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New piperidinium surfactants containing *N*-ethylcarbamate fragment: aggregation properties and antimicrobial activity

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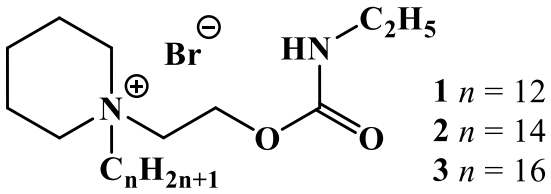
Experimental section

The synthesis method and characteristics of piperidinium surfactants containing an *N*-ethylcarbamate fragment.



General procedure for synthesis of 1-alkyl-1-[2-(N-ethylcarbamoyloxy)ethyl]piperidinium bromides. Ethyl isocyanate (5 mM) was added to a solution of the appropriate 1-alkyl-1-(2-hydroxyethyl)piperidinium bromide (2.5 mM) and DABCO (0.45 mM) in 30 mL dry acetonitrile. The reaction mixture was stirred for 16 h at 82 °C. The solvent was removed under vacuum (20 Torr), and the solid residue was recrystallized from ethyl acetate. The precipitate was filtered, washed with diethyl ether and dried on a water bath (40 °C) under vacuum (15 Torr). Data of elemental analysis, IR spectroscopy, NMR spectroscopy, and mass spectrometry were used to confirm the structures of the compounds. Elemental analysis was carried out on a EuroEA3028-HT-OM CHNS analyzer (Eurovector SpA, Italy). IR spectra were recorded on a Vector-27 FT-IR spectrometer (Bruker, Germany) with KBr pellets. Mass spectra with electrospray ionization (ESI) were obtained on an Amazon X mass spectrometer (Bruker, Germany) with the ion trap. ^{1}H NMR spectra were recorded on a Bruker Avance spectrometer (Bruker, Germany) with the working frequency 600 MHz. ^{1}H NMR chemical shifts (400 MHz, solvent $CDCl_3$) are given relative to the residual signal of $CHCl_3$ (δH 7.27).

1-[2-(*N*-Ethylcarbamoyloxy)ethyl]-1-dodecylpiperidinium bromide (1). Yield 1.09 g (97.4 %). Light yellow solid. M.p. 76-79 °C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (J, Hz): 0.88 m (N^+-$(CH_2)_{11}$-$\underline{CH_3}$, 3H); 1.16 t (-NH-CH_2-$\underline{CH_3}$, 3H, $^3J_{HH}$ 7.3); 1.26-1.31 m (-$(CH_2)_2$-$(\underline{CH_2})_7$-$(CH_2)_2$-

CH_3, 14H); 1.37 m (-$(CH_2)_9$-($\underline{CH_2}$)$_2$-CH_3, 4H); 1.68 m (N^+-$(CH_2)_2$-$\underline{CH_2}$-$(CH_2)_2$-N^+, 2H); 1.87-1.95 m (N^+-CH_2-$\underline{CH_2}$-Alk, N^+-CH_2-$\underline{CH_2}$-CH_2-$\underline{CH_2}$-CH_2-N^+, 6H); 3.21 q (C(O)-NH-$\underline{CH_2}$-CH_3, 2H, $^3J_{HH}$ 7.2); 3.50-3.54 m (N^+-$\underline{CH_2}$-Alk, 2H); 3.70 m (N^+-$\underline{CH_2}$-CH_2-O-C(O)-, 2H); 3.89 m (N^+-$\underline{CH_2}$-$(CH_2)_3$-$\underline{CH_2}$-N^+, 4H); 4.52 m (N^+-CH_2-$\underline{CH_2}$-O-C(O)-, 2H). IR (KBr) ν: 3419, 3219, 3027, 2956, 2923, 2853, 1709, 1625, 1526, 1469, 1447, 1379, 1358, 1309, 1252, 1198, 1138, 1087, 1053, 1032, 1010, 996, 969, 942, 893, 819, 779, 723, 629 cm^{-1}. Elemental analysis calcd for $C_{22}H_{45}BrN_2O_2$ (%): C 58.78; H 10.09; Br 17.78; N 6.23. Found (%): C 58.85; H 10.00; Br 17.75; N 6.18. ESI mass spectrum, *m/z*: $[M]^+$ 369.31 (calcd 369.61).

1-[2-(*N*-Ethylcarbamoyloxy)ethyl]-1-tetradecylpiperidinium bromide (2). Yield 1.07 g (90 %). White solid. M.p. 88-91 °C. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (J, Hz): 0.88 t (N^+-$(CH_2)_{13}$-$\underline{CH_3}$, 3H, $^3J_{HH}$ 7.0); 1.17 t (-NH-CH_2-$\underline{CH_3}$, 3H, $^3J_{HH}$ 7.3); 1.25-1.30 m (-$(CH_2)_2$-($\underline{CH_2}$)$_9$-$(CH_2)_2$-CH_3, 18H); 1.37 m (-$(CH_2)_{11}$-($\underline{CH_2}$)$_2$-CH_3, 4H); 1.68 m (N^+-$(CH_2)_2$-$\underline{CH_2}$-$(CH_2)_2$-N^+, 2H); 1.84-1.96 m (N^+-CH_2-$\underline{CH_2}$-Alk, N^+-CH_2-$\underline{CH_2}$-CH_2-$\underline{CH_2}$-CH_2-N^+, 6H); 3.22 q (C(O)-NH-$\underline{CH_2}$-CH_3, 2H, $^3J_{HH}$ 7.2); 3.50-3.54 m (N^+-$\underline{CH_2}$-Alk, 2H); 3.69 m (N^+-$\underline{CH_2}$-CH_2-O-C(O)-, 2H); 3.88 m (N^+-$\underline{CH_2}$-$(CH_2)_3$-$\underline{CH_2}$-N^+, 4H); 4.52 m (N^+-CH_2-$\underline{CH_2}$-O-C(O)-, 2H). IR (KBr) ν: 3428, 3217, 2956, 2922, 2852, 1709, 1626, 1526, 1468, 1378, 1309, 1253, 1138, 1087, 1053, 962, 943, 893, 780, 722, 633 cm^{-1}. Elemental analysis calcd for $C_{24}H_{49}BrN_2O_2$ (%): C 60.36; H 10.34; Br 16.73; N 5.87. Found (%): C 60.25; H 10.37; Br 16.67; N 5.88. ESI mass spectrum, *m/z*: $[M]^+$ 397.35 (calcd 397.67).

1-[2-(*N*-Ethylcarbamoyloxy)ethyl]-1-hexadecylpiperidinium bromide (3). Yield 88 %. White solid. M.p. 90-93 °C. ^{1}H NMR spectrum (600 MHz, $CDCl_3$), δ, ppm (J, Hz): 0.88 t (N^+-$(CH_2)_{15}$-$\underline{CH_3}$, 3H, $^3J_{HH}$ 7.0); 1.17 t (-NH-CH_2-$\underline{CH_3}$, 3H, $^3J_{HH}$ 7.2); 1.30-1.26 m (-$(CH_2)_2$-($\underline{CH_2}$)$_{11}$-$(CH_2)_2$-CH_3, 22H); 1.37 m (-$(CH_2)_{13}$-($\underline{CH_2}$)$_2$-CH_3, 4H); 1.68 m (N^+-$(CH_2)_2$-$\underline{CH_2}$-$(CH_2)_2$-N^+, 2H); 1.96-1.84 m (N^+-CH_2-$\underline{CH_2}$-Alk, N^+-CH_2-$\underline{CH_2}$-CH_2-$\underline{CH_2}$-CH_2-N^+, 6H); 3.22 q (CO-NH-$\underline{CH_2}$-CH_3, 2H, $^3J_{HH}$ 7.1); 3.53 m (N^+-$\underline{CH_2}$-Alk, 2H); 3.71 m (N^+-$\underline{CH_2}$-CH_2-O-CO-, 2H); 3.91 m (N^+-$\underline{CH_2}$-$(CH_2)_3$-$\underline{CH_2}$-N^+, 4H); 4.51 m (N^+-CH_2-$\underline{CH_2}$-O-CO-, 2H). IR (KBr) ν: 3428, 3217, 3027, 2955, 2921, 2852, 1710, 1625, 1526, 1468, 1445, 1360, 1310, 1253, 1199, 1139, 1089, 1053, 967, 941, 892, 860, 779, 723, 631 cm^{-1}. Elemental analysis calcd for $C_{26}H_{53}BrN_2O_2$ (%): C 61.76; H 10.57; Br 15.80; N 5.54. Found (%): C 61.62; H 10.48; Br 15.91; N 5.39. ESI mass spectrum, *m/z*: $[M]^+$ 425.34 (calcd 425.71).

Aggregation properties. Surface tension measurements were performed by the anchor-ring method using KRUSS 6 tensiometer (KRŰSS, Germany). The CMC values were defined as the

concentration corresponding to the breakpoints in the γ *vs*. logarithm of surfactant concentration plots. The dynamic contact angle was determined at 25°C using a KRUSS 100 (KRŰSS, Germany) by measuring the wetting force when a solid sample (Parafilm M type) was immersed in the test liquid with a known surface tension.

Solubilization effect of micellar solutions on hydrophobic compounds, such as Orange OT, tebuconazole, and carbendazim, was determined using spectrophotometry, following the methodology as described [R. A. Kushnazarova, A. B. Mirgorodskaya, S. S. Lukashenko, A. D. Voloshina, A. S. Sapunova, I. R. Nizameev, M. K. Kadirov and L. Ya. Zakharova J. Mol. Liq., 2020, 318, 113894. https://doi.org/10.1016/j.molliq.2020.113894]. Spectral measurements were carried out on a Specord 250 Plus spectrophotometer (Analytik Jena, Germany) using quartz cells with the absorbing layer thickness 1 cm.

The absorption dependencies of Orange OT in micellar solutions at 495 nm (A) were analyzed using the Schott's method [H. Schott, J. Phys. Chem., 1996, 70, 2966–2973 https://doi.org/10.1021/j100881a041] by the linear eq. $C = \mathrm{CMC} + b \times A$, where C is represents the concentration of surfactant above the CMC ($g \cdot L^{-1}$), b is the slope of the linear part of the dependence. The molecular mass of the micelle (*MM*m) was calculated using the following formula: $MM\mathrm{m} = \varepsilon \times (C - \mathrm{CMC})/A$, where ε is the molar absorption coefficient of Orange OT which is equal to 18,720 $L \cdot mol^{-1} \cdot cm^{-1}$. The aggregation numbers (N_{agg}) were determined by dividing *MM*m by the molecular mass of the surfactant.

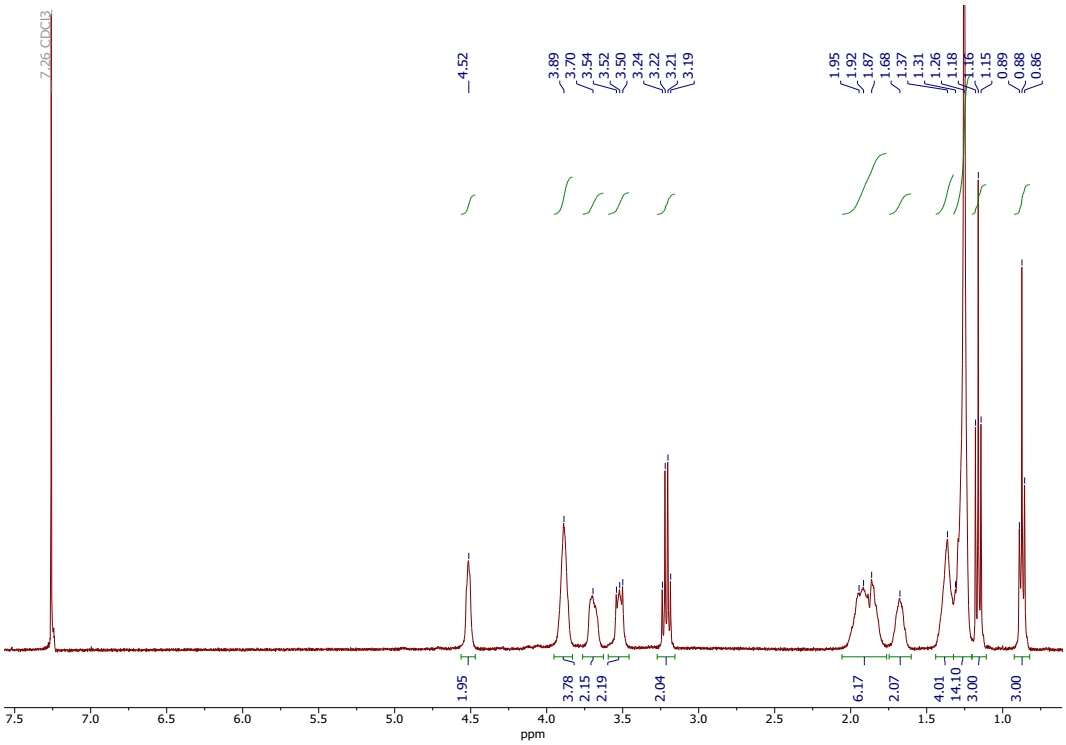


Figure S1 ^{1}H NMR spectrum of **1**.

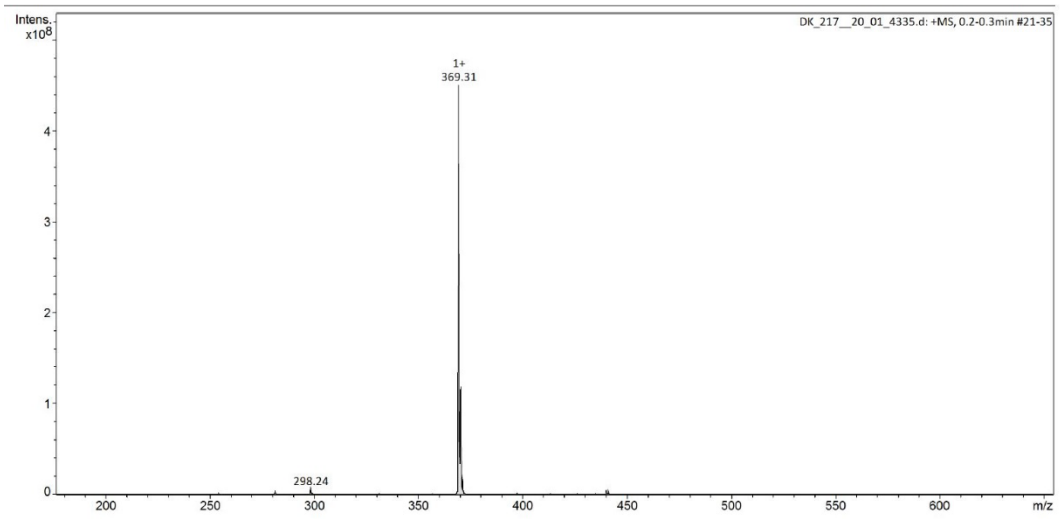


Figure S2 ESI mass spectrum of **1**.

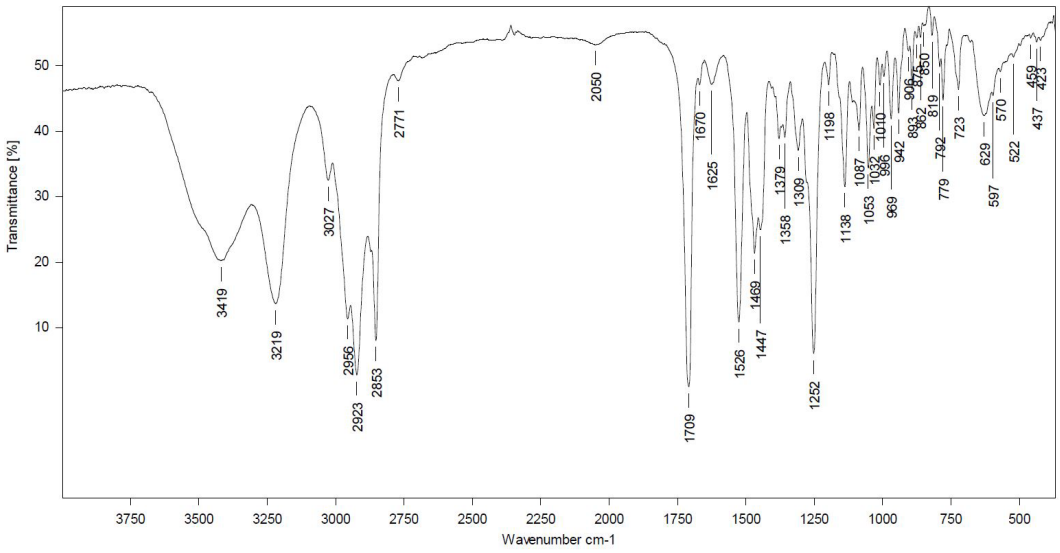


Figure S3 IR spectrum of **1**.

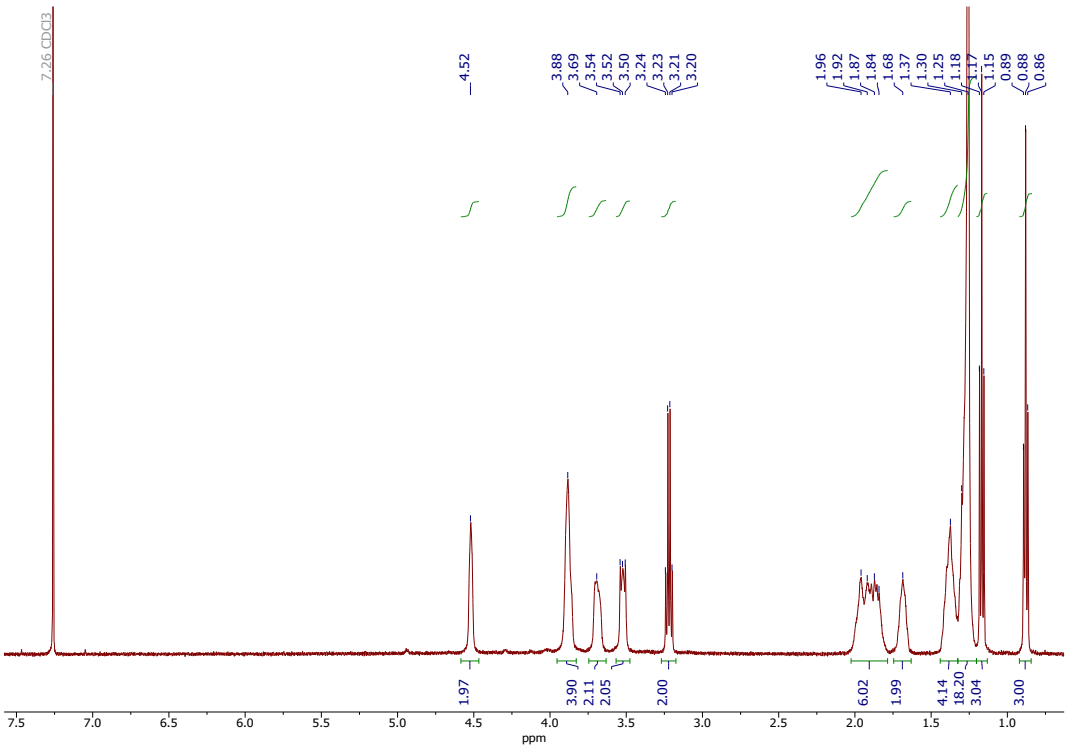


Figure S4 ^{1}H NMR spectrum of **2**.

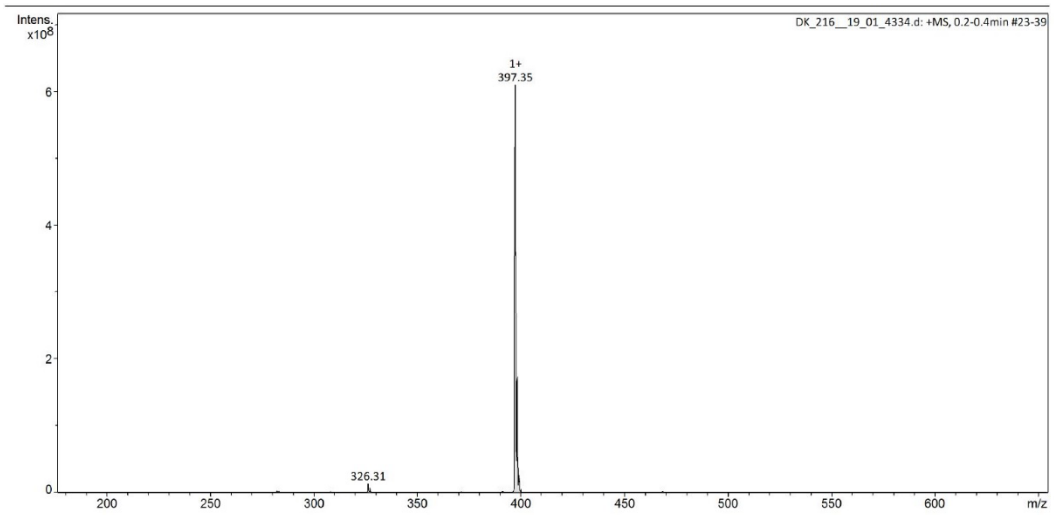


Figure S5 ESI mass spectrum of **2**.

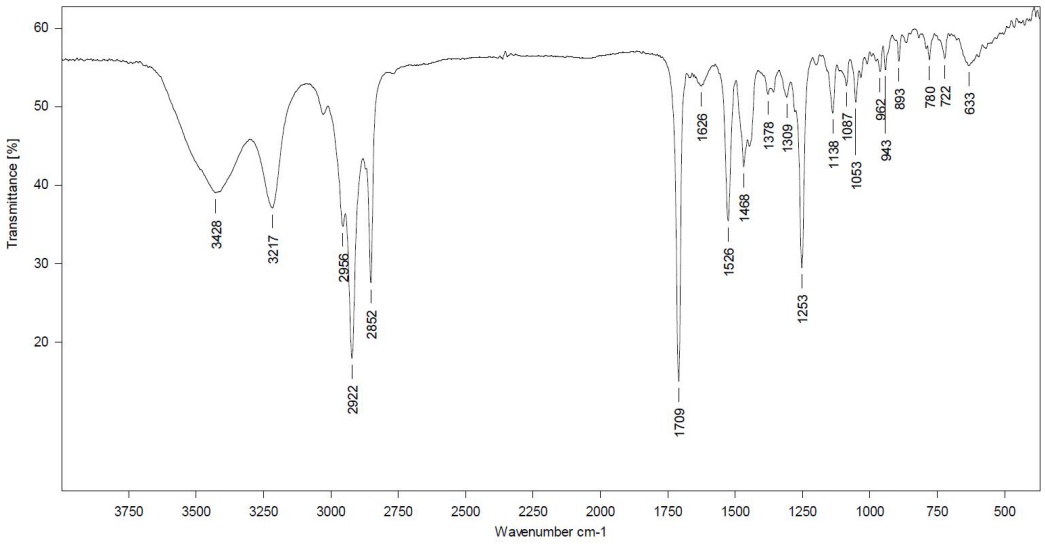


Figure S6 IR spectrum of **2**.

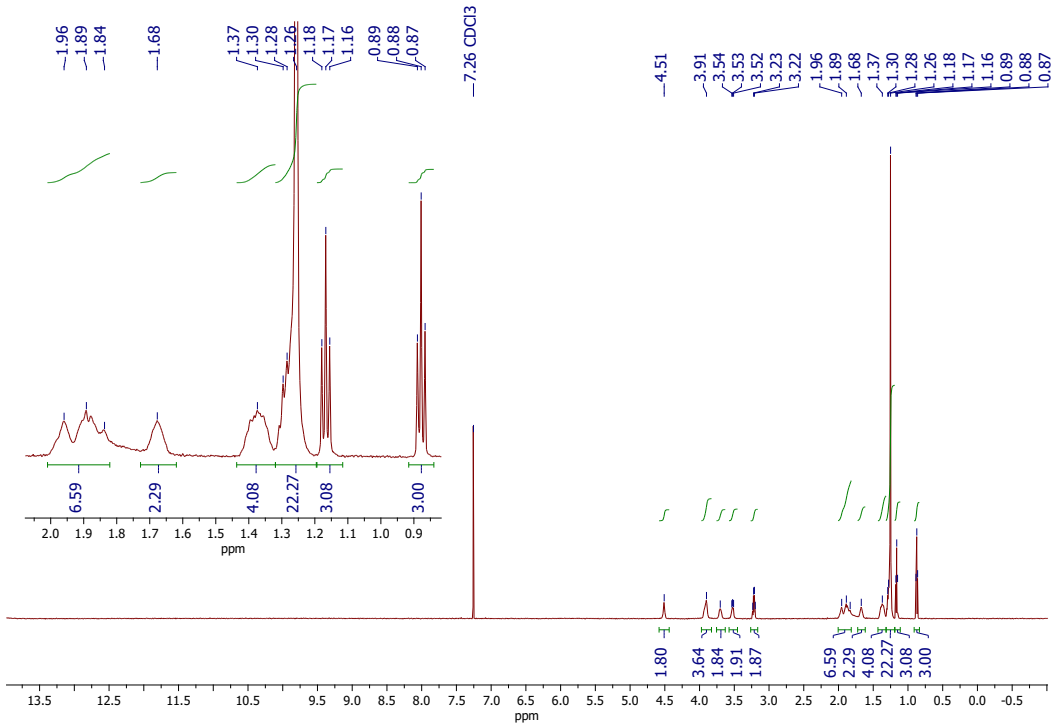


Figure S7 ^{1}H NMR spectrum of **3**.

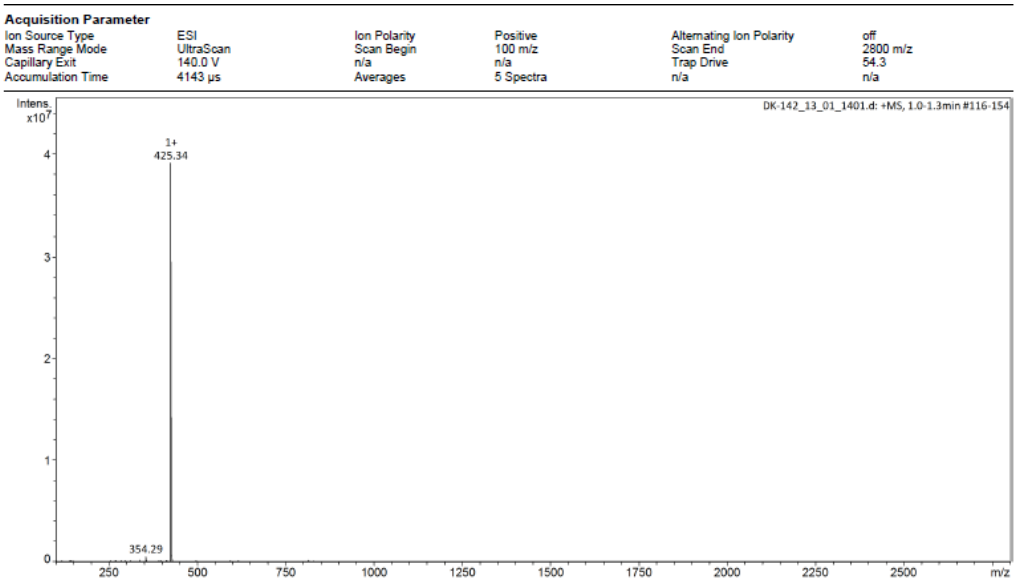


Figure S8 ESI mass spectrum of **3**.

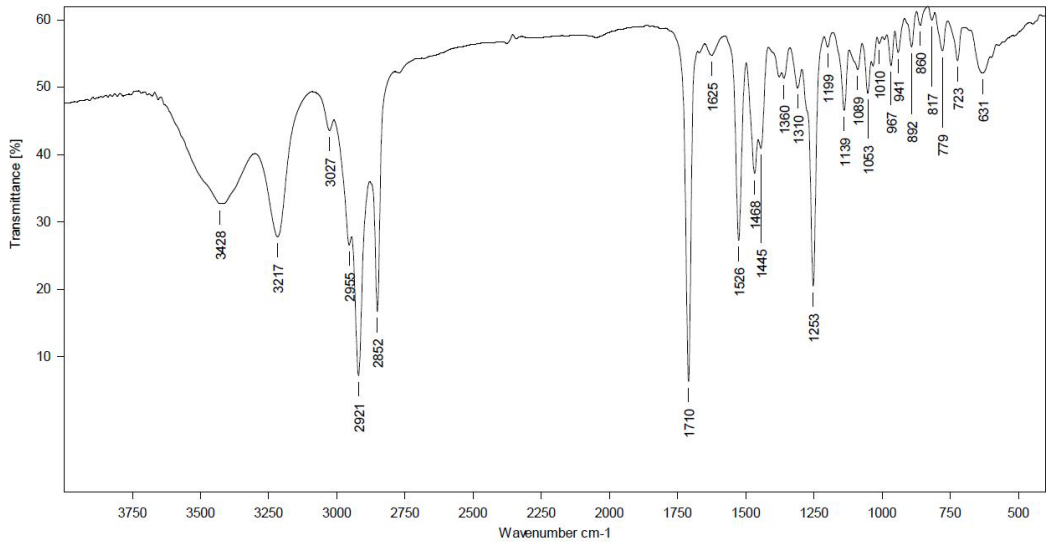


Figure S9 IR spectrum of **3**.

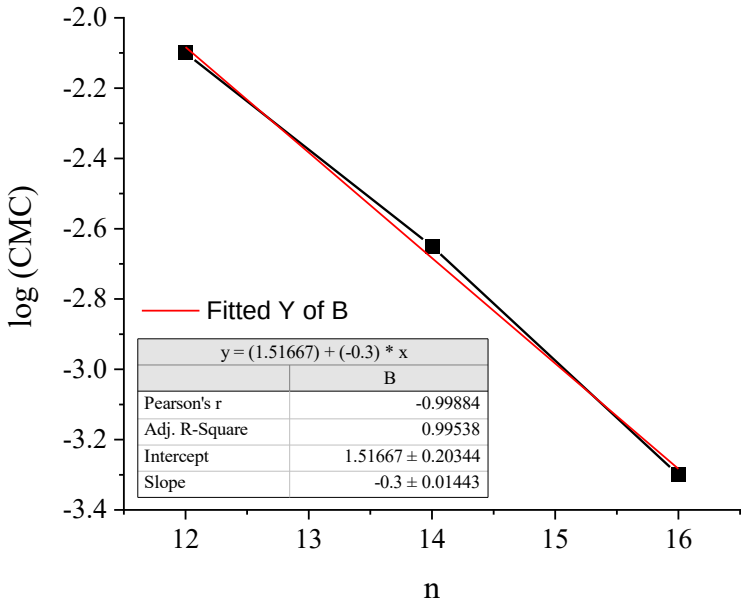


Figure S10 The dependence of the log(CMC) on the number of carbon atoms (n) in the hydrophobic tail of the piperidinium surfactants containing ethylcarbamate group (n = 12, 14, 16).

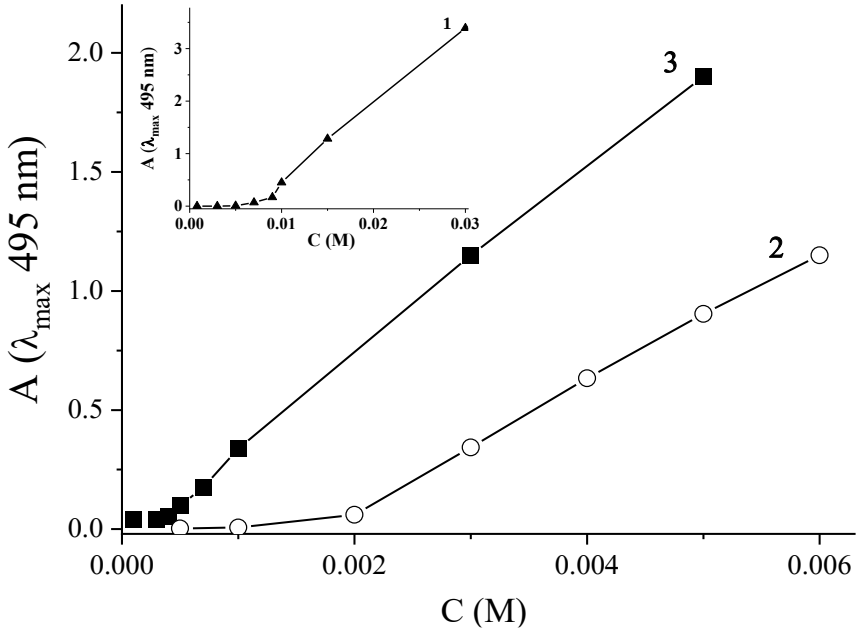


Figure S11 The change in absorbance of saturated solutions of Orange OT at a wavelength of 495 nm depending on the concentration of surfactants **2**, **3** and **1** (inset), optical path 1 cm, 25°C.

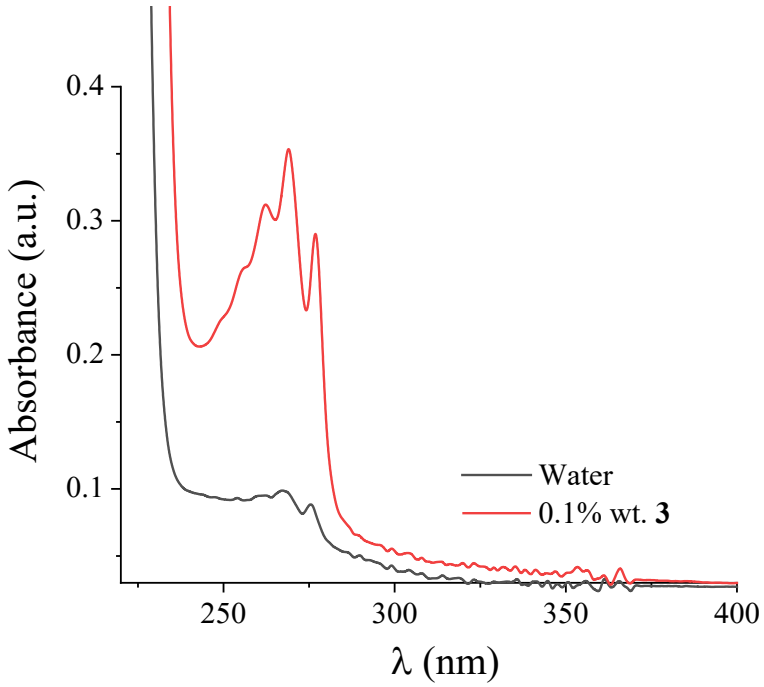


Figure S12 Absorption spectra of saturated solutions of tebuconazole in the presence and absence of surfactants at a concentration of 0.1% wt., optical path 1 cm, 25°C.

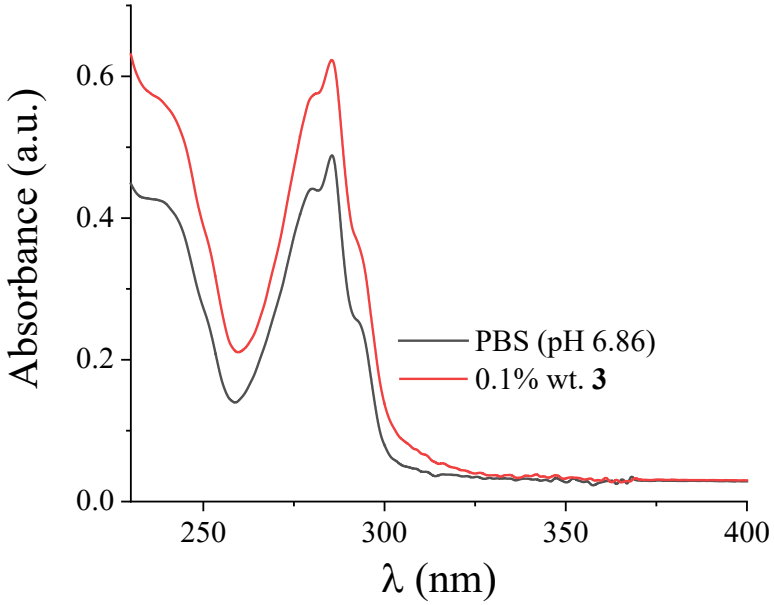


Figure S13 Absorption spectra of saturated solutions of carbendazim in the presence and absence of surfactants at a concentration of 0.1% wt., optical path 1 cm.

Table S1 Antifungal activity of homologous series of piperidinium surfactants with an ethyl carbamate fragment against various phytopathogenic microorganisms.

Compound	Minimum inhibitory concentration (MIC), μg·mL^{-1}				
	Cc	*Aa*	*As*	*Fg*	*Fo*
1	125.0±8.3	250.0±19.0	500.0±60.8	62.5±4.4	125.0±14.0
2	125.0±11.4	250.0±15.6	125.0±14.2	>250.0	125.0±12.8
3	125.0±12.5	125.0±10.5	62.5±7.2	125.0±10.5	125.0±12.4
Tebuconazole	19.5±2.0	9.8±1.2	39.1±4.0	78.1±5.2	78.1±6.5
Carbendazim	312.5±28.0	625.0±57.0	1250.0±138.0	4.9±0.2	0.6±0.1
Minimum fungicidal concentration (MFC), μg·mL^{-1}					
1	250.0±16.6	250.0±19.0	500.0±60.8	125.0±8.8	250.0±28.0
2	250.0±22.8	250.0±15.6	250.0±28.4	250.0±20.2	250.0±25.6
3	250.0±25.0	250.0±21.0	125.0±14.4	250.0±21.0	250.0±24.8
Tebuconazole	39.1±4.0	19.5±2.4	78.1±8.0	78.1±5.2	78.1±6.5
Carbendazim	625.0±56.0	1250.0±114.0	2500.0±276.0	9.76±0.6	–

Table S2 Antimicrobial activity of compositions based on **3** and fungicides carbendazim or tebuconazole against phytopathogenic bacteria and fungi.

Compound	Minimum inhibitory concentration (MIC), μg·mL^{-1}			
	Cm	*Ec*	*Aa*	*Fg*
3/carbendazim	1.9±0.05	3.8±0.1	>60.0	15.0±0.7
	1.6/0.3	*3.1/0.6*	*>50.0/10.0*	*12.5/2.5*
Carbendazim	>500.0	>500	625.0±57.0	4.9±0.2
3/tebuconazole	6.2±0.4	12.5±1.2	50.0±8.1	6.2±0.2
	1.6/4.7	*3.1/9.4*	*12.5/37.5*	*1.6/4.7*
Tebuconazole	>500.0	>500.0	9.8±1.2	78.1±5.2
3	3.1±0.2	6.3±0.4	125.0±10.5	125.0±10.5
Minimum bactericidal concentration (MBC) or Minimum fungicidal concentration (MFC), μg·mL^{-1}				
3/carbendazim	3.8±0.1	15.0±0.5	>60.0	30.0±1.3
	3.1/0.6	*12.5/2.5*	*>50.0/10.0*	*25.0/5.0*
Carbendazim	–	–	2500.0±114.0	9.76±0.6
3/tebuconazole	12.5±0.8	25.0±2.3	100.0±16.2	12.5±0.5
	3.1/9.4	*6.3/18.8*	*25.0/75.0*	*3.1/9.4*
Tebuconazole	–	–	19.5±2.4	78.1±5.2
3	6.3±0.3	12.5±0.8	250.0±21.0	250.0±21.0

*Italicized are the ratios of the reagents of **3** and fungicide.