

Synthesis of Tricyclic Spiro Compounds on the Basis of Alloocimene

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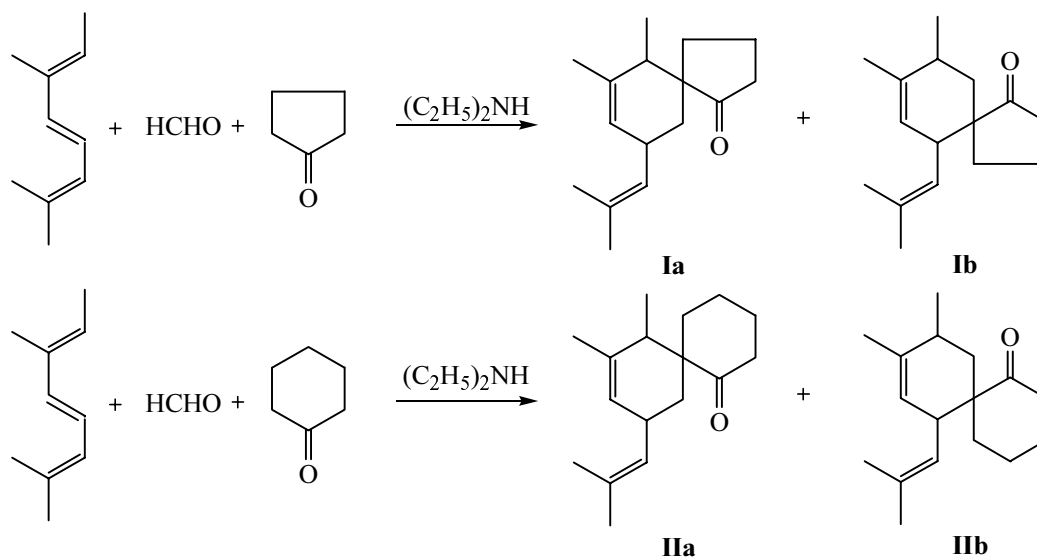
Abstract—Cyclization of 2- and 5-(2-methyl-1-propenyl)-3-cyclohexene-1-spiro-1'-cyclopentan-2'-ols and 2- and 5-(2-methyl-1-propenyl)-3-cyclohexene-1-spiro-1'-cyclohexan-2'-ols in the presence of orthophosphoric acid leads to formation of isomeric tricyclic spiro compounds.

Fused spirocyclic compounds attract strong interest due to their unusual chemical properties [1–3]. In some procedures for the synthesis of macrocyclic compounds, the Diels–Alder reaction is the first step. In this way, we obtained spirobicyclic ketones from alloocimene and cyclopentanone or cyclohexanone and formaldehyde [4]. The cyclic structure of the initial compounds ensures selective character of the process which results in formation of isomer mixtures **Ia/Ib** or **IIa/IIb** at a ratio of 1 : 2 (Scheme 1). Ring closure is the key stage in the synthesis of any macrocyclic compound; here, formation

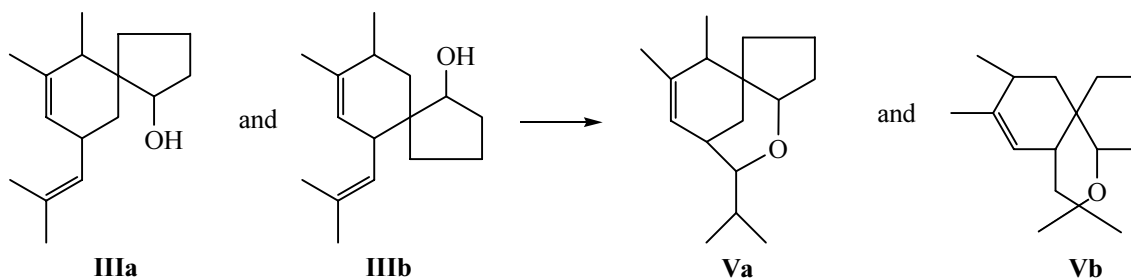
of a bond between a carbon atom and a heteroelement is the most important. The present communication reports on the synthesis of new tricyclic oxa spiro compounds **Va/Vb** and **VIa/VIb** (Scheme 2) on the basis of alloocimene via cyclization of isomeric bicyclic alcohols **IIIa/IIIb** and **IVa/IVb** which are obtained by selective hydrogenation of the carbonyl group in ketones **Ia/Ib** and **IIa/IIb** with sodium tetrahydridoborate.

Diels–Alder adducts derived from alloocimene and dienophiles undergo cyclization in strongly acidic medium. The amount of the acid ranges from 40 to 50 wt % with

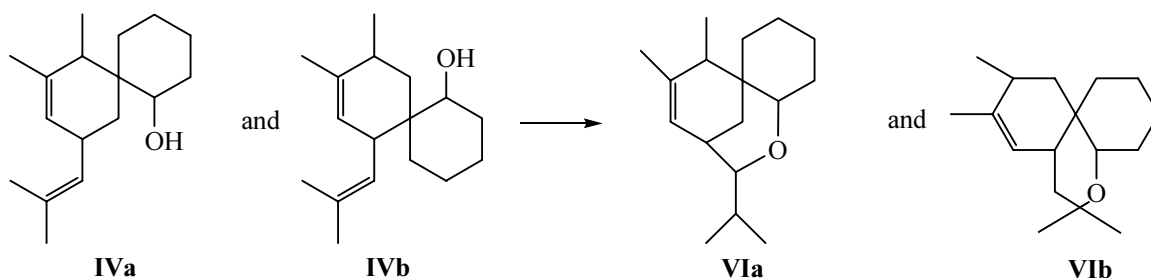
Scheme 1.



Scheme 2.



Scheme 3.

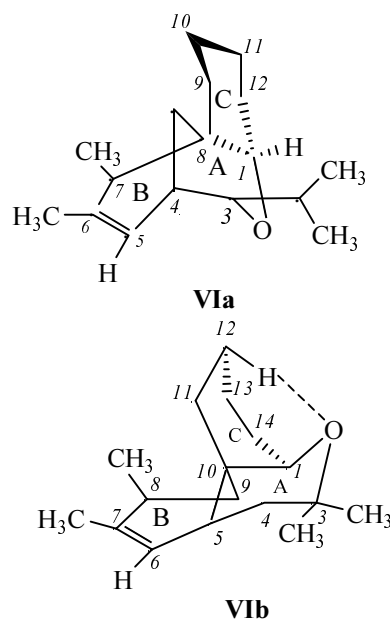


respect to the substrate. It is recommended to carry out the reaction in the temperature range from 25 to 115°C [5–7]. Experiments were performed in the presence of orthophosphoric acid (which is usually used in reactions with such substrates) at 110°C in toluene. The IR spectra of products **Va/Vb** and **VIa/VIb** lacked bending vibration band at 860 cm⁻¹, which is typical of the =C–H bond, but a new absorption band appeared at 1180 cm⁻¹ due to vibrations of the ether C–O bond; these data indicate the transformation of alcohols into ethers. As follows from the data given in table, a high selectivity (85 and 87%) in the formation of the target products and a high conversion of the initial compounds were attained.

The pure products can be isolated only by high-vacuum distillation followed by column chromatography. We thus succeeded in isolating isomer mixtures **Va/Vb** and **VIa/VIb** containing 95–97% of the main substance. The isomer ratio varied from 1 : 1.3 to 1 : 1.9. The structure

and purity of the isolated products were confirmed by their elemental compositions and IR, NMR, and mass spectra.

By computer simulation we determined the most stable conformations of new tricyclic spiro compounds **VIa** and **VIb**. The latter possesses a higher energy, and it is stabilized via intramolecular hydrogen bond.



Composition of the reaction mixture, conversion, and selectivity in the cyclization of spirobicyclic alcohols

Products	Composition of the reaction mixture, %			Conversion, %	Selectivity for ethers, %
	9.8 ^a	43.5 ^b	46.7 ^c		
Va+Vb	9.8 ^a	43.5 ^b	46.7 ^c	83.7	86.7
VIa+VIb	9.4 ^a	58.2 ^b	32.4 ^c	87.9	85.4

^a Bicyclic alcohols.

^b Tricyclic spiro compounds.

^c Other products.

The products were tested at the Research Institute of Synthetic and Natural Fragrant Substances (Plovdiv, Bulgaria); the results showed that isomer mixtures **Va/Vb**

and **VIa**/**VIb** possess a wood odor and that they can be recommended for use as fragrant components in perfume compositions.

EXPERIMENTAL

The IR spectra were recorded on a Specord M-80 spectrometer from samples prepared as thin films. The ^1H NMR spectra were measured on a JEOL spectrometer (Fourier transform, 270 MHz) from solutions in CDCl_3 using TMS as reference. Gas chromatographic–mass spectrometric analysis was performed on a Hewlett–Packard HP 5970B mass-selective detector coupled with an HP 5890 Series II gas chromatograph (25 000 \times 0.2-mm capillary column, 95% of methylsilicone + 5% of methylphenylsilicone; oven temperature 160°C; carrier gas helium, flow rate 1.2 ml/min). Vacuum distillation was performed on an HMS-500 setup (Donau Trading). Kieselgel 100 silica gel (Fluka) was used for column chromatography with hexane, methylene chloride, and methanol as eluents.

3,3,7,8-Tetramethyl-2-oxatricyclo[8.4.0^{1,10}.0^{5,10}]-tetradec-6-ene (VIa) and 6,7-dimethyl-3-(1-methylethyl)-2-oxatricyclo[6.4.1^{4,8}.0^{1,8}]dodec-5-ene (VIb) (mixture of isomers). A mixture of 2- and 5-(2-methyl-1-propenyl)-3-cyclohexene-1-spiro-1'-cyclohexan-2'-ols (**IVa**/**IVb**), 49.7 g (0.2 mol), was added under stirring over a period of 15 min to a mixture prepared from 120 g of 85% orthophosphoric acid and 120 ml of toluene, heated to 110°C. The mixture was heated for 6 h under reflux and washed in succession with 10% aqueous sodium chloride (300 ml), 10% aqueous sodium carbonate (300 ml), and 10% aqueous sodium chloride again. The solvent was distilled off, and the residue was subjected to fractional distillation in a high vacuum, a fraction boiling in the range 108–116°C (0.01–0.02 hPa) being collected. Yield 37.3 g. IR spectrum, ν , cm^{-1} : 1180 (C–O, C–O–C); 1665 (C=C_{ring}); 1140, 1170 [C(CH₃)₂]. ^1H NMR spectrum (CDCl_3), δ , ppm: 0.96–1.07 m (3H, CHCH₃), 1.19–1.24 m [6H, CH(CH₃)₂], 1.27–1.34 (3H, HC=CCH₃), 1.54–1.71 m (10H, CH₂, ring), 3.64–3.73 s (2H, CHOCH), 5.17 (1H, HC=CCH₃). Mass spectrum,

m/z (I_{rel} , %): 248 [M]⁺ (70), 205 [M – Pr]⁺ (18), 175 [M – C₅H₁₃]⁺ (100), 159 [M – C₅H₁₃O]⁺ (39), 119 [M – C₉H₁₁]⁺ (61), 91 [M – C₁₁H₉O]⁺ (93), 79 [M – C₁₁H₂₁O]⁺ (57), 41 [M – C₁₄H₂₃O]⁺ (89). Found, %: C 74.3; H 10.1. C₁₇H₂₈O. Calculated, %: C 75.1; H 10.5.

3,3,7,8-Tetramethyl-2-oxatricyclo[8.3.0^{1,10}.0^{5,10}]-tridec-6-ene (Va) and 6,7-dimethyl-3-(1-methylethyl)-2-oxatricyclo[6.3.1^{4,8}.0^{1,8}]undec-5-ene (Vb) (mixture of isomers) were synthesized in a similar way with the difference that 46.9 g (0.2 mol) of a mixture of 2- and 5-(2-methyl-1-propenyl)-3-cyclohexene-1-spiro-1'-cyclopentan-2'-ols (**IIIa**/**IIIb**) was added first. A fraction boiling at 101–108°C (0.01–0.02 hPa) was collected. Yield 34.0 g. IR spectrum, ν , cm^{-1} : 1180 (C–O, C–O–C); 1665 (C=C_{ring}); 1140, 1170 [C(CH₃)₂]. ^1H NMR spectrum (CDCl_3), δ , ppm: 0.98–1.01 m (3H, CHCH₃), 1.09–1.23 m [6H, CH(CH₃)₂], 1.27–1.34 (3H, HC=CCH₃), 1.59–1.70 m (8H, CH₂, ring), 3.61–3.72 s (2H, CHOCH), 5.25 (1H, HC=CCH₃). Mass spectrum, m/z (I_{rel} , %): 234 [M]⁺ (29), 201 [M – Et]⁺ (5), 178 [M – C₄H₈]⁺ (69), 145 [M – C₅H₁₃O]⁺ (84), 122 [M – C₈H₁₆]⁺ (100), 91 [M – C₁₁H₁₁]⁺ (47), 77 [M – C₁₁H₉O]⁺ (27), 41 [M – C₁₃H₂₁O]⁺ (33). Found, %: C 74.8; H 10.8. C₁₆H₂₆O. Calculated, %: C 75.5; H 11.1.

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