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SYNTHESIS AND STRUCTURE—AROMA CORRELATION OF CITRAL OXIME ESTERS

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Citral (3,7-dimethyl-2,6-octadienal, **1**) occurs in lemongrass, cubeb, citrus, and other essential oils as a mixture of the *E*- and *Z*-isomers in a 7:3 ratio. This aldehyde (**1**) has a strong lemon odor [1] and is used widely in many perfume compositions.

The goal of our work was to develop preparative synthetic methods of citral oxime esters through the reaction of citral oxime (**2**) with alkylcarboxylic acid anhydrides or alkyl- and arylcarboxylic acid chlorides in the presence of pyridine. The synthesis was performed at 20-23°C for 24-36 h by simply mixing the appropriate reagents and proceeded without using cooling and prolonged stirring. Citral oxime esters **3-22** were prepared in 74-88% yield.

$$\underset{\mathbf{1}}{\mathrm{Me_2C{=}CH(CH_2)_2C(Me){=}CHCH{=}O}} \longrightarrow \underset{\mathbf{2}}{\mathrm{Me_2C{=}CH(CH_2)_2C(Me){=}CHCH{=}NOH}} \longrightarrow$$

$$\longrightarrow \underset{\mathbf{3\text{ - }22}}{\mathrm{Me_2C{=}CH(CH_2)_2C(Me){=}CHCH{=}NOC(O)R}}$$

R = Me (**3**), Et (**4**), Pr (**5**), $CHMe_2$ (**6**), CH_2CHMe_2 (**7**), $(CH_2)_4Me$ (**8**), $(CH_2)_5Me$ (**9**),
$(CH_2)_6Me$ (**10**), $(CH_2)_7Me$ (**11**), $(CH_2)_{11}Me$ (**12**), $(CH_2)_{16}Me$ (**13**), C_6H_{11}-*cyclo* (**14**),
C_6H_5 (**15**), $(CH_2)_2C_6H_5$ (**16**), $CH{=}CHC_6H_5$-*cis* (**17**), $C(C{\equiv}N){=}CHC_6H_5$ (**18**),
$C_6H_4NO_2$-3 (**19**), OMe (**20**), OEt (**21**), $(CH_2)_2C(O)OMe$ (**22**)

Esters **3-22** are colorless or slightly colored liquids (**3-17** and **19-22**) or a crystalline compound (**18**, crystallized from hexane). The esters did not need further purification; contained no impurities of starting materials, benzene, and pyridine; and were suitable for direct use in the perfumery and food industries. The products were 96-98% pure according to PMR spectroscopy. Esters **3-22** are very stable at temperatures below +5°C if protected from air and light. They were stabilized against polymerization by adding hydroquinone (0.5%).

The structures and compositions of esters **3-22** were confirmed by elemental analysis, cryoscopic determination of molecular weights, PMR spectra, and IR spectra. The analytical results and determined molecular weights of all synthesized compounds agreed with those calculated.

IR spectra of **3-22** contained absorption bands in the range 3000-2800 cm^{-1} for (CH_{Alk}), 3050-3020 (=CH), 1770-1740 (C=O), 1670-1665 (C=C), 1645-1635 (C=N), 1667-1663 (CH_2), and 1250-1180 (C–O). IR spectra of esters of aromatic carboxylic acids (**15-19**) had absorption bands for (CH_{Ar}) in the range 3100-3000 and 707-690 cm^{-1}; 1600-1595, 1455-1450, 1370-1370, and 1315-1313 (Ar). The IR spectrum of **18** had an absorption band for (C≡N) at 2219 cm^{-1}. The NO_2 band for **19** appeared as two characteristic absorption bands at 1535 and 1350 cm^{-1}. IR spectra of the compounds as thin layers or KBr disks were recorded on a Nicolet Protege-460 IR Fourier spectrophotometer.

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TABLE 1. Aroma of Citral Oxime (**2**) and Citral Oxime Esters **3 - 17** and **20 - 22**

No.	Aroma
2	Citrus-woody with a trace of dry fruit
3	Sweet lemon with a hint of grapefruit
4	Sweet lemon with a hint of anise and ripe apple
5	Citrus with a hint of viburnum
6	Citrus with a hint of apricot peel
7	Citrus-herbaceous with a hint of pineapple
8	Citrus with a hint of plum peel
9	Citrus with a hint of wood bark
10	Citrus and ozone with a hint of resin
11	Citrus and plum with a hint of tarragon
12	Citrus and oily with a hint of pear
13	Citrus and bitter with a hint of berry
14	Citrus with a trace of sharp apple
15	Lemon and cologne with a hint of ozone
16	Lemon with a hint of medicinal herbs
17	Lemon with a hint of coriander
20	Lime with a hint of cranberry
21	Lime with a hint of bilberry
22	Lime with a hint of wormwood

PMR spectra of **3-22** showed resonances for the moiety ($Me_2C=C$) as two broad singlets at 1.60 ± 0.05 and 1.66 ± 0.04 ppm; (MeC=C), a broad singlet at 2.05 ± 0.05; and (HC=C), resonances at 4.90-6.40. Resonances of aromatic protons of esters **15-19** appeared as a multiplet at 7.10-9.00 ppm. PMR spectra of **3-22** contained characteristic resonances corresponding to the ester group [2]. PMR spectra in $CDCl_3$ (5% solutions) were obtained on a BS-587A spectrometer (100 MHz, Tesla). Chemical shifts were determined relative to TMS internal standard.

The Tasting Council of accredited monitoring-analytical laboratory OOO Tereza-Inter (Moscow) evaluated the organoleptic aromas of the synthesized citral oxime esters **3-17** and **20-22**. Table 1 lists the statistical average data for the pure products. Practically all prepared esters have some citrus aroma with different traces of fruit, berry, or spice. This enables them to be used as imitation food flavors and fruit and berry fragrances. Ester **15** is interesting because it has a clear fresh ozone and cologne aroma, which makes it promising for use in perfumery.

Citral oxime (**2**) was synthesized by the literature method [3]. Its physical chemical properties agreed with those published [4].

Citral Oxime Esters 3-6. Citral oxime (**2**, 0.01 mol) and the appropriate acid anhydride (0.011 mol) were mixed, shaken, left at 20-23°C for 24-36 h, and diluted with water. The product was extracted with hexane. The organic layer was separated, washed with water and $NaHCO_3$ solution (5%), and dried over $CaCl_2$. Solvent was removed at reduced pressure ($p = 10\text{-}15$ mm Hg), keeping the temperature below 25-30°C. The product was dried in vacuo ($p = 2\cdot10^{-2}$ mm Hg). Esters **3-6** were purified finally by preparative column chromatography over Al_2O_3 (Brockman activity II, neutral) with elution by benzene with hexane. The molecular weights were determined by cryoscopy in benzene.

The following compounds were prepared by this method.

***N*-Acetyloxyimino-3,7-dimethyl-2,6-octadiene (3).** Yield 86%, d_{20}^{20} 1.0589, n_D^{20} 1.4968, $C_{12}H_{19}NO_2$.

***N*-Propionyloxyimino-3,7-dimethyl-2,6-octadiene (4).** Yield 90%, d_{20}^{20} 0.9758, n_D^{20} 1.4920, $C_{13}H_{21}NO_2$.

***N*-Butyryloxyimino-3,7-dimethyl-2,6-octadiene (5).** Yield 83%, d_{20}^{20} 0.9859, n_D^{20} 1.4794, $C_{14}H_{23}NO_2$.

***N-iso*-Butyryloxyimino-3,7-dimethyl-2,6-octadiene (6).** Yield 85%, d_{20}^{20} 1.0035, n_D^{20} 1.4750, $C_{14}H_{23}NO_2$.

Citral Oxime Esters 7-22. Citral oxime (**2**, 0.01 mol) was dissolved in absolute pyridine (0.011 mol), cooled to 15°C, stirred, treated carefully with the appropriate acid chloride (0.011 mol), left at 20-23°C for 24-36 h, and diluted with water. The product was extracted with hexane (**7-14**, **20-22**) or benzene (**15-19**). The organic layer was separated, washed with water and $NaHCO_3$ solution (5%), and dried over $CaCl_2$. Solvent was removed at reduced pressure ($p = 10\text{-}15$ mm Hg), keeping the temperature below 25-30°C. The product was dried in vacuo ($p = 2\cdot10^{-2}$ mm Hg). Esters **7-22** were finally purified by preparative column chromatography over Al_2O_3 (Brockman activity II, neutral) with elution by benzene with hexane.

The following compounds were prepared by this method.

***N-iso*-Valeroyloxyimino-3,7-dimethyl-2,6-octadiene (7).** Yield 92%, d_{20}^{20} 0.9785, n_D^{20} 1.4876, $C_{15}H_{25}NO_2$.

***N*-Caproyloxyimino-3,7-dimethyl-2,6-octadiene (8).** Yield 88%, d_{20}^{20} 0.8114, n_D^{20} 1.4798, $C_{16}H_{27}NO_2$.

***N*-Enanthoyloxyimino-3,7-dimethyl-2,6-octadiene (9).** Yield 93%, d_{20}^{20} 0.8901, n_D^{20} 1.4808, $C_{17}H_{29}NO_2$.

***N*-Caprylyloxyimino-3,7-dimethyl-2,6-octadiene (10).** Yield 84%, d_{20}^{20} 0.9974, n_D^{20} 1.4839, $C_{18}H_{31}NO_2$.

***N*-Pelargonyloxyimino-3,7-dimethyl-2,6-octadiene (11).** Yield 85%, d_{20}^{20} 0.9785, n_D^{20} 1.4842, $C_{19}H_{33}NO_2$.

***N*-Tridecanoyloxyimino-3,7-dimethyl-2,6-octadiene (12).** Yield 86%, d_{20}^{20} 0.9130, n_D^{20} 1.4798, $C_{23}H_{41}NO_2$.

***N*-Stearyloxyimino-3,7-dimethyl-2,6-octadiene (13).** Yield 85%, d_{20}^{20} 1.0580, n_D^{20} 1.4798, $C_{28}H_{51}NO_2$.

***N*-Cyclohexanecarboxyloxyimino-3,7-dimethyl-2,6-octadiene (14).** Yield 80%, d_{20}^{20} 1.0501, n_D^{20} 1.5025, $C_{17}H_{27}NO_2$.

***N*-Benzoyloxyimino-3,7-dimethyl-2,6-octadiene (15).** Yield 84%, d_{20}^{20} 1.0224, n_D^{20} 1.5208, $C_{17}H_{21}NO_2$.

***N*-(3-Phenylpropionyloxyimino)-3,7-dimethyl-2,6-octadiene (16).** Yield 87%, d_{20}^{20} 0.9530, n_D^{20} 1.5268, $C_{19}H_{25}NO_2$.

***N-trans*-Cinnamyloxyimino-3,7-dimethyl-2,6-octadiene (17).** Yield 81%, d_{20}^{20} 1.0752, n_D^{20} 1.5724, $C_{19}H_{23}NO_2$.

***N-trans*-2-Cyanocinnamyloxyimino-3,7-dimethyl-2,6-octadiene (18).** Yield 80%, mp 38-39°C, $C_{20}H_{22}N_2O_2$.

***N*-3-Nitrobenzoyloxyimino-3,7-diemthyl-2,6-octadiene (19).** Yield 83%, d_{20}^{20} 1.1376, n_D^{20} 1.5424, $C_{17}H_{22}N_2O_4$.

***N*-3,7-Dimethyl-2,6-octadieniminomethylcarbonate (20).** Yield 82%, d_{20}^{20} 0.9310, n_D^{20} 1.4856, $C_{12}H_{19}NO_3$.

***N*-3,7-Dimethyl-2,6-octadieniminoethylcarbonate (21).** Yield 84%, d_{20}^{20} 0.9836, n_D^{20} 1.4860, $C_{13}H_{21}NO_3$.

***N*-3,7-Dimethyl-2,6-octadieniminomethylsuccinate (22).** Yield 86%, d_{20}^{20} 0.8945, n_D^{20} 1.4848, $C_{15}H_{23}NO_4$.

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