SYNTHESIS AND STRUCTURE OF AMINO ESTERS OF FENCHOL. II.

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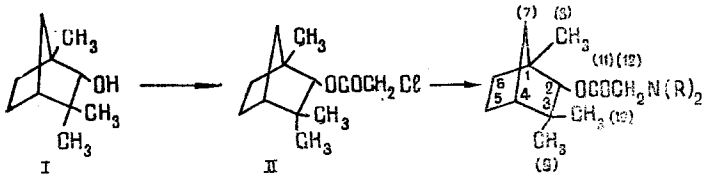
UDC 547.496.2+333.3

Amino derivatives of fenchol have been synthesized. Their structure and properties have been studied by physicochemical methods.

Continuing work on the synthesis of amino derivatives of terpene alcohols [1], we have studied the esterification of (+)-fenchol (I) with monochloroacetyl chloride and from the (+)-fenchol endo-monochloroacetate (II) so obtained we have synthesized amino esters (III-VII) in accordance with the scheme given below.



$N(R)_2 = N(CH_3)_2$ (III); $N(C_2H_5)_2$ (IV); $N(C_4H_9)_2$ (V); N⟨O⟩ (VI); N⟨⟩ (VII)

The esterification of the fenchol with monochloroacetyl chloride took place with the formation of 20% of by-products in addition to fenchol monochloroacetate. By the method of adding authentic substances in GLC analysis the presence in the reaction products of α,β-fenchenes was established. The appearance of the latter can be explained by the fact that under the action of acid catalysts fenchol is readily dehydrated with the formation of fenchyl carbonium ions, the stabilization of which leads to the formation of a mixture of fenchenes [2].

A rise in the temperature of the reaction favored the occurrence of the side reaction of dehydration, but no new products were formed under these conditions and the reaction was restricted to the mutual transformations of the fenchenes. The decrease in the yield of desired products with a rise in the reaction temperature was also connected with the polymerization of the fenchenes, which took place irreversibly and rapidly at temperatures as low as 60-80°C.

According to ^{13}C NMR results, the fenchol monochloroacetate obtained retained the original configuration of the alcohol (I). This means that the reaction took place at the oxygen atom and the bond of the asymmetric carbon atom (C_2) was not affected.

The sign of the specific rotation of the initial fenchol and of the monochloroacetate (II) obtained did not change in the process of esterification from which it may be assumed that monomolecular nucleophilic substitution took place by a S_NI mechanism [3].

The amino esters of fenchol (III-VII) were synthesized by the nucleophilic replacement of the chlorine in (II) by amino groups. It was observed that the exchange reaction took place more readily with amines the basicity of which was higher. Furthermore, the spatial accessibility of the nitrogen atom in the initial amine had a great influence on its reactivity in the exchange reaction and, therefore, on the yield of desired products. Thus, at equal induction effects of the radicals of piperidine and diethylamine, the better accessibility of the nitrogen atom in the piperidine ensured a higher reactivity of this amine.

The characteristics of 1,3,3-trimethylbicyclo[2,2,1]heptyl monochloroacetate (II), 1,3,3-trimethylbicy-

Institute of Physical Organic Chemistry, Academy of Sciences of the Belorussian SSR, Minsk. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 305-308, May-June, 1983. Original article submitted May 12, 1982.

0009-3130/83/1903-0289$07.50

TABLE 1. Characteristics of the Compounds Synthesized

Compound	Yield, %	bp, °C (mm Hg)	n_D^{20}	d_4^{20}	MR_D	Empirical formula	$[\alpha]_D^{20}$
II	82	110–111 (5)	1,4765	0,959	67,75	$C_{12}H_{19}O_2Cl$	+102.40 (c 0.996; alc.)
III	67	125–126 (6)	1,4700	0,962	68,40	$C_{14}H_{25}O_2N$	+ 88.36 (c 1.05; alc.)
IV	62	148–149 (8)	1,4730	0,962	77,62	$C_{16}H_{29}O_2N$	+ 85.71 (c 1.05; alc.)
V	58	210–214 (14)	1,4723	0,950	95,30	$C_{20}H_{37}O_2N$	+ 63.49 (c 1.008; alc.)
VI	71	148–150 (6)	1,4862	1,076	74,98	$C_{16}H_{27}O_3N$	+ 74.14 (c 0.998; alc.)
VII	74	142–143 (6)	1,4850	1.057	75,56	$C_{17}H_{29}O_2N$	+ 60.36 (c 0,994; alc.)

TABLE 2. ^{13}C NMR Chemical Shifts (δ, ppm) of Amino Esters of Fenchol

Compound	R	1	2	3	4	5	6	7	8
II	Cl	48,4	88.2	39 6	48,3	26,8	25,5	41,3	19,4
III	$N(CH_3)_2$	48,3	86.3	39,4	48,2	26 8	25,7	41,3	19,4
IV	$N(C_2H_5)_2$	48,3	86.3	39,4	48,2	25,8	26,7	41.3	16,4
V	$N(C_4H_9)_2$	48,4	86 3	39,0	48 2	25,8	26,6	41,4	19,4
VI	C_4H_8NO	48,2	86,5	39,4	48,1	25,8	26,5	41,3	19,4
VII	$C_5H_{10}N$	48,1	86,2	39,0	48,4	26,8	26,6	41,4	19,4

Compound	R	9	10	11	12	13	14	15	16
II	Cl	20,2	29,6	167,7	41,0	—	—	—	—
III	$N(CH_3)_2$	20,3	29,6	170,8	53,1	45 1	—	—	—
IV	$N(C_2H_5)_2$	20.3	29,6	170,9	53,5	47,6	12,5	—	—
V	$N(C_4H_9)_2$	20,2	29,6	170,9	55.2	54.4	30 1	20,6	14.1
VI	C_4H_8NO	20,2	29,5	170,5	59,3	53,2	66.7	—	—
VII	$C_5H_{10}N$	20,2	29,6	170,9	59,9	54,1	25,8	24,0	

clo[2,2,1]heptyl dimethylaminoacetate (III), 1,3,3-trimethylbicyclo[2,2,1]heptyl diethylaminoacetate (IV), 1,3,3-trimethylbicyclo-[2,2,1]heptyl dibutylaminoacetate (V), 1,3,3-trimethylbicyclo[2,2,1]heptyl morpholinoacetate (IV) and 1,3,3-dimethylbicyclo[2,2,1]heptyl piperidinoacetate (VII) are given in Table 1.

The structures of the compounds synthesized were confirmed by the results of elementary analysis and by GLC, and mass, IR, and ^{13}C NMR spectra.

In the performance of the GLC analysis, the relative retention times (RRTs) of compounds (III-VII) were determined on two stationary phases (SPs) of different polarities; the values of the RRTs are given below:

Compound	Column I	Column II
III	0,094	0,082
IV	0,14	0,11
V	0,37	0,29
VI	0,38	0,44
VII	0,29	0,31
Tetracosane as standard	1,00	1,00

The mass spectra of compounds (III-VII) were each characterized by appreciable peak of the molecular ion, the intensity of which amounted to 8-12% of the maximum. A characteristic feature of the mass spectra of (III-VII) was the presence of fairly intense peaks of the ions formed as the result of simple cleavages at the bonds adjacent to the nitrogen atom, with m/z 44, 72, 128, 84, and 86, respectively. These ions are characteristic, and their position in the spectrum serves as a proof of the presence of a particular amino grouping in the molecule.

The infrared spectra of all the compounds investigated confirmed their structures and permitted their functional groups to be identified unambiguously. In the 3000-2800 cm^{-1} region we observed a set of bands at (cm^{-1}) 2996 (νC–H at C_2), 2975 (ν_{as} CH_3), 2960 (ν_{as} CH_2), 2940 (ν_{as} CH_3), and 2880 (ν_s CH_2). In compound (V), to those mentioned must be added a band at 2864 cm^{-1}, ν_s of a CH_2 group of a butyl radical. The ratio of the relative intensities of the overlapping bands in this region changed according to the relative numbers of the corresponding CH_3 and CH_2 groups in the molecule of the substance concerned. Thus, in (III) the maximum at

2960 cm^{-1} predominated; (IV) – 2975 cm^{-1}; (V) – 2962 cm^{-1}; (VI) – 2940 cm^{-1}; and (VII) – 2962 cm^{-1}. Corresponding changes were also observed in the regions of the symmetrical and antisymmetrical deformation vibrations (1490-1440 and 1390-1360 cm^{-1}) of these groups. A methylene group conjugated with a carbonyl group was identified from the presence of a band in the 1425-1415 cm^{-1} region. The ester groups in these compounds were determined by the presence of strong absorption bands due to the vibrations of the C=O group at 1757 and 1735 cm^{-1} in (III); 1740 and 1730 cm^{-1} in (IV); 1750 and 1730 cm^{-1} in (V); 1754-1733 cm^{-1} in (VI); and 1743 and 1730 cm^{-1} in (VII), and also by bands at 1185 and 1165 cm^{-1} in all the spectra due to the vibrations of a C–O bond.

The assignment of the chemical shifts of the ^{13}C nuclei was made on the basis of a comparison of the results obtained and the previously known chemical shifts of fenchone [4] and of α- and β-fenchols [5]. The chemical shifts of the ^{13}C nuclei of the fenchol ring in the compound (III-VII) synthesized differed little from the chemical shifts of the corresponding ^{13}C nuclei in fenchol. The ^{13}C NMR spectra show the endo orientation of the functional substituent at C_2. According to ^{13}C NMR results, the purity of all the samples was 95%. The ^{13}C NMR chemical shifts of the amino esters of fenchol are given Table 2.

EXPERIMENTAL

GLC analysis was performed on a Chrom-4 chromatograph with a flame-ionization detector at a column temperature of 200°C and an evaporator temperature of 220°C. Two stainless steel columns (380 × 0.3 cm) containing 5% of the silicone elastomer SKTFV-803 + 1% Na_3PO_4 and 5% of Versamid 900 + 1% Na_3PO_3 deposited on Chromaton NAW-DMCS (grain size 0.2-0.25 mm) were used. The rate of flow of carrier gas (helium) was 30 ml/min. The mean values of the RRTs were calculated from three parallel determinations. The reproducibility of the RRT values was ±0.01 unit.

Mass spectra were recorded on a Varian MAT-311 instrument with a cathode emission current of 1000 mA and an energy of the ionizing electrons of 10 eV. The temperature of the ion source was 200°C.

IR spectra were recorded on a UR-20 spectrometer in the range of frequencies of 400-3800 cm^{-1} using slit program 4 at a rate of scanning of 60 cm^{-1}/min. The compounds were taken in the form of liquid films between KBr plates and in CCl_4 solution in concentrations of 0.2 and 0.001 M.

The ^{13}C NMR spectra were taken in $CDCl_3$ on a Bruker CXP-200 spectrometer with a resonance frequency for ^{13}C of 50.31 MHz in the regime of complete decoupling from protons. The chemical shifts were determined relative to an internal standard – tetramethylsilane (TMS). To interpret the spectra, in some cases monoresonance spectra with the nuclear Overhauser effect (NOE) were also taken.

The amino esters of fenchol (III-VII) were synthesized by a procedure described previously [6].

SUMMARY

The esterification of fenchol by monochloroacetyl chloride has been studied. From fenchol monochloroacetate new amino esters of fenchol have been synthesized and their structures have been demonstrated with the aid of physicochemical methods.

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