Furan derivatives
199. Preparation and nucleophilic substitution reactions of ethyl ester of 4-bromo-3-(2-furyl)-2-butenoic acid

K. ŠPIRKOVÁ and J. KOVÁČ

Department of Organic Chemistry, Slovak Technical University, CS-812 37 Bratislava

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In the paper, preparation of ethyl ester of 4-bromo-3-(2-furyl)-2-butenoic acid is described and also its nucleophilic substitution reactions with the oxygen nucleophiles. IR, UV, and ^{1}H NMR spectra of the compounds prepared are discussed.

В работе описывается получение этилового эфира 4-бром-3-(2-фурил)-2-бутеновой кислоты и его реакции нуклеофильного замещения с кислородными нуклеофилами. Интерпретируются ИК-, УФ- и ^{1}H ЯМР-спектры полученных соединений.

In paper [1], we described preparation of ethyl ester of 4-bromo-3-(2-furyl)-2-butenoic acid using Horner—Wittig olefinization method. Despite of good yields (60—70 %), this procedure is laborious and time-consuming.

In the present paper, we describe a new, more effective and quicker method of its preparation. Using Claisen condensation we prepared ethyl ester of 3-(2-furyl)-2-propenoic acid. We allowed to react diazomethane with its double bond in anhydrous ether. In the first stage, unstable substituted 1-pyrazoline [2] was formed as the intermediate, which was stabilized already at low temperatures by the hydrogen rearrangement from the position 3 to 2-pyrazoline [3]. The thermal decomposition of 4-(2-furyl)-3-ethoxycarbonyl-2-pyrazoline gave ethyl ester of 3-(2-furyl)-2-butenoic acid in the 80 % yield. As the main reason for the formation of trisubstituted ethylene derivative and not of cyclopropane ring, as it could be expected from the literature data [4—6], we presume preservation of conjugation in the whole system. We prepared by bromination of the ester with *N*-bromosuccinimide under the conditions of selective bromination of the methyl in double bond ester of 4-bromo-3-(2-furyl)-2-butenoic acid [1].

In this work, we selected nucleophilic substitution reactions [7] with the oxygen nucleophiles for studies of properties of this substituted allyl system. In the solvolytic reactions of ethyl ester of 4-bromo-3-(2-furyl)-2-butenoic acid with alkoxides, we obtained 4-alkoxy derivatives of 3-(2-furyl)-2-butenoic acid. Ethyl ester of 4-hydroxy-3-(2-furyl)-2-butenoic acid was obtained by reaction with

sodium hydroxide in 50 % aqueous solution of dioxan and also in 50 % aqueous solution of acetone at room temperature (Table 1).

In this reaction, a nucleophilic substitution of bromine by a hydroxyl ion took place, but the hydrolysis of the ester group did not occur. We obtained the same results when the solvolytic reactions were performed at room temperature. From

Table 1

Characteristic data of 4-X-3-(2-furyl)-2-butenoic acids

Compound	X	M_r	M.p./°C Yield/%	w_i(calc.)/% w_i(found)/%	
				C	H
I	—OCH_3	$C_9H_{10}O_4$	123—124	59.36	5.49
		182.09	65.9	58.98	5.21
II	—OC_2H_5	$C_{10}H_{12}O_4$	127—128	61.19	6.11
		196.10	58.6	60.83	6.03
III	—O—i-C_3H_7	$C_{11}H_{14}O_4$	130—131	62.82	6.66
		210.11	52.4	62.47	6.38
IV	—O—t-C_4H_9	$C_{12}H_{16}O_4$	134—135	64.25	7.13
		224.12	44.6	64.01	7.10
V	—O-C_6H_5	$C_{14}H_{12}O_4$	133—134	68.82	4.91
		244.14	67.6	68.59	4.83

the given data, we can assume the reactivity of both reaction centres. The carbon atom of methylene group with bromine is more reactive for a nucleophilic attack than the carbon of ethoxycarbonyl group. We assume a normal bimolecular S_N2 reaction course in the reaction as we isolated products of the normal substitution only. We did not isolate products of the so-called abnormal nucleophilic substitution S_N2', which is also described with allylic compounds.

The structures of the products synthesized were studied by IR, UV, and ^1H NMR spectroscopy.

In IR spectra we observed an intense band in the $\tilde{\nu}$ range of 1694 cm^{-1}. It was assigned to stretching vibrations of the carbonyl group. Intensive bands in the $\tilde{\nu}$ range of 1614—1622 cm^{-1} were assigned to stretching vibrations of the ethylene C=C bond. A moderate band in the $\tilde{\nu}$ range of 1300 cm^{-1} belongs to asymmetric vibration and a sharp band in the $\tilde{\nu}$ range of 1025 cm^{-1} belongs to symmetric vibration of C—O—C bond. A band in the $\tilde{\nu}$ range of 880 cm^{-1} was assigned to the antiplanar bending vibrations of furan ring and a characteristic broad band in the $\tilde{\nu}$ range of 3450 cm^{-1} was assigned to stretching vibrations of OH group (Table 2).

The absorption spectra revealed two maxima, the first one in the λ range of 211—218 nm. This band corresponds to $\pi^* \leftarrow \pi$ electron transition of furan ring.

Table 2

IR spectra ($\tilde{\nu}_i/cm^{-1}$)

Compound	δ(C—H)	ν_s(COC)	ν_{as}(COC)	ν(C=C)	ν(C=O)	ν(OH)
I	884	1028	1300	1614	1695	
II	879	1022	1302	1615	1694	3460
III	880	1026	1301	1617	1693	3455
IV	879	1025	1298	1614	1695	3452
V	875	1033	1302	1622	1693	3426

Compounds *I*—*IV* measured in chloroform; compound *V* measured by using KBr technique.

Table 3

UV spectrum

Compound	λ_{max}/nm	log (ε/(dm³ mol⁻¹ cm⁻¹))	λ_{max}/nm	log (ε/(dm³ mol⁻¹ cm⁻¹))
I	211	3.96	301	4.35
II	211	3.89	301	4.25
III	211	3.93	301	4.31
IV	212	3.90	301	4.30
V	218	4.25	298	4.33

More intensive band in the range of 300 nm corresponds to $\pi^* \leftarrow \pi$ electron transition through the whole furylacrylic system (Table 3).

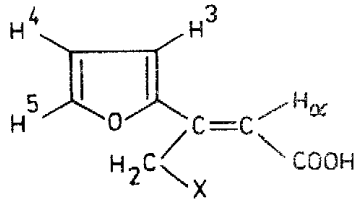
In the selected compounds, we determined their structures by ^{1}H NMR spectroscopy. The compounds prepared — trisubstituted derivatives of ethylene can exist as geometric isomers [8, 9]. The genuine ester of 4-bromo-3-(2-furyl)--2-butenoic acid was prepared by the given method as *Z* isomer. Identification of the individual isomers was made on the basis of comparison of calculated and measured values of the chemical shifts of olephinic protons. The calculation was made on the basis of the additive relation [10], in which increments of the aromatic system were used for the furan ring.

Z isomer	*E* isomer
$\delta(H_\alpha, \text{calc.}) = 6.34$ ppm	$\delta(H_\alpha) = 5.76$ ppm
$\delta(H_\alpha, \text{found}) = 6.36$ ppm	

Substitution nucleophilic reactions with the oxygen nucleophiles took place with the retention of configuration. The obtained values of chemical shifts are given in Table 4.

Table 4

^{1}H NMR data



Compound	δ/ppm				
	H_α, s	H_3, d	H_4, dd	H_5, d	CH_2, s
I	6.42	6.89	6.48	7.56	4.80
II	6.51	6.93	6.45	7.46	4.89
V	6.56	6.92	6.46	7.46	5.45

Experimental

Ethyl ester of 3-(2-furyl)-2-butenoic acid was prepared according to [1], 4-(2-furyl)--3-ethoxycarbonyl-2-pyrazoline according to [3].

IR spectra were measured with a (Zeiss, Jena) UR-20 spectrometer using KBr technique and concentration of the sample 1 mg for 300 mg of KBr, and in chloroform with 0.26 mm cell. Calibration of the apparatus was made on the polystyrene foil with the thickness of 25 μm.

UV spectra were measured with a (Zeiss, Jena) Specord UV VIS spectrophotometer using concentrations 10^{-5}—10^{-4} mol dm^{-3} of methanol.

^{1}H NMR spectra were recorded with a 80 MHz Tesla BS 487 C spectrometer in $CDCl_3$ using tetramethylsilane as the internal standard.

Ethyl ester of 4-hydroxy-3-(2-furyl)-2-butenoic acid (VI)

An aqueous solution of NaOH (1 g; 0.025 mol; 30 cm^3 H_2O) was added to ethyl ester of 4-bromo-3-(2-furyl)-2-butenoic acid (2.59 g; 0.01 mol) in dioxan (30 cm^3). The reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated and the residue was diluted with water (30 cm^3) and acidified with HCl (V(conc. HCl): $V(H_2O) = \alpha = 1:1$) to pH = 1. After acidification, the solution was extracted with chloroform (4×50 cm^3). The extract was dried, concentrated and the crude product was further purified by chromatography on a column of silica gel using benzene—ethyl acetate (volume ratio = 1 : 1) as the eluant. Hydrolysis in 50 % aqueous solution of acetone can be accomplished in a similar way. This yields the same product. Yield 69 %, formula $C_{10}H_{12}O_4$ (M_r = 196.10), oil, w_i(calculated): 61.22 % C, 6.12 % H; w_i(found): 60.83 % C, 5.91 % H. IR

spectrum—$\tilde{\nu}(CHCl_3)/cm^{-1}$: 1620 (C=C), 1705 (C=O), 3480 (OH). UV spectrum—λ_{max}/ /nm (log (ε/(dm^3 mol^{-1} cm^{-1}))): 215 (3.89), 294 (4.29). ^{1}H NMR spectrum—$\delta(CDCl_3)$/ /ppm: 6.49 (H_a, s), 6.92 (H-3, d), 6.38 (H-4, dd), 7.39 (H-5, d), 3.76 (CH_2, s), 3.51 (OCH_2, q), 1.21 (CH_3, t), 9.90 (OH, s).

4-X-3-(2-Furyl)-2-butenoic acids (I—V)

A. A solution of NaOH (3 g; 0.075 mol) in methanol (40 cm^3) is added to ethyl ester of 4-bromo-3-(2-furyl)-2-butenoic acid (0.01 mol) dissolved in methanol (20 cm^3). The reaction mixture was refluxed for 1 h and NaBr separated after cooling was filtered off, and the solvent was evaporated. The residue was dissolved in water (30 cm^3) and acidified with HCl ($\alpha = 1:1$) to pH = 1. The crystalline compounds *I—IV* separated were recrystallized from methanol.

B. Phenol (0.94 g; 0.01 mol) was dissolved in acetone (30 cm^3) and sodium (0.23 g; 0.01 mol) was added. Sodium phenolate thus formed was then added to a solution of ethyl ester of 4-bromo-3-(2-furyl)-2-butenoic acid (2.59 g; 0.01 mol) in acetone (30 cm^3). The reaction proceeded immediately and NaBr separated was filtered off, acetone was evaporated, and the residue was dissolved in water (30 cm^3) and acidified with HCl ($\alpha = 1:1$) to pH = 1. The crude product *V* was crystallized from methanol.

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