K), δ: 0.79 (t, $\mathcal{J}_{HH}$ = 6.76 Hz, 3H, –CH_3), 1.50 (m, 2H, –CH_2–), 2.75 (t, $\mathcal{J}_{HH}$ = 7.2Hz, 2H, –CH_2–), 5.24 (br, s, 1H, Ar-OH), 7.05 (d, $\mathcal{J}_{HH}$ = 6.84 Hz, 1H, Ar-$H_{6'}$), 7.06 (s, 1H, Ar-$H_{2'}$), 7.08 (d, $\mathcal{J}_{HH}$ = 6.80 Hz,1H, Ar-$H_{4'}$), 7.16 (t, $\mathcal{J}_{HH}$ = 6.48 Hz, 1H, Ar-$H_{5'}$). ^{13}C NMR (100 MHz, CD_2Cl_2, δ = ppm, 295.8 K) δ: 14.06 (C_3), 23.03 (C_2), 39.36 (C_1), 112.88 ($C_{2'\&6'}$), 120.11 ($C_{4'}$), 129.45 ($C_{5'}$), 140.33 ($C_{3'}$), 157.34 ($C_{1'}$). MS [*m*/*z*, relative intensity (%)]: 41 (7), 77 (30), 107 (100), 121 (16), 136 (M^+, 37).

2.7 Synthesis of 3-(dec-8-enyl)phenol (13)

A glass pressure bottle was cleaned with acetone and dried in an oven. It was charged with a magnetic stirrer and brought into the glove box. In the glove box, 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(*o*-isopropoxyphenylmethylene)ruthenium (**HG$_2$**, 0.02 g, 0.03mmol) was weighed and put into the glass pressure bottle which was well tightened before it was removed from the box. To the glass pressure bottle placed in a cold bath (−60°C), *cis*-2-butene (ca. 7 mL) (boils at 3.7°C) was added. A solution of cardanol (2.00 g, 6.60 mmol) dissolved in dry dichloromethane (2 mL) was prepared and degassed in three cycles. Then the solution was transferred into the pressure bottle containing the catalyst and *cis*-2-butene by means of a syringe and stirred at RT for 24 h. The reaction was quenched by adding vinylethylether (0.5 mL) to the reaction mixture. The solvents were evaporated prior to separation by column chromatography through silica gel which afforded 3-(dec-8-enyl)phenol (1.50 g, 6.50 mmol, 97.7%; 63:37 *E*/*Z*) as a brownish liquid mixture. FTIR (film): 740.00 cm^{-1} (*s*), 896 cm^{-1} (*w*), 1457.02 cm^{-1} (*m*), 2856.07 cm^{-1} (*s*), 2928.70 cm^{-1} (*s*), 3054.38 cm^{-1} (*s*), 3401.17 cm^{-1} (*s*, br). ^{1}H NMR (400 MHz, CD_2Cl_2, δ = ppm, 297.2 K) 0.80 (t, $\mathcal{J}_{HH}$ = 7.92 Hz, 3H, H_{10}), 1.18 (m, 8H, $H_{3,4,5\&6}$), 1.50 (m, 2H, H_2), 1.55 (d, $\mathcal{J}_{HH}$ = 5.32 Hz, 3H, H_{10}), 1.91 (q, $\mathcal{J}_{HH}$ = 18.50 Hz, 2H, H_7), 2.46 (t, $\mathcal{J}_{HH}$ = 6.64 Hz, 2H, H_1), 5.01 (s, 1H, Ar-OH), 5.34 (m,1H, $H_{8\&9}$), 6.55 (d, $\mathcal{J}_{HH}$ = 7.22 Hz, 1H, Ar-$H_{6'}$), 6.57 (br, s, 1H, Ar-$H_{2'}$), 6.66 (d, $\mathcal{J}_{HH}$ = 8.08 Hz, 1H, Ar-$H_{4'}$), 7.03 (t, $\mathcal{J}_{HH}$ = 8.12 Hz, 1H, Ar-$H_{5'}$).^{13}C NMR (100 MHz, CD_2Cl_2, δ = ppm, 297.2 K) 18.01 (C_{10}), 124.91 (C_9), 132.03 (C_8), 32.93 (C_7), 29.63 ($C_{4\&5}$), 29.99 (C_6), 36.16 (C_1), 112.79 ($C_{6'}$), 115.53 ($C_{2'}$), 121.17 ($C_{4'}$), 124.91 (C_9), 129.70 ($C_{5'}$), 145.49 ($C_{3'}$) 156.14 ($C_{1'}$). MS [*m*/*z*, relative intensity (%)]: 41 (10), 55 (16), 77 (12), 108 (100), 120 (24), 133 (6), 147 (5), 232 (M^+, 6).

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2.8 Synthesis of sodium 2-(dec-8-enyl)-6-hydroxybenzenesulfonate (6)

A solution of 3-(dec-8-enyl)phenol (1.50 g, 6.50 mmol) in 10 mL of methanol in a round bottomed flask (100 mL) was cooled in an ice bath to about 10°C. To this solution, oleum (SO_3 (20%) in H_2SO_4, 2.0 mL) was added dropwise using a dropping funnel over 2 h. The mixture was kept at RT for 3 h and then neutralized by careful addition to NaOH (15 mL, 5 mol/dm^3) while stirring for 1 h. The brown solid formed was suspended in hexane (5 mL) such that all the solids settled at the bottom of the separating funnel and were separated. The solids were dried in an oven overnight and a beige powdery solid (2.09 g, 6.30 mmol, 96.1%, m.p 366.5–367.0°C) was obtained. FTIR (KBr): 621.00 cm^{-1} (*s*), 865.52 cm^{-1} (*w*), 995.85 cm^{-1} (*m*), 1137.00 cm^{-1} (*s*), 1448.35 cm^{-1} (*s*), 2854.86 cm^{-1} (*s*), 2927.18 cm^{-1} (*s*), 3039.47 cm^{-1} (*s*), 3416.33 cm^{-1} (*s*, br). ^{1}H NMR (400 MHz, D_2O, ppm, 297.2 K): δ = 0.93 (t, $\mathcal{J}_{HH}$ = 8.08 Hz, 3H, H_{10}), 1.34 (m, 8H, $H_{3,4,5\&6}$), 1.64 (m, 2H, H_2), 1.92 (d, $\mathcal{J}_{HH}$ = 3.03 Hz, 3H, H_{10}), 2.45 (t, $\mathcal{J}_{HH}$ = 8.00 Hz, 2H, H_1), 5.09 (s, 1H, Ar-O*H*), 5.44 (m, 2H, $H_{8\&9}$), 6.49 (d, $\mathcal{J}_{HH}$ = 6.68 Hz, 1H, Ar-$H_{6'}$), 6.59 (d, $\mathcal{J}_{HH}$ = 8.00 Hz, 1H, Ar-$H_{4'}$), 6.99 (t, $\mathcal{J}_{HH}$ = 8.00 Hz, 1H, Ar-$H_{5'}$).

2.9 Synthesis of 1-octene (7) and 3-(non-8-enyl)phenol (8)

In the glove box, the catalyst 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(*o*-isopropoxyphenylmethylene)ruthenium (**HG$_2$**, 0.01 g, 0.02 mmol) was weighed and put into an autoclave. A solution of cardanol (2.00 g, 6.60 mmol) dissolved in dry dichloromethane (15 mL) was degassed in three cycles using the vacuum system and transferred by means of a syringe into the autoclave charged with a magnetic stirrer and the catalyst under a nitrogen atmosphere. The autoclave was then pressurized with ethene gas (20 bar) and the mixture stirred for 24 h at RT. The reaction was quenched by adding ethylvinylether (0.5 mL) [34]. Distillation of the mixture afforded a colorless liquid, 1-octene (0.48 g, 4.30 mmol, 65%) which had a boiling point in the range 121–123°C (lit. 123°C) [35]. *1-Octene* (**7**) ^{1}H NMR (400 MHz, CD_2Cl_2, δ = ppm, 295.8 K) δ: 0.80 (t, $\mathcal{J}_{HH}$ = 6.80 Hz, 3H, –CH_3), 1.26 (m, 8H, –CH_2CH_2CH_2CH_2–), 1.95 (q, $\mathcal{J}_{HH}$ = 11.98 Hz, 2H, –CH_2–), 4.85 ppm (t, $\mathcal{J}_{HH}$ = 11.68 Hz, 1H, =CH_2), 4.90 (t, $\mathcal{J}_{HH}$ = 2.16 Hz, 1H, =CH_2), 5.73 (m, CH_2 = C*H*–CH_2–). ^{13}C NMR (100 MHz, CD_2Cl_2, δ = ppm, 296.9 K) δ: 13.99 (C_8), 23.03 (C_7), 29.20 ($C_{4\&5}$), 32.21 (C_6), 34.17 (C_3), 114.10 (C_1), 139.69 (C_2). MS [*m*/*z*, relative intensity (%)]: 32 (4), 36 (7), 39 (40), 41 (89), 43 (91), 55 (100), 70 (80), 83 (33), 112 (M$^+$, 9). Cyclohexa-1,4-diene was detected by GC–MS in the crude reaction mixture.

The residue was purified by passing it through a silica gel column using hexane:ethanol (80:20) eluant to give brownish liquid, 3-(non-8-enyl)phenol **8** (1.10 g, 5.05 mmol, 76.4%). FTIR (film): 1050.85 cm^{-1} (*s*), 1380.63 cm^{-1} (*w*), 1446.38 cm^{-1} (*w*), 1483.08 cm^{-1} (*m*), 1639.30 cm^{-1} (*m*), 2886.39 cm^{-1} (*s*), 2976.17 cm^{-1} (*s*), 3029.28 cm^{-1} (*m*), 3384.47 cm^{-1} (*s*, br). ^{1}H NMR (400 MHz, CD_2Cl_2, δ = ppm, 295.8 K) δ: 1.18 (m, 8H, –CH_2CH_2CH_2CH_2–), 1.54 (m, 2H, –CH_2), 1.87 (q, $\mathcal{J}_{HH}$ = 11.36 Hz, CH_2), 2.45 (t, $\mathcal{J}_{HH}$ = 7.2 Hz, 2H, –CH_2–), 5.01 (s, 1H, O*H*), 5.87 (m, 1H, =C*H*), 6.53 (d, $\mathcal{J}_{HH}$ = 6.98 Hz, 1H, Ar-$H_{6'}$), 6.56 (s, 1H, Ar-$H_{2'}$), 6.65 (d, $\mathcal{J}_{HH}$ = 6.88 Hz, 1H, Ar-$H_{4'}$) 7.02 (t, $\mathcal{J}_{HH}$ = 8 Hz, 1H, Ar-$H_{5'}$). ^{13}C NMR (100 MHz, CD_2Cl_2, δ = ppm, 296.9 K) δ: 29.98 ($C_{4,5\&6}$), 31.70 (C_2), 32.80 (C_7), 35.92 (C_1), 112.90 ($C_{2'}$), 115.56 (C_9), 121.33 ($C_{4'}$), 131.02 ($C_{5'}$), 134.61 (C_8), 139.60 ($C_{3'}$), 156.31 ($C_{1'}$). MS [*m*/*z*, relative intensity (%)]: 41 (10), 55 (7), 77 (14), 108 (100), 120 (19), 133 (6), 147 (4), 218 (M$^+$, 7).

3 Results and discussion

3.1 Preparation of starting material, cardanol

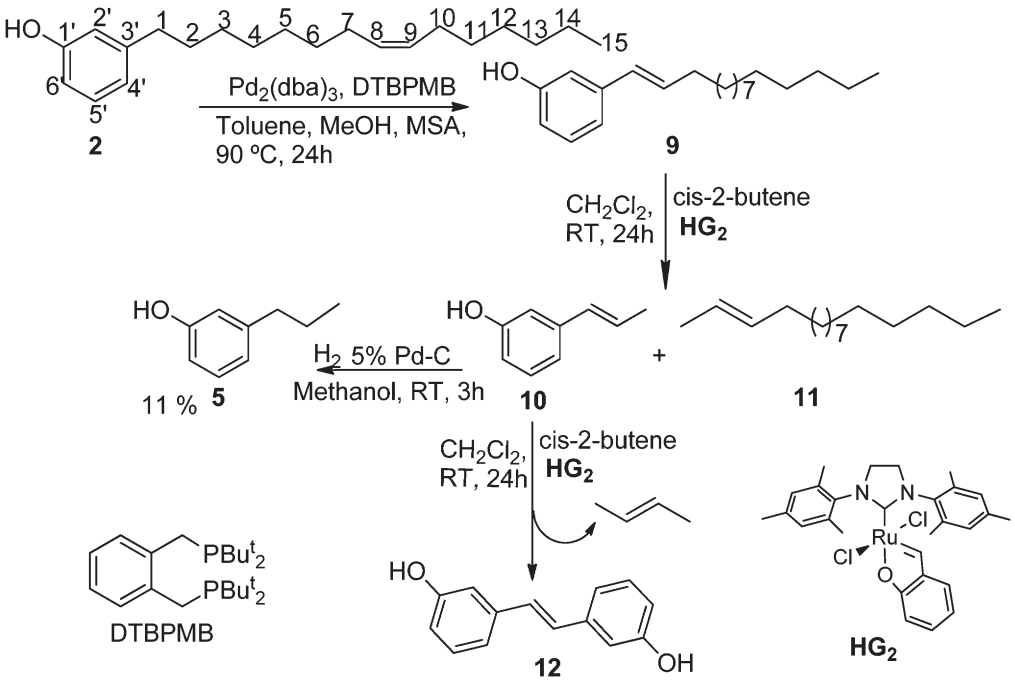
Heating anacardic acid (prepared as reported in the literature) [3] to 200°C for 3 h furnished cardanol in high yield (99.7%). The GC–MS quantitative analysis of cardanol from Naliendele, Tanzania showed that 87% was monoene cardanol, 7.5% saturated cardanol, 2.7% diene cardanol, and 1.7% triene cardanol. Isolation of monoene cardanol (*m*/*z* = 302) from traces of diene, triene, and saturated cardanol using chromatographic techniques proved difficult. We, therefore, used cardanol without purification and, because of its high proportion, we assumed monoene cardanol (3-pentadec-8-enylphenol) to be the predominant starting material in most reactions in this work. The ^{1}H NMR spectrum was in agreement with this analysis [27–29].

3.1.1 Synthesis of 3-propylphenol (5): A kairomone component

The synthesis of a natural tsetse fly attractant, 3-propylphenol, **5**, comprised three steps: carbon–carbon double bond isomerization of cardanol, **2**, cross-metathesis reaction of the isocardanol [3-(pentadec-2-enyl)phenol], **9**, with *cis*-2-butene and hydrogenation (Scheme 1).

In order to determine the optimum conditions, we carried out a series of palladium catalyzed double bond isomerization reactions of cardanol, **2**, at different catalyst loadings, temperatures and time durations. The highest conversion, at 40%, was attained using [$Pd_2(dba)_3$] [*tris*(dibenzylideneacetone)dipalladium(0)] (12 wt% Pd), and the ligand, [*bis*(ditertiarybutylphosphinomethyl)benzene] (DTBPMB), at 90°C for over 24 h. We have shown this system to provide an excellent isomerization catalyst [30]. Under these conditions, the carbon–carbon double bond migrated from its natural position (C8) in cardanol to the benzylic position

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Scheme 1. The synthesis of 3-propylphenol, **5**, from cardanol and some side reactions.

(C1) in isocardanol, **9**. We reasoned that the energy gained by conjugation might be sufficient to make **9** selectively, but this was not in fact the case. Although this isomer predominated, accounting for about 40% of the isomers, many other isomers were also present as indicated by GC–MS studies.

Cross-metathesis of the mixture of positional isomers containing 40% compound **9** with *cis*-2-butene using Hoveyda–Grubbs catalyst $\mathbf{HG_2}$ [31] gave rise to *trans*-3-(prop-2-enyl)phenol, **10**. The catalyst $\mathbf{HG_2}$ showed excellent performance in the metathesis of the isomeric mixture of cardanols (Fig. 4) and alkenes although its ruthenium residues caused undesirable coloration in the products [32]. Column chromatography of the crude product on silica gel afforded *trans*-3-(prop-2-enyl)phenol (**10**), as a brown liquid in low overall yield (11%). The low yield may be attributed to the observed low selectivity of the carbon–carbon double bond isomerization of cardanol and a possible self-metathesis (dimerization) of compound **10** to yield compound **12** [*E*-3,3′-(ethene-1,2-dyl)diphenol] (Scheme 1). This latter compound was detected by GC–MS which showed a peak at 11.5 min retention time with molecular fragment $M^+ = 212$ (Fig. 4).

Compound **10**, the immediate precursor for the targeted 3-propylphenol (**5**), was characterized spectroscopically. Hydrogenation of compound **10** afforded the target molecule, 3-propylphenol, **5**, with spectral data consistent with those in literature [20]. The overall synthesis of compound **5** from cardanol (**2**) is summarized in Scheme 1. The numbering assigned to cardanol (**2**) in Scheme 1, also applies to all target compounds, **5**, **6**, **7**, **8**, **9**, **10**, and **13**.

E-Hexadec-2-ene (**11**) was not a target compound of this study but it was detected as a major product in the crude reaction mixture by GC–MS.

*3.1.1.1 Synthesis of sodium 2-(dec-8-enyl)-6-hydroxybenzenesulfonate (**6**): A new detergent*

Compound **13** (3-(dec-8-enyl)phenol) was prepared by cross-metathesis of cardanol with *cis*-2-butene, it was then sulfonated and the sulfonated product neutralized with sodium hydroxide solution to afford the detergent **6** (Scheme 2).

Compound **13**, obtained in excellent yield (98%) in 63:37 *E*/*Z* ratio, was characterized spectroscopically The ^{1}H NMR spectrum showed olefinic peaks at δ 5.34 ppm and a doublet at δ 1.55 ppm from the methyl protons (H_{10}). However, a triplet was also observed at δ 0.80 ppm, which suggests that some molecules may have undergone isomerization (double bond migration) during cross-metathesis, leaving a terminal $-CH_2CH_3$ unit. It is known that such isomerization can be caused by the ruthenium residues of the metathesis catalyst [32].

Sulfonation of **13** with 20% oleum introduced a sulfonic acid group to the aromatic ring (Scheme 2). Subsequent neutralization of the sulfonated product with NaOH (5 mol/dm^3) solution yielded the detergent, sodium 2-(dec-8-enyl)-6-hydroxybenzenesulfonate (**6**) as a beige powder (96% yield, m.p. = 367–368°C). The powder dissolved in polar solvents: methanol, ethanol, THF, and water, but was insoluble in non-polar solvents such as dichloromethane

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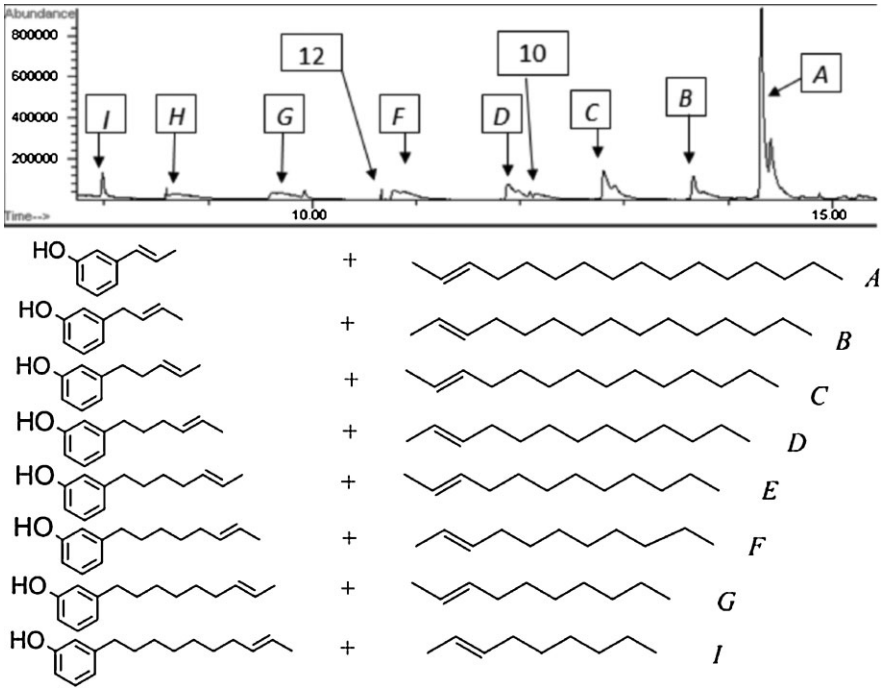
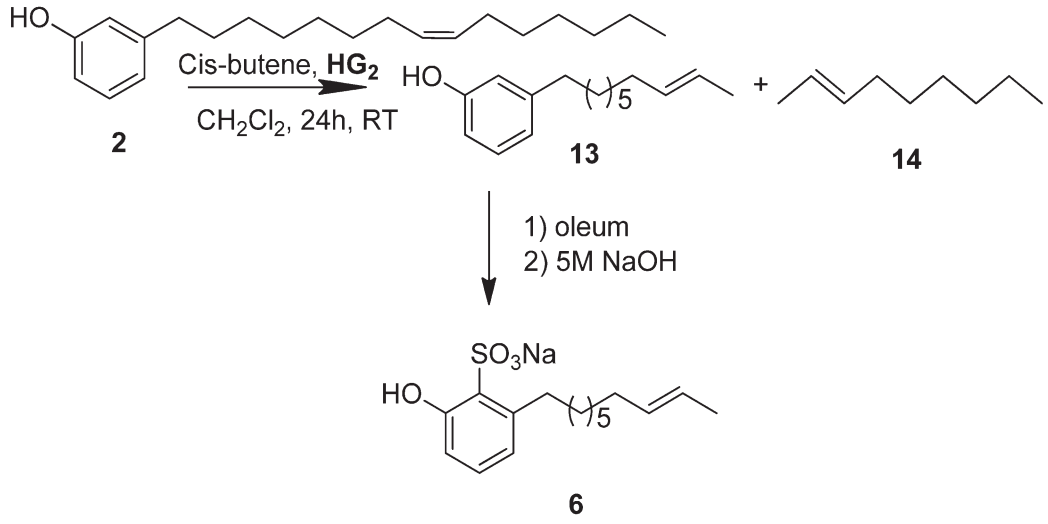


Figure 4. GC–MS trace of products from the but-2-eneolysis of isomerized cardanol with assigments of major peaks (A corresponds to compound **11**, *E*-2-hexadeceene). The high lighted alkene peaks correspond to *E* isomers, the smaller peaks beside them are from the *Z* isomers.

and toluene. The powder made a strong lather with water (Fig. 5), confirming its surface active properties. Its ^{1}H NMR spectrum showed signals for aromatic protons as a triplet at δ_H 6.99 ppm (for $H_{5'}$), doublet at 6.49 ppm ($H_{6'}$), and doublet at 6.59 ppm ($H_{4'}$). The singlet signal expected for $H_{2'}$ had disappeared. The explanation for this disappearance could be that sulfonation occurred at $C_{2'}$ between the alkenyl group and phenolic group. In other words, the sulfonic group assumed the position of the former carboxylic acid group of anacardic acid which enabled us to propose the structure of a new detergent, **6**. This substitution pattern contrasts with that reported for the sulfonation of cardanol, **2**, itself, which occurred at the $C_{4'}$ and $C_{6'}$ positions [6]. It may be that the bulkier and lengthier alkenyl group [3-(pentadec-8-enyl)]



Scheme 2. Formation of surfactant, **6**, from cardanol, **2**.

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Figure 5. Foaming of water on shaking with compound **6**.

of cardanol sterically hindered the sulfonation at $C_{2'}$ and also determined the regioselectivity of the overall reaction. Sulfonation of **13** did not affect the phenolic group (Ar-O*H*) since the ^{1}H NMR spectrum showed a broad singlet at δ_H 5.09 ppm which is assigned to the proton belonging to aromatic hydroxyl group. Once again a triplet at δ_H 0.93 ppm is attributable to the methyl protons for some isomers where the double bond has been isomerized closer to the ring.

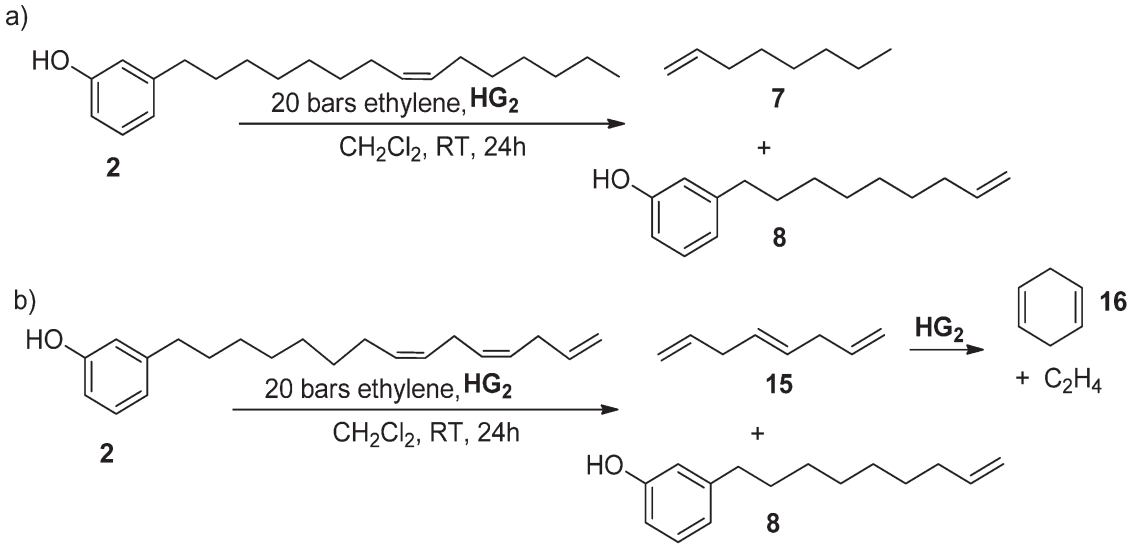
The beige coloration of **6** may be attributable to ruthenium residues from the Hoveyda–Grubbs catalyst **HG$_2$**, which could not be removed by conventional filtration methods because the catalyst residues formed a homogeneous solution with 3-(dec-8-enyl)phenol. This problem can be circumvented by treating the solution with triphenylphosphine oxide or DMSO which immobilizes the residues so that the solution cleans up when it is passed through a silica gel column [33].

Like compound **11**, non-2-ene (**14**) was not a target compound of this study. However, it was detected by GC–MS in the crude reaction mixture.

3.1.2 Synthesis of 1-octene (7) and 3-(non-8-enyl)phenol (8)

Synthesis of 1-octene and 3-(non-8-enyl)phenol from cardanol requires only one step. It involves cross-metathesis of monoene cardanol with ethylene using Hoveyda–Grubbs catalyst, **HG$_2$** (Scheme 3).

Cross-metathesis of cardanol with ethylene followed by distillation yielded 1-octene (**7**) (65%) (Scheme 3a). In addition, the GC–MS showed that 1,4-cyclohexadiene was also a product of the metathesis reaction. We believe that this comes from cardanol containing 3 double bonds. Metathesis with ethene would give 1,4,7-octatriene, **15**, which would undergo ring closing metathesis to give 1,4-cyclohexadiene, **16**, and ethene (Scheme 3b). Compound **8**, which should be formed as the phenolic component whether there are 1, 2, or 3 double bonds in the C_{15} chain (76% yield) was obtained as a residue from the distillation of **7**. It has been fully characterized spectroscopically. The less than perfect yield in this reaction partly arises from incomplete conversion of cardanol, but also from the formation of products with a variety of chain lengths, which were removed during the chromatographic separation of **8**. These compounds arise from isomerization of the double bond followed by metathesis. We believe the isomerization is catalyzed by decomposition products of **HG$_2$**, because attempting to improve the yield by restarting a reaction after depressurization and repressurization led to a



Scheme 3. The formation of 3-nonylphenol, 1-octene, and 1,4-cyclohexadiene from cardanol.

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much larger proportion of compounds with different chain lengths.

4 Conclusions

Double bond isomerization in cardanol (**2**) to obtain 3-(pentadec-2-enyl)phenol (**9**), which is a key intermediate towards the targeted kairomone component, 3-propylphenol, **5**, was achieved to a significant extent (40–50% conversion). The observed self-metathesis of 3-(prop-2-enyl)phenol (**10**), the immediate precursor for **5**, to form *trans*-3,3′-(ethene-1,2-diyl)diphenol (**12**), further reduced the overall yield of 3-propylphenol **5** (11%), although this can potentially be avoided by use of excess 2-butene. The new detergent sodium 2-(dec-8-enyl)-6-hydroxybenzenesulfonate (**6**), the possible detergent precursor, 3-(non-8-enyl)phenol (**8**), and 1-octene (**7**) have been successfully synthesized from cardanol (**2**). Overall, the present work has once again proved the potential utility of the phenolic components of CNSL in the synthesis of useful chemicals.

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The authors have declared no conflict of interest.

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