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Aminomethylated Derivatives of 2-Propenyl- and 4-Isopropenylphenols as Antimicrobial Additives for Petroleum Products

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Abstract—A number of aminomethylated derivatives of 2-propenyl-, 4-isopropenylphenols have been synthesized and their antimicrobial properties have been studied in M-12 engine oil and TS-1 jet fuel (at concentrations of 1–2% and 0.3–0.5%, respectively). They have been found to possess bactericidal and fungicidal properties and significantly improve the antimicrobial properties of both of the materials (as compared to the well-known antimicrobial additive, 8-hydroxyquinoline). The presence of an alkenyl substituent along with an aminomethyl group in the structure of the substances in question has been demonstrated to enhance the antimicrobial properties. The formation of an intermolecular and intramolecular hydrogen bond in the initial and synthesized phenolic compounds has been studied.

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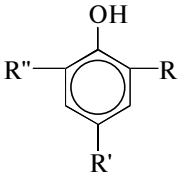
Functionally substituted phenols are an object of systematic research. Compounds containing heteroatoms, multiple bonds, and other moieties that allow for their modification in order to obtain new compounds with useful properties are of the greatest interest both theoretically and practically [1–5].

We have previously synthesized aminomethyl derivatives of allylphenols, which were studied as antimicrobial additives for petroleum products [6, 7]. In a continuation of these studies, we synthesized aminomethyl derivatives of 2-propenyl- and 4-isopropenylphenols and also examined them as antimicrobial additives.

EXPERIMENTAL

Aminomethylated 2-propenylphenol and 4-isopropenylphenol derivatives have been synthesized using a known technique [6, 7] by their triple condensation with formaldehyde and secondary amines (by the Mannich reaction). The reaction was carried out at 70–75°C and an equimolar reactant ratio for 4–5 h. The desired substances were extracted from the reaction mixture by converting them into the corresponding quaternary ammonium salts through treatment with hydrogen chloride and subsequent decomposition by aqueous ammonia. The following substances have been synthesized:



where (1) R' = H; R'' = –CH=CH–CH_3

R = $-CH_2-N(C_2H_5)_2$ (I), $-CH_2-N$ (II), $-CH_2-N$O (III);

(2) R'' = H; R' = $-C(CH_3)=CH_2$

R = $-CH_2-N(C_2H_5)_2$ (IV), $-CH_2-N$ (V), $-CH_2-N$O (VI).

The structures of these substances have been established by NMR spectroscopy.

6-Diethylaminomethyl-2-propenylphenol (I): yield 88.3%, n_D^{20} 1.5114; d_4^{20} 1003.6 kg/m^3, ^{1}H NMR (acetone d_6, δ, ppm): 1.18 t (6H, $2CH_3$); 1.89 d (3H, CH_3); 2.58 q (4H, $2CH_2$); 3.75 s (2H, CH_2-N); 6.29 m (1H, CH=); 6.63 (1H, CH=); 6.65–7.3 (3H, aromatic); 10.5 s (1H, OH). ^{13}C NMR spectrum: 12.3; 18.7; 46.8; 57.1; 118.7; 123.1; 123.9; 124.6; 125.2; 126.8; 128.5; 157.5.

6-Piperidinomethyl-2-propenylphenol (II): yield 76.0%; n_D^{20} 1.5085; d_4^{20} 1043.4 kg/m^3; ^{1}H NMR (acetone d_6, δ, ppm): 1.35–1.71 m (6H, $3CH_2$); 1.9 d (3H, CH_3); 3.59 s (2H,CH_2–N); 6.15 m (1H, CH=); 6.62 (1H, CH=); 6.55–7.2 (3H, aromatic); 10.4 s (1H, ÎH). ^{13}C NMR spectrum: 18.9; 24.8; 26.7; 44.9; 62.8; 118.6; 123.4; 124.1; 124.8; 125.2; 128.1; 128.6; 156.9.

6-morpholinomethyl-2-propenylphenol (III): yield 80.7%, n_D^{20} 1.5085; d_4^{20} 1043.4 kg/m^3; ^{1}H NMR (acetone d_6, δ, ppm): 1.89 d (3H, CH_3); 2.55 t (4H, $N(CH_2)_2$); 3.65 t (4H, $O(CH_2)_2$); 3.66 s (2H, CH_2–N); 6.3 t (1H, CH=); 6.67 (1H, CH=); 6.7–7.4 (3H, aromatic); 10.55 s (1H, OH). ^{13}C NMR: 18.3; 43.4; 62.3; 66.7; 118.3; 118.9; 121.8; 125.7; 126.1; 126.9; 127.4; 135.8

2-Diethylaminomethyl-4-isopropenylphenol (IV): yield 70%; n_D^{20} 1.5492; d_4^{20} 1002.2 kg/m^3; ^{1}H NMR (acetone d_6, δ, ppm): 1.04 t (6H, $2CH_3$); 2.05 c (3H, CH_3–C); 2.57 q (4H, $N(CH_2)_2$); 3.5 s (2H, N–CH_2–Ar); 4.91 and 5.13 AB (2H, CH_2=); 6.8–7.2 (3H, C_6H_3); 8.9 (1H, OH).

2-Piperidinomethyl-4-isopropenylphenol (V): yield 65.0%; n_D^{20} 1.5612; d_4^{20} 1022.8 kg/m^3; ^{1}H NMR (acetone d_6, δ, ppm): 1.71 m (6H, of the $3CH_2$ cycle), 2.01 s (3H, CH_3–C); 2.62 m (4H, of the $N(CH_2)_2$ cycle); 3.49 s (2H, NCH_2–Ar); 4.90 and 5.12 AB (2H, CH_2=); 6.96–7.3 (3H, C_6H_3); 9.2 (1H, OH).

2-Morpholinomethyl-4-isopropenylphenol (VI): yield 75.7%; n_D^{20} 1.5645; d_4^{20} 1021.8 kg/m^3; ^{1}H NMR (acetone d_6, δ, ppm): 1.99 s (3H, CH_3); 2.32 m (4H, $N(CH_2)_2$); 3.45 s (2H, NCH_2–Ar); 3.55 m (4H, $O(CH_2)_2$); 4.8 and 5.12 s (2H, CH_2=); 6.6–7.2 (3H, aromatic); 9.5 (1H, OH). ^{13}C NMR: 22.3; 53.6; 62.3; 66.7; 109.9; 116.4; 119.9; 126.4; 126.6; 133.1; 143.1; 157.4.

NMR spectroscopy was also used to investigate the formation of an intermolecular and intramolecular hydrogen bond in the precursors and products (I–VI) in the temperature range of 25–70°C and at concentrations of 0.1–50% in CCl_4.

The antimicrobial properties of the aminomethylated derivatives of 2-propenyl- and 4-isopropenylphenols in M-12 engine oil (at a concentration of 1–2%) and TS-1 jet fuel (at a concentration of 0.3–0.5%) were tested by zone diffusion assay according to GOST (State Standard) 9.052-88 and GOST 9.082-77. The following microorganisms were studied: *Mycobacterium lacticolium*, *Staphyilococcus albus*, *E. coli, Mucor*, *Pinicillium*, and *Aspergillus niger*.

Meat-peptone agar (MPA) and wort agar (WA) were taken to cultivate bacterial cultures and fungi, respectively. In order to compare and detect the antimicrobial activity of these compounds, 8-hydroxyquinoline, a well-known antimicrobial additive for lubricants and fuels, was used. Inoculation and cultivation were carried out as described in [6]. The efficiency of the antimicrobial action of the compounds was determined in terms of the diameter of the microorganism growth inhibition area.

Microorganisms were inoculated in Petri dishes on the surface of an agarized culture medium; then, pits of a 4- to 5-mm depth were made with a sterile 10-mm drill bit into which 0.3–0.5 ml of the samples were introduced. The dishes were subsequently placed in a thermostat and left to stay at 29–30°C over 2 days (for bacterial growth) or 3–4 days (for fungi).

RESULTS AND DISCUSSION

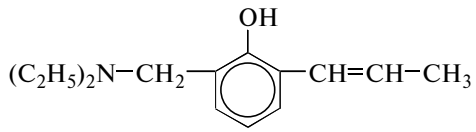
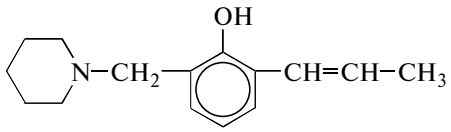
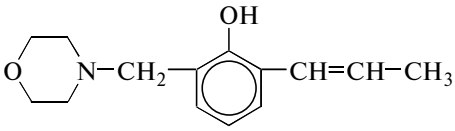
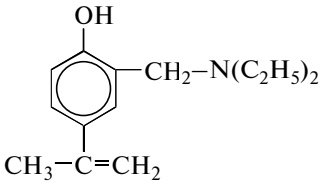
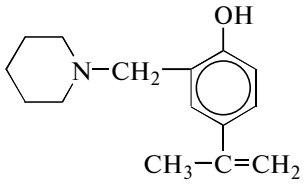
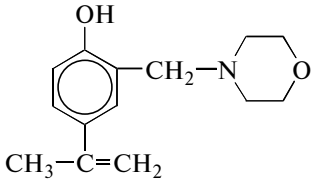
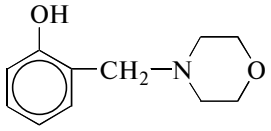
The results of the study show that the yields of the desired compounds vary from 65.0 to 88.3% depending on the nature of the reactant amines and phenols. The greatest yields can be achieved with the use of morpholine or diethylamine and 2-propenylphenol. The aminomethylated 2-propenyl- and 4-isopropenylphenol derivatives and the reactant alkenylphenols were investigated by the NMR spectroscopy technique. It was found that these phenols experience intermolecular hydrogen bonding and the products' Mannich bases contain a rather strong intramolecular bond, supposedly due to the electron pair of the aminomethyl nitrogen atom located in the *o*-position with respect to the phenol hydroxyl and the OH hydrogen.

The ^{1}H NMR spectra of dilute solutions of 2-propenyl- and 4-isopropenylphenols in CCl_4 feature a shift of hydroxyl proton signals from 6.5 to 4.8 ppm. However, no such concentration-induced shift is observed for the *o*-aminomethyl derivatives. Owing to the formation of the N...H intramolecular hydrogen bond, hydroxyl group signals in these compounds are detected in the range of 8.9–10.55 ppm.

Furthermore, ^{1}H NMR spectroscopic studies of the aminomethyl derivatives of alkenylphenols up to the boiling temperature of CCl_4 revealed a minor shift of the hydroxyl group signals, thereby unequivocally confirming that the intramolecular hydrogen bond is quite strong [8, 9].

The nature of the aminomethyl moiety in all derivatives of both 2-propenyl- and 4-isopropenylphenol does not have any significant influence on the strength of the intramolecular hydrogen bond.

Table 1. Results of testing the substances in M-12 oil in MPA and WA culture media

No.	Compound	Conc., %	Microorganism killing zone, cm					
			Bacteria			Fungi		
			Mycobacterium lacticolium	*Staphylococcus*	*E. coli*	*Mucor*	*Penicillium*	*Aspergillus niger*
I		2 1	1.3–1.5 0.8–0.9	+ +	2.0–2.4 1.1–1.2	+ +	+ +	+ +
II		2 1	1.7–1.8 1.1–1.2	+ +	+ +	+ +	1.5–1.7	+ +
III		2 1	1.7–1.9 1.2–1.4	1.9–2.1 1.1–1.3	+ +	2.1–2.5 1.3–1.6	+ +	+ +
IV		2 1	1.7–1.8 0.9–1.2	+ +	2.0–2.5 1.5–1.8	+ +	+ +	1.3–1.5 0.5–0.6
V		2 1	2.2–2.7 1.1–1.3	+ +	2.5–2.7 1.2–1.5	1.8–2.2 0.8–1.1	2.6–3.0 1.5–1.7	+ +
VI		2 1	2.5–2.8 1.2–1.6	+ +	2.8–3.3 1.5–1.8	2.9–3.3 1.3–1.5	2.5–2.7 1.5–1.8	0.9–1.1 0.4–0.5
VII		2 1	+ +	+ +	0.9–1.1 0.5–1.6	+ +	1.8–2.1 1.2–1.3	+ +
VIII	8-Hydroxyquinoline (reference)	2 1	0.7–0.9 +	0.9–1.1 +	1.6–1.8 0.7–1.0	+ +	+ +	+ +
IX	M-12 oil (control)	–	+	+	+	+	+	+

As can be seen from the above NMR data, the intramolecular hydrogen bond in the structures of aminomethylated 2-propenylphenol is stronger (10.4–10.55 ppm) than in the derivatives of 4-isopropylphenol (8.9–9.5 ppm).

The results of spectral analyses of aminomethylated derivatives of 2-propenylphenol also have shown that they consist of 95% *trans*- and 5% *cis*-isomers (this is proved by the corresponding signals).

The results of testing the aminomethylated derivatives of 2-propenyl- and 4-isopropenylphenols for antimicrobial properties are given in Tables 1 and 2.

The data of Tables 1 and 2 make it evident that all of the substances in question (I–VI) in M-12 engine

Table 2. Results of testing the substances in TS-1 fuel in MPA and WA culture media (compound numbers as in Table 1)

No.	Conc., %	Microorganism killing zone, cm				
		Bacteria		Fungi		
		Staphylococcus	*E. coli*	*Mucor*	*Penicillium*	*Aspergillus niger*
I	0.5	1.5–2.0	+ +	+ +	3.7–3.8	2.7–3.5
	0.3	0.7–0.9			1.8–1.9	1.6–1.8
II	0.5	3.7–3.0	+ +	3.7–3.9	3.1–3.5	3.3–3.8
	0.3	1.0–1.3		1.8–2.0	1.7–1.8	1.4–1.7
III	0.5	+ +	+ +	3.9–4.1	+ +	3.3–3.7
	0.3			1.9–2.3		1.7–1.8
IV	0.5	3.5–3.7	3.7–4.2	3.7–4.0	+ +	2.9–3.5
	0.3	1.9–2.2	1.8–2.1	1.8–2.1		1.5–1.6
V	0.5	3.3–3.5	+ +	3.1–3.4	+ +	3.1–3.5
	0.3	1.9–2.0		1.6–1.9		1.5–1.7
VI	0.5	+ +	+ +	2.6–2.9	+ +	2.2–2.5
	0.3			1.7–2.0		1.3–1.4
VII	0.5	2.2–2.5	+ +	+ +	+ +	1.9–2.0
	0.3	1.1–1.2				1.0–1.1
VIII	0.5	3.3–3.5	2.9–3.0	+ +	+ +	+ +
	0.3	1.7–1.8	1.5–1.6			
IX	–	+	+	+	+	+

oil and TS-1 jet fuel at the investigated concentrations possess bactericidal and fungicidal properties. In terms of efficiency, they are not inferior to the well-known antimicrobial additive 8-hydroxyquinoline and often prove superior to it. Of the aminomethyl derivatives of alkenylphenols tested in M-12 oil, compound I only has bactericidal properties, whereas compound VI containing the morpholinomethyl moiety in the *o*-position and the conjugate isopropenyl group in the *p*-position with respect to the hydroxyl group efficiently inhibits the growth of both bacteria and fungi.

Studies of the phenol compounds in TS-1 fuel revealed that the best bactericidal and fungicidal properties are exhibited by compounds containing both piperidine and propenyl (compound II), as well as diethylaminomethyl and isopropenyl (IV) fragments.

In order to clarify the contribution of the multiple bond to the antimicrobial properties of aminomethyl derivatives of 2-propenyl- and 4-isopropenylphenols, we examined 2-morpholinomethylphenol (VII), which has been obtained by the condensation of phenol with formaldehyde and morpholine and does not contain an alkenyl group. A comparison of the results of the investigation shows that the presence of a substituent with a multiple bond on the phenyl ring enhances the antimicrobial properties of the compounds.

A comparison of the data obtained with the results of previously performed investigations [6, 7] indicated that unlike aminomethyl derivatives of allylphenols, the substances in question exhibit fungicidal properties in addition to bactericidal properties at the same concentrations in oil and fuel.

Thus, the Mannich bases bearing alkenyl groups on the aromatic ring synthesized in this work exhibit quite a high antimicrobial activity and can be used for the protection of petroleum products against microbial degradation during their storage and transportation.

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