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ESTERS OF VANILLIN AND VANILLAL OXIMES

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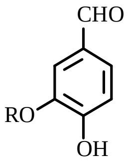
*Vanillin and vanillal oximes **2a** and **2b** were used to prepare the corresponding esters **3a-k**, **4a-k**, and **5a-c** by reaction with acyl chlorides in the presence of pyridine.*

Key words: oximes, vanillin, vanillal, esters, acyl chlorides.

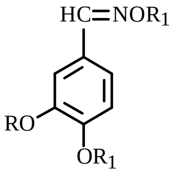
Ethers and esters of oximes exhibit anti-inflammatory, antimicrobial, pesticidal, insecticidal, fungicidal, and other types of physiological activity [1-8].

Oximes of plant phenols (**2a** and 2**b**) prepared from vanillin and vanillal (**1a** and **1b**) are convenient and available synthons for the synthesis of new biologically active compounds and fragrances and can be used as reagents for separating and concentrating chemical elements [9].

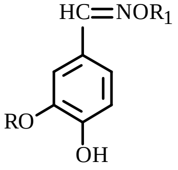
Our goal was to prepare new esters of vanillin and vanillal oximes (**2a** and **2b**) in order to study their biological activities and to seek compounds with valuable practical properties based on them. The corresponding esters of vanillin and vanillal oximes **3a-k** and **4a-k** were isolated by reacting **2a** and **2b**, which were synthesized as before [10, 11], with acyl chlorides in the presence of pyridine (reagent ratio 1:2:2) in absolute diethylether. The esterification was carried out by simple mixing of the reagents at room temperature (18-20°C) for 8-10 h in product yields of 80-96% for **3a-k** and **4a-k**. It should be noted that the hydroxyls of **2a** and **2b** are more reactive than the phenols.



1: R = Me (**a**),
R = Et (**b**)



2a, b; 3a - k; 4a - k



5a - c

2: R = Me, R_1 = H (**a**); R = Et, R_1 = H (**b**); **3:** R = Me;
4: R = Et; **3, 4:** R_1 = $Me(CH_2)_nC(O)$, n = 0 (**a**), 1 (**b**), 2 (**c**) 3 (**d**),
4 (**e**), 5 (**f**), 6 (**g**); R_1 = $Me_2CHC(O)$ (**h**), $MeCHCH_2C(O)$ (**i**),
$C_6H_5C(O)$ (**j**), $ClCH_2C(O)$ (**k**); **5:** R = Me, R_1 = $Me(CH_2)_2C(O)$ (**a**);
$Me(CH_2)_6C(O)$ (**b**); R = Et, R_1 = $Me(CH_2)_6C(O)$ (**c**)

Hydroxyesters **5a-c** form in 88-92% yield for reagent ratios 1:1:1 under the same conditions.

The structures of the synthesized vanillin and vanillal oxime esters **3a-k**, **4a-k**, and **5a-c** were confirmed by elemental analysis, molecular-weight determination, and IR, UV, and PMR spectra. The purity of the products was 98 ± 1%. The IR spectra of **3a-k**, **4a-k**, and **5a-c** contain absorption bands of aromatic rings at 3100-3000, 1600-1570, 1520-1505, 1420-1410, and 780-600 cm^{-1}; of alkyls at 3000-2820 and 1470-1450 cm^{-1}; of asymmetric C=O stretching vibrations at 1780-1750 cm^{-1}; and of C–O deformations at 1200-1000 cm^{-1}. The IR spectra of **5a-c** also exhibit OH absorption bands at 3500-3200 cm^{-1}. The UV spectra of **3a-i** and **-k**; **4a-i** and **-k**; and **5a-c** have absorption maxima at 215 (ε 16,000), 220 (ε 12,000), 305 nm (ε 6000);

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3j and **4j**, 207 (ε 36,000), 234 (ε 44,000), 268 (ε 37,000), and 305 nm (ε 12,000). PMR spectra of **3a-k** and **5a** and **5b**, which are vanillin derivatives, have an MeO signal as a singlet near 3.9 ppm; **4a-k** and **5c**, which are vanillal derivatives, a EtO signal as a triplet near 1.4 ppm (CH_3) and a quartet near 4.1 ppm (CH_2). The aromatic protons (C_6H_3) of **3a-i** and **-k**, **4a-i** and **-k**, and **5a-c** appear in the range 7.0-7.6 ppm; of benzoic-acid esters **3j** and **4j**, at 7.3-8.30 ppm (C_6H_3 and 2 × C_6H_5). Protons of the HC=N group in **3a-i** and **-k**, **4a-i** and **-k**, and **5a-c** give singlets in the range 8.3-8.7 ppm. The two MeC(O)O groups of acetic-acid esters **3a** and **4a** appear as two singlets near 2.25 and 2.35 ppm. The EtC(O)O groups of propionic-acid esters **3b** and **4b** are observed as two triplets at 1.1-1.5 ppm (2 × Me) and two quartets at 2.4-2.9 ppm (2 × CH_2). The PMR spectra of esters **3c-g**, **4c-g**, and **5a-c** have regions for the terminal CH_3 groups at 0.9-1.2 ppm and of the $CH_2C(O)O$ groups at 2.3-2.8 ppm. Signals of Me_2C in spectra of **3h** and **3i** and **4h** and **4i** appear as two doublets in the range 0.9-1.4 ppm. Esters of monochloroacetic acid **3k** and **4k** have signals for protons of the two $ClCH_2C(O)O$ groups as two singlets near 4.28 and 4.37 ppm. The OH group in PMR spectra of **5a-c** is found as a broad singlet near 6.3 ppm.

EXPERIMENTAL

IR spectra were recorded on a Protege-460 Fourier spectrometer in KBr disks (esters **3a-c**, **-h**, **-j**, **-k**; **4a-d**, **-h**, **-j**, **-k**; **5a-c**) or in thin layers (**3d-g**; **i**; **4e-g**, **-i**); PMR spectra, on a Tesla-567A spectrometer (100 MHz) in $CDCl_3$, chemical shifts measured relative to TMS. UV spectra were recorded on a Specord UV Vis instrument for $1 \cdot 10^{-4}$ M solutions in CH_3OH. Molecular weights (M) were determined by cryoscopy in benzene. We used neutral aluminum oxide L 40/250 μm, Brockman activity II, for column chromatography.

Vanillin and vanillal oximes (**2a** and **2b**) were prepared by oximation of vanillin and vanillal (**1a** and **1b**) as before [10, 11]. Acyl chlorides were synthesized by the literature method [12]. Elemental analyses of all compounds agreed with those calculated.

Vanillin and Vanillal Oxime Esters 3a-k, 4a-k, and 5a-c (General Method). A solution of **2a** or **2b** (20 mmol) in absolute diethylether (200 mL) was treated at 20-23°C with pyridine (40 mmol) and one portion of the appropriate acyl chloride (40 mmol, reagent ratio 1:2:2, for **3a-k** and **4a-k**). Compounds **5a-c** were prepared using a 1:1:1 ratio of reagents. The reaction mixture was vigorously shaken and left for 24-36 h at 20-23°C. The pyridinium hydrochloride precipitate was filtered off and washed with ether. The ether solutions were combined, washed with water and $NaHCO_3$ solution (5%), and dried over $CaCl_2$. The solid was filtered off. Solvent was removed. Compounds **3a-c**, **-h**, **-j**, **-k**; **4a-d**, **-h**, **-j**, **-k**; and **5a-c** were purified by crystallization at low temperature of a benzene:hexane (1:1) mixture; **3d-g**, **-i**; **4e-g**, **-i**, by column chromatography over Al_2O_3 with elution by benzene:hexane (1:1). Solvents were regenerated for repeated use by boiling and distilling over $LiAlH_4$.

This method produced:

1-Acetyloxy-4-(N-acetyloxyiminomethyl)-2-methoxybenzene 3a. Yield 80%, mp 88-89°C. $C_{12}H_{13}NO_5$. M: found 243.4, calc. 251.2.

1-Propionyloxy-4-(N-propionyloxyiminomethyl)-2-methoxybenzene 3b. Yield 92%, mp 61-62°C. $C_{14}H_{17}NO_5$. M: found 264.7, calc. 279.3.

1-*n*-Butyryloxy-4-(N-*n*-butyryloxyiminomethyl)-2-methoxybenzene 3c. Yield 87%, mp 52-53°C. $C_{16}H_{21}NO_5$. M: found 291.4, calc. 307.3.

1-*n*-Valeroyloxy-4-(N-*n*-valeroyloxyiminomethyl)-2-methoxybenzene 3d. Yield 94%, d_{20}^{20} 1.1244, n_D^{20} 1.5208. $C_{18}H_{25}NO_5$. M: found 326.5, calc. 335.4.

1-*n*-Capronoyloxy-4-(N-*n*-capronoyloxyiminomethyl)-2-methoxybenzene 3e. Yield 90%, d_{20}^{20} 1.1036, n_D^{20} 1.5188. $C_{20}H_{39}NO_5$. M: found 347.8, calc. 363.5.

1-*n*-Enanthoyloxy-4-(N-*n*-enanthoyloxyiminomethyl)-2-methoxybenzene 3f. Yield 95%, d_{20}^{20} 1.0995, n_D^{20} 1.5090. $C_{22}H_{33}NO_5$. M: found 373.6, calc. 391.5.

1-*n*-Capryloyloxy-4-(N-*n*-capryloyloxyiminomethyl)-2-methoxybenzene 3g. Yield 96%, d_{20}^{20} 1.0932, n_D^{20} 1.5120. $C_{24}H_{37}NO_5$. M: found 398.2, calc. 419.6.

1-*i*-Butyryloxy-4-(N-*i*-butyryloxyiminomethyl)-2-methoxybenzene 3h. Yield 91%, mp 43-44°C. $C_{16}H_{21}NO_5$. M: found 296.9, calc. 307.3.

1-*i*-Valeroyloxy-4-(N-*i*-valeroyloxyiminomethyl)-2-methoxybenzene 3i. Yield 92%, d_{20}^{20} 1.1230, n_D^{20} 1.5225. $C_{18}H_{25}NO_5$. M: found 322.7, calc. 335.4.

1-Benzoyloxy-4-(N-benzoyloxyiminomethyl)-2-methoxybenzene 3j. Yield 86%, mp 111-112°C. $C_{21}H_{17}NO_5$. M: found 340.0, calc. 363.4.

1-Chloroacetyloxy-4-(N-chloroacetyloxyiminomethyl)-2-methoxybenzene 3k. Yield 92%, mp 127-128°C. $C_{12}H_{11}NCl_2O_5$. M: found 309.3, calc. 320.1.

1-Acetyloxy-4-(N-acetyloxyiminomethyl)-2-ethoxybenzene 4a. Yield 83%, mp 99-100°C. $C_{13}H_{15}NO_5$. M: found 246.7, calc. 265.3.

1-Propionyloxy-4-(N-propionyloxyiminomethyl)-2-ethoxybenzene 4b. Yield 93%, mp 67-68°C. $C_{15}H_{19}NO_5$. M: found 275.4, calc. 293.3.

1-*n*-Butyryloxy-4-(N-*n*-butyryloxyiminomethyl)-2-ethoxybenzene 4c. Yield 90%, mp 75-76°C. $C_{17}H_{23}NO_5$. M: found 308.8, calc. 321.4.

1-*n*-Valeroyloxy-4-(N-*n*-valeroyloxyiminomethyl)-2-ethoxybenzene 4d. Yield 94%, mp 20-30°C. $C_{19}H_{27}NO_5$. M: found 329.7, calc. 349.4.

1-*n*-Capronoyloxy-4-(N-*n*-capronoyloxyiminomethyl)-2-ethoxybenzene 4e. Yield 91%, d_{20}^{20} 1.1007, n_D^{20} 1.5084. $C_{21}H_{31}NO_5$. M: found 361.0, calc. 377.5.

1-*n*-Enanthoyloxy-4-(N-*n*-enanthoyloxyiminomethyl)-2-ethoxybenzene 4f. Yield 93%, d_{20}^{20} 1.0920, n_D^{20} 1.5026. $C_{23}H_{35}NO_5$. M: found 387.4, calc. 405.5.

1-*n*-Carpyloyloxy-4-(N-*n*-capryloyloxyiminomethyl)-2-ethoxybenzene 4g. Yield 95%, d_{20}^{20} 1.0811, n_D^{20} 1.5025. $C_{25}H_{39}NO_5$. M: found 407.7, calc. 433.6.

1-*i*-Butyryloxy-4-(N-*i*-butyryloxyiminomethyl)-2-ethoxybenzene 4h. Yield 88%, mp 47-48°C. $C_{17}H_{23}NO_5$. M: found 311.3, calc. 321.4.

1-*i*-Valeroyloxy-4-(N-*i*-valeroyloxyiminomethyl)-2-ethoxybenzene 4i. Yield 91%, d_{20}^{20} 1.1204, n_D^{20} 1.5166. $C_{19}H_{27}NO_5$. M: found 329.9, calc. 349.4.

1-Benzoyloxy-4-(N-benzoyloxyiminomethyl)-2-ethoxybenzene 4j. Yield 90%, mp 106-107°C. $C_{22}H_{19}NO_5$, M: found 361.6, calc. 377.4

1-**Chloroacetyloxy-4-(N-chloroacetyloxyiminomethyl)-2-ethoxybenzene 4k.** Yield 90%, mp 108-109°C. $C_{13}H_{13}NCl_2O_5$. M: found 321.5, calc. 334.2.

4-(N-*n*-Butyloxyiminomethyl)-2-methoxy-1-phenol 5a. Yield 92%, mp 91-92°C. $C_{12}H_{15}NO_4$. M: found 229.8, calc. 237.3.

4-(N-*n*-Capryloyloxyiminomethyl)-2-methoxy-1-phenol 5b. Yield 89%, mp 61-62°C. $C_{16}H_{23}NO_4$. M: found 271.1, calc. 293.4.

4-(N-*n*-Capryloyloxyiminomethyl)-2-ethoxy-1-phenol 5c. Yield 88%, mp 79-80°C. $C_{17}H_{25}NO_4$. M: found 285.9, calc. 307.4.

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