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ALKYLATION OF PHENOL BY NEROL IN THE PRESENCE OF ORGANOALUMINUM COMPOUNDS

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Alkylation of aluminum phenolate by nerol and of phenol by nerol in the presence of the organoaluminum compounds aluminum phenolate and aluminum isopropylate was studied. The reaction products were isolated and characterized. Several features of the process were determined. It was found that ortho*-substitution of the aromatic ring occurred primarily. In several instances nerol was cyclized. The fraction of allyl rearrangement was insignificant.*

Keywords: phenol, nerol, aluminum phenolate, aluminum isopropylate, alkylation.

Prenylphenols and their oxidized forms, prenylquinones, are classified as biosynthetic natural compounds. Geranyl derivatives of phenols exhibit a high level of biological activity [1, 2]. One method for preparing analogs of such natural compounds is alkylation. Under the conditions of this reaction, the effects of temperature and catalysts can modify the terpene substituent (closure into heterocyclic and carbocyclic structures). This is responsible for a variety of resulting products and can produce compounds with novel structures and possibly with specific biological activity. Therefore, great significance is placed on elucidation of the features of the alkylation reaction, owing to which the preparation of certain products can be targeted. In this respect, the effects of the catalyst, reaction temperature regime, and structure of the alkylating agent on the composition of the alkylation products must be studied.

Previously reported studies [3–5] provided a basis for proposing that alkylation in the presence of organoaluminum catalysts occurred in the Al coordination sphere, the result of which was the formation primarily of *ortho*-alkylated phenols, in particular, in yields reaching 73% via the reaction of phenol with geraniol [$(PhO)_3Al$ catalyst] [6, 7].

Herein results from the alkylation of aluminum phenolate $(PhO)_3Al$ by nerol (**2**) (*cis*-isomer of geraniol) and of phenol (**1**) by nerol (**2**) using catalytic amounts of Al-containing compounds [$(PhO)_3Al$ and $(i\text{-PrO})_3Al$] are reported. The product composition was studied as a function of reaction temperature and amount and type of Al-containing catalyst (Scheme 1, Table 1).

Alkylation of $(PhO)_3Al$ by nerol (**2**) and of phenol (**1**) by nerol (**2**) in the presence of equimolar amounts of $(i\text{-PrO})_3Al$ occurred with 93–98% conversion.

Monoterpenes **3** and **4** were obtained in overall yield 47% upon refluxing the reagents in benzene using $(PhO)_3Al$. Furthermore, products of C-alkylation, the principal one of which was *ortho*-alkylated phenol **9** (26%), were isolated in yields up to 35%. Polymerization products represented 4% of the mix. Increasing the reaction temperature to 120°C without using a solvent formed ethers **5** and **14** in yields of 14 and 10%, respectively. The overall amount of **3** and **4** in this instance decreased to 5% whereas the yield of polymerization products increased to 32%. Alkylation of $(PhO)_3Al$ by **2** at 140°C gave primarily chromane-type ethers **6**, **7**, **15**, and **16** in overall yield 74%. Compounds **15** and **16** contained two aromatic rings. Furthermore, bisphenol **17** was formed in 3% yield. A side product of *ortho*-alkylated phenol **18** was isolated pure and characterized structurally.

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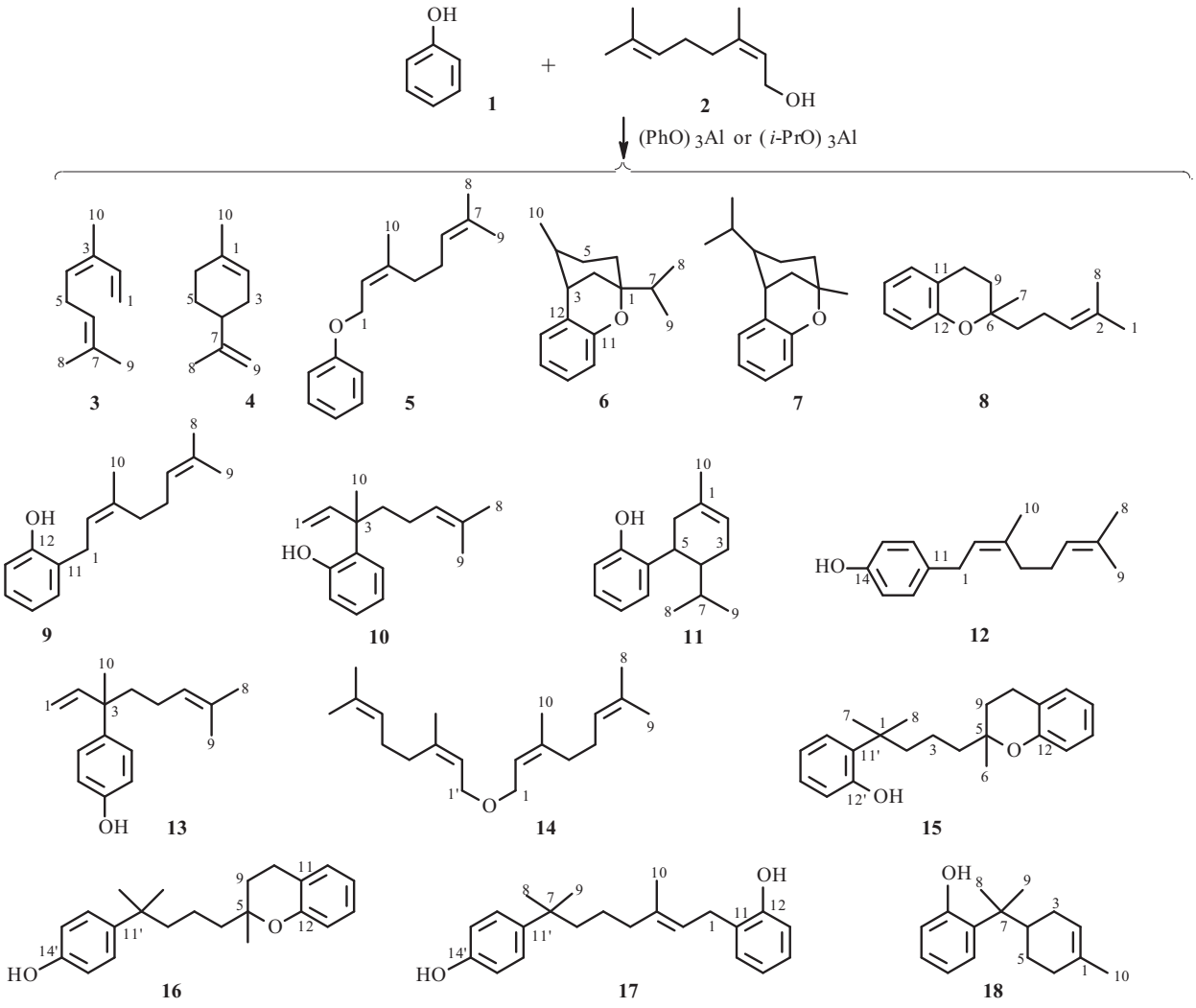

Scheme 1

Alkylation of **1** by **2** using equimolar amounts of $(i\text{-PrO})_3Al$ at 120 and 140°C formed a complicated C-alkylation product mixture (37–40%). Apparently the reaction occurred with isomerization of the terpene substituent and addition of it to both the *ortho*- and *para*-positions of the phenol aromatic ring. The fraction of chromanes among the identified products obtained under these reaction conditions was 44% (120°C) and 32% (140°C). Their structures corresponded to **7**, **8**, **15**, and **16**. Chromane **8**, which was obtained in the reactions using $(i\text{-PrO})_3Al$, was not formed in the presence of $(PhO)_3Al$. The yield of polymerized compounds reached 15–17%. Compound **1** was not alkylated by **2** upon refluxing in benzene for 4 h.

The reaction of **1** and **2** in the presence of catalytic amounts of $(PhO)_3Al$ and $(i\text{-PrO})_3Al$ occurred at temperatures above 160°C and formed a mixture of O- and C-alkylation products. The reaction at 160°C occurred with 40–60% conversion; at 180°C, 90% (Table 1), regardless of the catalyst used. However, the nature of the organoaluminum compound affected the composition of the alkylation products. Primarily *ortho*-nerylphenol **9** (35 and 44%) was formed by using $(PhO)_3Al$ at 160 and 180°C, respectively; phenylneryl ether **5** (50%, 160°C), by using $(i\text{-PrO})_3Al$.

A study of the alkylation of phenol by nerol in the presence of organoaluminum compounds showed that primarily *ortho*-substitution of the aromatic ring occurred. In certain instances, nerol underwent cyclization. The fraction of allyl rearrangement was negligible. The yield of alkylation products as a function of reaction temperature and ratio of reagents and catalyst was followed when $(PhO)_3Al$ was used. A stoichiometric ratio of catalyst and reagents provided practically complete conversion of the starting compounds. However, a detailed study of the reaction products showed that the fraction of side products was large in the range 80–120°C. These were hydrocarbons at 80°C (47%) and polymerization products of them at 120°C. Primarily tetrahydro-2,6-methanobenzo[*b*]oxacines (41%) and diarylalkanoids (36%) were formed at 140°C. This could be used for practical purposes considering the activity of natural diarylalkanoids [8]. Catalytic alkylation involving $(PhO)_3Al$ occurred with high conversion of the starting reagents at 180°C. Highly selective formation (44%) of *ortho*-nerylphenol **9** was observed. However, polymerization products and resins (19%) were formed in significant quantities under these conditions.

TABLE 1. Conditions and Products of Phenol Alkylation by Nerol

Product	Ratio of reaction products, %								
	$(PhO)_3Al$–nerol 1:1			$(PhO)_3Al$ = 10% of starting phenol, PhOH–nerol 1:1		$(i\text{-}PrO)_3Al$–PhOH–nerol 1:1:1		$(i\text{-}PrO)_3Al$ = 10% of starting phenol, PhOH–nerol 1:1	
	Reaction conditions								
	80°C, 4 h, C_6H_6	120°C, 4 h	140°C, 1 h	160°C, 1 h	180°C, 6 h	120°C, 4 h	140°C, 4 h	160°C, 1 h	180°C, 1 h
Conversion,%	**93**	**95**	**97**	**40**	**90**	**95**	**98**	**60**	**90**
3, 4	47	5	–	–	5	2	3	–	13
5	14	14	–	18	5	–	–	50	–
6	–	–	18	–	–	–	1	–	6
7	–	–	23	–	–	18	17	–	–
8	–	–	–	–	–	12	11	–	–
9	26	29	–	35	44	–	–	25	23
10	–	–	–	6	–	–	–	–	–
11	–	–	–	–	–	1	10	–	–
12	6	6	13	18	16	–	–	12	25
13	3	4		3	2	–	–	8	–
14	–	10	–	14	9	–	–	–	8
15	–	–	24	–	–	10	–	–	–
16	–	–	9	–	–	4	3	–	–
17	–	–	3	–	–	–	–	–	–
18	–	–	1	–	–	–	–	–	–
*	4	32	9	6	19	17	15	5	25
**	–	–		–	–	36	40	–	–

*Polymerization products; **complicated mixture of C-alkylation products.

The reaction occurred with high conversion to form up to 36–40% of a difficultly separated mixture of C-alkylation products at 120–140°C in the presence of a stoichiometric amount of $(i\text{-}PrO)_3Al$. Furthermore, 15–17% of the products were polymerized compounds. Catalytic alkylation in the presence of $(i\text{-}PrO)_3Al$ at 160°C occurred with 60% conversion of the starting reagents and gave good yields of nerylphenyl ether (50%) and *ortho*-nerylphenol **9** (25%). The analogous reaction at 180°C was complicated by polymerization (25%) although it occurred with high conversion (90%). The ratio of *ortho*- and *para*-nerylphenol was 23 and 25%, respectively.

The structures of the products were confirmed by NMR spectral methods. Thus, the PMR spectrum of **8** exhibited three singlets characteristic of protons for three methyls at 1.40 ppm, 1.65, and 1.73. A multiplet corresponding to H-3 on the double bond appeared in the range 5.16–5.18 ppm. The resonance of quaternary C-6 bonded to oxygen was found at 74.63 ppm in the ^{13}C NMR spectrum of **8**. Resonances of C atoms of the double bond (C-2 and C-3) were observed at 130.59 and 124.29 ppm, respectively. Elemental analyses and the ratio of integrated intensities of resonances for the aromatic and terpene substituent protons confirmed that **15**–**17** each contained two aromatic rings. Chromanes **15** and **16** had resonances in the ^{13}C NMR spectrum for quaternary C atom C-5 bonded to an O atom at 76.48 and 76.34 ppm, respectively. Resonances for protons of *para*-substituted aromatic ring (AB system) were observed in PMR spectra of phenols **16** and **17**.

EXPERIMENTAL

PMR and ^{13}C NMR spectra were recorded in $CDCl_3$ at room temperature on a Bruker Avance II 300 spectrometer (300 and 75 MHz, respectively). The internal standards were $CD(H)Cl_3$ resonances (δ_H 7.25 ppm, δ_C 76.90 ppm). Resonances were assigned using ^{13}C NMR spectra recorded in JMOD mode and two-dimensional NMR spectroscopy (HSQC, COSY, NOESY). IR spectra were recorded as thin layers on a Shimadzu IR Prestige 21 IR-Fourier spectrometer. Elemental analyses were performed on a Vario Microcube Elementar CHNS analyzer. The course of reactions was monitored using TLC on Sobrfil plates and GC on a Shimadzu GC-2010AF chromatograph using an SLB^{TM}-5ms capillary column (Supelco, 60 m × 0.25 mm, 0.5 μm, 70–230°C temperature regime, 6°C/min heating rate, flame-ionization detector, He carrier gas). Column chromatography used Alfa Aesar 70/230 μm silica gel. Compounds **3**–**18** were detected by spraying plates with an

alcohol solution of vanillin with subsequent heating to 100–150°C and by using $KMnO_4$ solution. Phenol (chemically pure) and nerol (Alfa Aesar) were used in the reactions. The catalysts were $(i\text{-PrO})_3Al$ (Alfa Aesar) and $(PhO)_3Al$ (synthesized *in situ*).

Alkylation of $(PhO)_3Al$ by Nerol. A 100-mL two-necked flask equipped with a thermometer and reflux condenser was charged with phenol (**1**, 1.8 g, 19.5 mmol), heated to 160°C, treated in portions with Al turnings (0.17 g, 6.5 mmol), held at this temperature until the Al dissolved completely, cooled to room temperature, and treated with nerol (**2**, 1.0 g, 6.5 mmol). The reaction was carried out at 80°C (in benzene) and 120 and 140°C (without solvent). The course of the reaction was followed using TLC (hexane:Et_2O, 3:1, detector alcohol solution of vanillin:H_2SO_4). When the reaction was finished, the mixture was cooled, diluted with Et_2O, treated with HCl solution (10%) to decompose the catalyst, and washed with NaOH solution (5%) and H_2O until neutral. The organic layer was dried over anhydrous Na_2SO_4. The solvent was removed. The products were separated by column chromatography over SiO_2 (petroleum ether:Et_2O with increasing fraction of Et_2O). The reagents were added simultaneously if $(i\text{-PrO})_3Al$ was used. The work up of the reaction mixture and the separation of reaction products were carried out by the method described above.

Alkylation of Phenol by Nerol in the Presence of $(PhO)_3Al$ and $(i\text{-PrO})_3Al$. A 100-mL two-necked flask equipped with a thermometer and reflux condenser was charged with phenol (0.62 g, 6.5 mmol), heated to 160°C, and treated in small portions with Al turnings (0.0054 g, 0.2 mmol). After the Al was completely dissolved, the solution was cooled to 40°C and treated with nerol (**2**, 1 g, 6.5 mmol). For $(i\text{-PrO})_3Al$ (10% of starting phenol), the reagents were added simultaneously. The reaction was carried out at 160°C until nerol was completely converted (GC and TLC monitoring). The work up of the reaction mixture and separation of reaction products were carried out by the method described above.

(*Z*)-3,7-Dimethylocta-1,3,6-triene (3), light-yellow oil.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 1.70 (3H, s, CH_3-8), 1.77 (3H, s, CH_3-9), 1.81 (3H, s, CH_3-10), 2.76–2.78 (2H, m, H-5), 4.98–5.02 (2H, m, H-1), 5.17–5.20 (1H, m, H-2), 5.55–5.58 (1H, m, H-4), 6.75–6.88 (1H, m, H-6).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 17.84 (C-8), 20.50 (C-10), 23.70 (C-9), 28.00 (C-5), 108.40 (C-1), 120.80 (C-6), 131.84 (C-4), 132.10 (C-7), 133.10 (C-3), 134.91 (C-2).

1-Methyl-4-(1-methylethenyl)cyclohexene (4), light-yellow oil. The spectral data agreed with those in the literature [9].

(*E*)-(3,7-Dimethylocta-2,6-dienyloxy)benzene (5), light-yellow oil. IR spectrum (KBr, ν, cm^{-1}): 1604, 1592 and 1500 (ν C=C of aromatic ring), 756 (δ CH, out-of-plane vibrations of mono-substituted aromatic ring), 1242 (ν =C–O), 1460 and 1380 [=$C(CH_3)_2$], 1676 (ν C=C of nerol), 835 (δ CH of nerol).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.67 (3H, s, CH_3-9), 1.75 (3H, s, CH_3-8), 1.86 (3H, s, CH_3-10), 2.19–2.20 (4H, m, 2H-4, 2H-5), 4.55–4.57 (2H, m, H-1), 5.18–5.21 (1H, m, H-6), 5.58 (1H, t, J = 6.0, H-2), 6.96–6.99 (3H, m, 1H-12, 1H-14, 1H-16), 7.33 (2H, t, J = 8.4, 1H-13, 1H-15).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 17.70 (C-10), 22.32 (C-8), 24.28 (C-9), 26.64 (C-5), 32.46 (C-4), 64.40 (C-1), 114.68 (C-12, C-16), 120.50 (C-14), 120.58 (C-2), 123.74 (C-6), 129.42 (C-13, C-15), 132.19 (C-7), 141.55 (C-3), 158.89 (C-11).

1-Isopropyl-10-methyl-2-oxatricyclo[7.3.1.0.^{3,8}]trideca-3(8),4,6-triene (6), light-yellow oil. The spectral data agreed with those in the literature [10, 11].

10-Isopropyl-1-methyl-2-oxatricyclo[7.3.1.0.^{3,8}]trideca-3(8),4,6-triene (7), light-yellow oil. The spectral data agreed with those in the literature [10, 11].

2-Methyl-2-(4-methylpent-3-enyl)chromane (8), yellow oil.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 1.40 (3H, s, CH_3-7), 1.65 (3H, s, CH_3-8), 1.73 (3H, s, CH_3-1), 1.82–1.91 (6H, m, 2H-9, 2H-4, 2H-5), 2.14–2.17 (2H, m, H-10), 5.16–5.18 (1H, m, H-3), 6.76–6.88 (1H, m, H-13), 6.91–7.03 (2H, m, 1H-15, 1H-14), 7.09 (1H, m, H-16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 19.94 (C-4), 20.05 (C-8), 22.32 (C-7), 22.16 (C-10), 24.29 (C-1), 30.72 (C-9), 38.42 (C-5), 74.63 (C-6), 117.32 (C-13), 119.54 (C-15), 121.32 (C-11), 124.29 (C-3), 127.85 (C-16), 129.40 (C-14), 130.59 (C-2), 153.02 (C-12).

2-(3,7-Dimethylocta-2,6-dienyl)phenol (9), yellow oil. IR spectrum (KBr, ν, cm^{-1}): 3472 (ν OH), 1260 (ArOH), 3040 (ν_{as} Car H), 1612 and 1594 (ν C=C aromatic ring), 754 and 884 (δ CH *ortho*-substituted aromatic ring), 1334 and 1492 (δ CH_3, CH_2, CH), 1380 (δ_s CH_3), 1676 and 835 (ν C=C, δ CH of nerol).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.66 (3H, s, CH_3-8), 1.68 (3H, s, CH_3-9), 1.83 (3H, s, CH_3-10), 2.16–2.27 (4H, m, 2H-4, 2H-5), 3.41–3.44 (2H, m, H-1), 5.18–5.19 (1H, m, H-6), 5.20 (1H, s, OH), 5.39 (1H, t, J = 7.05, H-2), 6.81–6.94 (2H, m, 1H-13, 1H-15), 7.14–7.18 (2H, m, 1H-14, 1H-16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 17.69 (C-9), 23.45 (C-10), 25.73 (C-8), 26.41 (C-5), 29.47 (C-1), 32.05 (C-4), 115.69 (C-13), 120.74 (C-15), 122.50 (C-2), 123.87 (C-6), 126.96 (C-11), 127.52 (C-14), 129.95 (C-16), 132.24 (C-7), 138.48 (C-3), 154.37 (C-12).

2-(3,7-Dimethylocta-1,6-dien-3-yl)phenol (10), yellow oil.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 1.64 (3H, s, CH_3-10), 1.72 (6H, s, CH_3-9, CH_3-8), 2.02–2.26 (4H, m, 2H-5, 2H-4), 5.11–5.13 (1H, m, H-6), 5.30–5.38 (2H, m, H-1), 5.91–5.93 (1H, m, H-2), 5.20 (1H, s, OH), 6.83 (1H, m, H-13), 7.14–7.16 (3H, m, 1H-14, 1H-15, 1H-16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 17.72 (C-9), 25.05 (C-10), 25.64 (C-8), 25.76 (C-5), 32.02 (C-4), 40.62 (C-3), 113.51 (C-1), 120.65 (C-13), 122.27 (C-15), 122.57 (C-6), 127.44 (C-16), 128.67 (C-14), 132.95 (C-7), 133.98 (C-11), 142.48 (C-2), 149.37 (C-12).

2-(6-Isopropyl-3-methylcyclohex-2-enyl)phenol (11), light-yellow oil.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 1.05 (6H, s, CH_3-8, CH_3-9), 1.23–1.32 (1H, m, H-4), 1.66 (3H, s, CH_3-10), 1.59–1.96 (5H, m, 2H-3, 2H-6, 1H-7), 2.76–2.79 (1H, m, H-5), 5.17–5.18 (1H, m, H-2), 5.30 (1H, s, OH), 6.77–6.85 (1H, m, H-13), 6.91–6.97 (1H, m, H-15), 7.02–7.15 (2H, m, 1H-14, 1H-16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 17.14 (C-9), 17.77 (C-8), 23.62 (C-10), 26.95 (C-3), 34.78 (C-7), 34.89 (C-4), 37.41 (C-5), 38.74 (C-6), 115.08 (C-13), 117.99 (C-2), 118.79 (C-15), 127.28 (C-14), 127.99 (C-16), 134.11 (C-1), 153.83 (C-12).

4-(3,7-Dimethylocta-2,6-dienyl)phenol (12), yellow oil. IR spectrum (KBr, ν, cm^{-1}): 3380 (ν OH), 2972 and 2864 (ν_{as} ν_s CH_3, CH_2), 1672 (ν C=C of nerol), 1454 and 1380 [ν_s =C$(CH_3)_2$], 3040 (ν C–H aromatic ring), 1618, 1604, and 1516 (ν C=C of aromatic ring), 828 (δ C–H *para*-substituted aromatic ring).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.66 (3H, s, CH_3-8), 1.76 (3H, s, CH_3-9), 1.83 (3H, s, CH_3-10), 2.16–2.27 (4H, m, 2H-4, 2H-5), 3.33–3.35 (2H, m, H-1), 5.19–5.20 (1H, m, H-6), 5.22 (1H, s, OH), 5.39 (1H, t, J = 7.06, H-2), 6.83–6.94 (2H, m, 1H-13, 1H-15), 7.14–7.18 (2H, m, 1H-14, 1H-16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 17.69 (C-9), 23.45 (C-10), 25.73 (C-8), 26.41 (C-5), 29.47 (C-4), 32.05 (C-1), 115.69 (C-13, C-15), 120.74 (C-15), 122.50 (C-2), 123.87 (C-6), 130.00 (C-12, C-16), 132.24 (C-7), 133.87 (C-11), 138.48 (C-3), 154.31 (C-14).

4-(5,7-Dimethylocta-1,6-dien-4-yl)phenol (13), yellow oil.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.34 (3H, s, CH_3-10), 1.65 (3H, s, CH_3-9), 1.66 (3H, s, CH_3-8), 2.16–2.17 (4H, m, 2H-4, 2H-5), 5.10–5.19 (1H, m, H-6), 5.24–5.34 (2H, m, 2H-1), 5.46 (1H, s, OH), 5.92–6.01 (1H, m, H-2), 6.78 (2H, d, J = 8.4, 1H-13, 1H-15), 7.07 (2H, d, J = 8.4, 1H-12, 1H-16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 17.67 (C-9), 23.42 (C-10), 25.71 (C-8), 23.42 (C-5), 39.73 (C-3), 42.03 (C-4), 111.86 (C-1), 115.22 (C-13, C-15), 123.47 (C-6), 129.37 (C-12, C-16), 132.87 (C-7), 133.85 (C-11), 144.87 (C-2), 153.76 (C-14).

Bis-(3,7-dimethyl-2,6-octadienyl)ether (14), light-yellow oil. IR spectrum (KBr, ν, cm^{-1}): 1676 (ν C=C of nerol), 1456 and 1380 [ν_s =C$(CH_3)_2$], 1108 and 1088 (ν_s C–O–C).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.65 (6H, s, CH_3-9, CH_3-9′), 1.72 (6H, s, CH_3-8, CH_3-8′), 1.80 (6H, s, CH_3-10, CH_3-10′), 2.12–2.20 (8H, m, 2H-4, 2H-4′, 2H-5, 2H-5′), 3.97–3.99 (4H, m, 2H-1, 2H-1′), 5.14–5.17 (2H, m, 1H-6, 1H-6′), 5.41 (2H, t, J = 6.6, 1H-2, 1H-2′).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 17.64 (C-9, C-9′), 23.59 (C-10, C-10′), 25.69 (C-8, C-8′), 26.43 (C-5, C-5′), 32.30 (C-4, C-4′), 66.27 (C-1, C-1′), 122.13 (C-2, C-2′), 123.97 (C-6, C-6′), 131.86 (C-7, C-7′), 140.14 (C-3, C-3′).

2-[1,1-Dimethyl-4-(2-methylchroman-2-yl)butyl]phenol (15), yellow oil. IR spectrum (KBr, ν, cm^{-1}): 3531 (ν OH), 2953 and 2866 (ν_{as} ν_s CH_3, CH_2), 1581 and 1604 (ν C=C aromatic ring), 1446 and 1380 [ν_s =C$(CH_3)_2$], 1242 (ν =C–O), 752 (δ C–H *ortho*-substituted aromatic ring).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 1.26 (3H, s, CH_3-6), 1.45 (6H, s, CH_3-7, CH_3-8), 1.60–1.63 (2H, m, H-4), 1.74–1.81 (4H, m, 2H-2, 2H-3), 1.91–1.94 (2H, m, 2H-9), 2.72–2.77 (2H, m, 2H-10), 4.92 (1H, s, OH), 6.66–6.69 (1H, m, H-13′), 6.83–6.96 (3H, m, 1H-14′, 1H-13, H-15), 7.08–7.16 (3H, m, H-15′, H-16′, H-14), 7.25–7.26 (1H, m, H-16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 19.31 (C-3), 22.15 (C-10), 24.29 (C-6), 28.24 (C-7, C-8), 30.81 (C-9), 38.03 (C-1), 40.38 (C-4), 41.35 (C-2), 76.48 (C-5), 116.44 (C-13′), 117.31 (C-13), 119.57 (C-15), 120.55 (C-15′), 121.34 (C-11), 127.05 (C-16), 127.24 (C-14), 128.20 (C-14′), 129.45 (C-16′), 134.56 (C-11′), 153.99 (C-12), 154.18 (C-12′). $C_{22}H_{28}O_2$.

4-[1,1-Dimethyl-4-(2-methylchroman-2-yl)butyl]phenol (16), light-yellow oil.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.26 (3H, s, CH_3-6), 1.32 (6H, s, CH_3-7, CH_3-8), 1.41–1.43 (2H, m, 2H-4), 1.55–1.65 (4H, m, 2H-2, 2H-3), 1.73–1.81 (2H, m, 2H-9), 2.71–2.78 (2H, m, 2H-10), 5.05 (1H, s, OH), 6.81 (2H, d, J = 8.6, 1H-13′, 1H-15′), 6.84–6.89 (2H, m, 1H-13, H-15), 7.08–7.13 (2H, m, 1H-16, 1H-14), 7.23 (2H, d, J = 8.6, H-12′, H-16′).

^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 18.85 (C-3), 22.12 (C-10), 24.24 (C-6), 28.27 (C-7, C-8), 30.83 (C-9), 37.20 (C-1), 40.36 (C-4), 45.06 (C-2), 76.34 (C-5), 114.85 (C-13′, C-15′), 117.31 (C-13), 119.60 (C-15), 121.27 (C-11), 126.84 (C-12′, C-16′), 127.27 (C-16), 129.45 (C-14), 141.85 (C-11′), 153.12 (C-12), 153.92 (C-14′). $C_{22}H_{28}O_2$.

4-(1,1,5-Trimethyl-7-*o*-phenylheptan-1-yl)phenol (17), yellow oil. IR spectrum (KBr, ν, cm^{-1}): 3525.88 and 3410 (ν OH), 1244 (ArOH), 1606 and 1583 (ν C=C aromatic ring), 754 (δ C–H, *ortho*-substituted aromatic ring), 1446 (δ CH_3, CH_2, CH), 1367 (δ_s CH_3 methyl), 830 (δ C–H *para*-substituted aromatic ring).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 1.28 (6H, s, CH_3-8, CH_3-9), 1.37–1.42 (2H, m, 2H-5), 1.72 (3H, s, CH_3-10), 1.83–1.85 (2H, m, 2H-6), 2.15–2.35 (2H, m, 2H-4), 3.54–3.55 (2H, m, 2H-1), 5.15 (2H, s, OH), 5.29–5.33 (1H, m, H-2), 6.65–6.67 (1H, m, H-13), 6.79–6.83 (2H, m, 1H-13′, 1H-15′), 6.86–6.89 (1H, m, H-15), 7.08–7.13 (2H, m, 1H-12′, 1H-16′), 7.18–7.21 (2H, m, H-14, H-16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 20.90 (C-10), 23.50 (C-5), 24.24 (C-9), 24.40 (C-8), 30.83 (C-1), 37.10 (C-7), 40.36 (C-4), 45.06 (C-6), 114.85 (C-13′, C-15′), 116.60 (C-13), 120.40 (C-15), 121.27 (C-2), 121.24 (C-11), 127.27(C-12′, C-16′), 127.95 (C-14), 129.41 (C-16), 135.85 (C-3), 141.72 (C-11′), 153.22 (C-14′), 154.41 (C-12). $C_{22}H_{28}O_2$.

2-[1-Methyl-1-(4-methylcyclohex-3-en-1-yl)ethyl]phenol (18), light-yellow oil.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 1.34 (3H, s, CH_3-9), 1.41 (3H, s, CH_3-8), 1.65 (3H, s, CH_3-10), 1.85–2.31 (6H, m, 2H-3, 2H-5, 2H-6), 2.49–2.51 (1H, m, H-4), 4.92 (1H, s, OH), 5.33–5.35 (1H, m, H-2), 6.60–6.66 (1H, m, H-13), 6.72–6.75 (1H, m, H-15), 7.09–7.11 (1H, m, H-14), 7.23–7.25 (1H, m, H-16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 23.40 (C-10), 23.70 (C-8), 24.40 (C-9), 24.70 (C-5), 27.50 (C-6), 31.70 (C-3), 39.6 (C-4), 40.30 (C-7), 116.69 (C-13), 120.34 (C-2), 121.50 (C-15), 128.30 (C-16), 129.90 (C-14), 133.92 (C-1), 135.55 (C-11), 154.37 (C-12).

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REFERENCES

1. K. M. Fisch, V. Bohm, A. D. Wright, and G. M. Konig, *J. Nat. Prod.*, **66**, 968 (2003).
2. H. Makabe, S. Miyazaki, T. Kamo, and M. Hirota, *Biosci. Biotechnol. Biochem.*, **67**, 2038 (2003).
3. L. A. Kheifits and I. S. Aul′chenko, in: *Chemistry and Technology of Fragrances and Essential Oils* [in Russian], Pishchevaya Promyshlennost′, Moscow, 1968.
4. I. Yu. Chukicheva and A. V. Kuchin, *Ross. Khim. Zh.*, **48** (3), 21 (2004).
5. I. Yu. Chukicheva, I. V. Fedorova, A. A. Koroleva, and A. V. Kuchin, *Dokl. Akad. Nauk*, **434** (6), 768 (2010).
6. I. Yu. Chukicheva, I. V. Timusheva, A. A. Koroleva, and A. V. Kuchin, *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, No. 1, 27 (2009).
7. I. Yu. Chukicheva, I. V. Timusheva, A. A. Koroleva, and A. V. Kuchin, RF Pat. No. 2,340,592; *Byull.*, No. 34, Dec. 10, 2008.
8. M. Tohikawa and F. Seiji, Jpn. Pat. 8-198791, 1996.
9. J. S. Zhang, N. N. Zhao, Q. Z. Liu, S. S. Du, L. Zhou, and Z. W. Deng, *J. Agric. Food Chem.*, **59**, 9910 (2011).
10. V. V. Fomenko, D. V. Korchagina, N. F. Salakhutdinov, and V. A. Barkhash, *Helv. Chim. Acta*, **85**, 2358 (2002).
11. J. C. Schmidhauser, G. L. Bryant, Jr., E. Donahue, M. F. Garbauskas, and E. A. Williams, *J. Org. Chem.*, **60**, 3612 (1995).