Chemistry of Natural Compounds, Vol. 41, No. 1, 2005

BRIEF COMMUNICATIONS

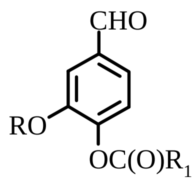
PREPARATIVE SYNTHESIS OF VANILLIN AND VANILLAL ESTERS OF SEVERAL CARBOXYLIC ACIDS

E. A. Dikusar and N. G. Kozlov

UDC 547.362

The natural plant aldehydophenols vanillin (4-hydroxy-3-methoxybnzaldehyde) (**1a**) and its close homolog vanillal (4-hydroxy-3-ethoxybenzaldehyde) (**1b**) are widely used in the food and perfume industries [1, 2].

Our goal was to prepare new derivatives of the natural compounds as esters of **1a** and **1b** with several aromatic and functionally substituted alkylcarboxylic acids (**3a-u** and **4a-e**). The esters of **3a-u** and **4a-e** were synthesized using a method that consists of reacting **1a** or **1b** with the corresponding acyl chlorides of the aromatic and functionally substituted alkylcarboxylic acids (**2**) in absolute CH_2Cl_2 with added pyridine. Acyl chlorides of the following acids (**2**) were used in the ester synthesis: capric, stearic, acrylic, methacylic, oleic, benzoic, *p*-toluic, phenylacetic, 2-phenylbutyric, cinnamic, 2-(*p*-toluyloxy)propionic, succinic, *o*-chlorobenzoic, *p*-chlorobenzoic, *o*,*p*-dichlorobenzoic, *o*,*p*-dichlorophenyoxyacetic, bromoacetic, 1,2-dibromohydrocinnamic, *p*-bromobenzoic, *m*-nitrobenzoic, and *p*-nitrobenzoic. This reaction converted the starting phenols **1a** and **1b** into the corresponding esters **3a-u** and **4a-e** in yields of 80-90%.



3a - u, **4a - e**

3a - u: R = CH_3; **4a - e:** R = CH_2-CH_3; **3a:** $R_1 = (CH_2)_8CH_3$; **3b:** $(CH_2)_{16}CH_3$; **3c:** CH=CH_2; **3d:** $C(CH_3)=CH_2$; **3e:** *cis*-$(CH_2)_7$CH=CH$(CH_2)_7CH_3$; **3f:** C_6H_5; **3g:** *n*-$C_6H_4CH_3$; **3h:** $CH_2C_6H_5$; **3i:** $CH_2CH(CH_3)C_6H_5$; **3j:** *trans*-CH=CHC_6H_5; **3k:** *n*-$(CH_2)_2OC_6H_4CH_3$; **3l:** ½-$(CH_2)_2$-; **3m:** *o*-C_6H_4Cl; **3n:** *n*-C_6H_4Cl; **3o:** *o*, *n*-$C_6H_3Cl_2$; **3p:** *o*, *n*-$CH_2OC_6H_3Cl_2$; **3q:** CH_2Br; **3r:** CHBrCHBrC_6H_5; **3s:** *n*-C_6H_4Br; **3t:** *m*-$C_6H_4NO_2$; **3u:** *n*-$C_6H_4NO_2$; **4a:** $R_1 = C_6H_5$; **4b:** *n*-$C_6H_4CH_3$; **4c:** ½-$(CH_2)_2$-; **4d:** *o*-C_6H_4Cl; **4e:** *n*-C_6H_4Cl

Aromatic compounds **3a-u** and **4a-e** contain aldehyde, ester, and methoxy or ethoxy groups in addition to several substituents associated with the structures of the starting carboxylic acid acyl chlorides (**2**). This enables them to be used as synthons for further chemical trnasformations. The prepared esters are expected to be promising for studying their antimicrobial and radioprotector activities [3, 4].

The structures of the synthesized esters were confirmed by elemental analysis, cryoscopic molecular-weight determination, and PMR, IR, and UV spectra. The purity of the prepared compounds according to PMR spectroscopy was 98 ± 1%.

Vanillin and Vanillal Esters 3a-u and 4a-e (general method). A solution of vanillin or vanillal (**1a** or **1b**, 0.2 mol) in absolute CH_2Cl_2 (500 mL) was treated with absolute pyridine (0.25 mol) and in small portions with stirring and shaking with the appropriate carboxylic acid acyl chloride (**2**, 0.2 mol, 0.1 mol for succinic acid). The reaction mixture was boiled for 1 h.

Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus, 220072, Minsk, ul. Surganova, 13, e-mail: loc@ifoch.bas-net.by. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 74-75, January-February, 2005. Original article submitted August 2, 2004.

The CH_2Cl_2 was distilled by heating on a water bath. The solid was dissolved in benzene (500 mL), washed three times with both water and $NaHCO_3$ solution (5%), and dried over $CaCl_2$. The solvent was removed. The solid was recrystallized from benzene—hexane or distilled in vacuo. The resulting esters have the following melting or boiling points, d_{20}^{20}, n_D^{20}, and compositions: **3a**, mp 35-36°C, $C_{18}H_{26}O_4$; **3b**, mp 32-33°C, $C_{26}H_{42}O_4$; **3c**, bp 140-141°C, (p = 0.5 mm Hg), d_{20}^{20} 1.3428, n_D^{20} 1.5555, $C_{11}H_{10}O_4$; **3d**, mp 46-47°C, $C_{12}H_{12}O_4$; **3e**, d_{20}^{20} 1.1563, n_D^{20} 1.5040, $C_{26}H_{40}O_4$; **3f**, mp 71-72°C, $C_{15}H_{12}O_4$; **3g**, mp 91-92°C, $C_{16}H_{14}O_4$; **3h**, bp 179-180°C (p = 0.5 mm Hg), d_{20}^{20} 1.2835, n_D^{20} 1.5810, $C_{16}H_{14}O_4$; **3i**, mp 69-70°C, $C_{18}H_{18}O_4$; **3j**, mp 59-60°C, $C_{17}H_{14}O_4$; **3k**, mp 63-64°C, $C_{18}H_{18}O_5$; **3l**, mp 130-131°C, $C_{20}H_{18}O_8$; **3m**, mp 91-92°C, $C_{15}H_{11}ClO_4$; **3n**, mp 98-99°C, $C_{15}H_{11}ClO_4$; **3o**, mp 102-103°C, $C_{15}H_{10}Cl_2O_4$; **3p**, mp 115-116°C, $C_{16}H_{12}Cl_2O_5$; **3q**, mp 43-44°C, $C_{10}H_9BrO_4$; **3r**, mp 82-83°C, $C_{17}H_{14}Br_2O_4$; **3s**, mp 108-109°C, $C_{15}H_{11}BrO_4$; **3t**, mp 114-115°C, $C_{15}H_{11}NO_6$; **3u**, mp 189-190°C, $C_{15}H_{11}NO_6$; **4a**, mp 68-69°C, $C_{16}H_{14}O_4$; **4b**, mp 103-104°C, $C_{17}H_{16}O_4$; **4c**, mp 114-115°C, $C_{22}H_{22}O_8$; **4d**, mp 83-84°C, $C_{16}H_{13}ClO_4$; **4e**, mp 84-85°C, $C_{16}H_{13}ClO_4$.

ACKNOWLEDGMENT

The work was supported financially by the Belorussian Republic Foundation for Basic Research (grant X 03-079).

REFERENCES

1. L. M. Shulov and L. A. Kheifits, *Fragrances and Intermediates for Perfume—Cosmetic Production* [in Russian], Agropromizdat, Moscow (1990).
2. Y. Shaikh, *Specialty Aroma Chemicals in Flavors and Fragrance*, Allured Publishing Corporation, Carol Stream, Illinois (2002).
3. N. N. Suvorov and V. S. Shashkov, *Chemistry and Pharmacology of Prophylactic Agents for Radiation Disease* [in Russian], Atomizdat, Moscow (1975), p. 230.
4. N. N. Karkishchenko, *Ecological Pharmacology* [in Russian], Izotekst, Moscow (1990), Vol. 1, p. 342.