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Synthesis and Isomerization
of Tricyclo[7.3.1.0²,⁷]tridecen-13-ones*

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Abstract—Dehydration of 2-hydroxy-8-R-tricyclo[7.3.1.0²,⁷]tridecan-13-ones (R = H, Me, Ph) effected by various reagents provided 8-R-tricyclo[7.3.1.0²,⁷]tridecen-13-ones with different positions of the double bond. In the presence of phosphoric acid arise isomers with the double bond in 2(3) position, a mixture of hydrochloric and acetic acid primarily affords isomers with the double bond in 2(7) position that further migrates into 7(8) position at R = Me, Ph.

From the plants of *Meliaceae* family were isolated so-called limonoids (mexicanolide, sweetenin etc.) [1]. The basic part of their structure is a tricyclo-[7.3.1.0²,⁷]tridecan-13-one system (**I**) where in the positions *2(3)*, *2(7)* or *6(7)* can be located a double bond.
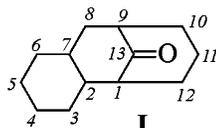
As a convenient model for the study of specific features inherent to structure **I** may serve the products of intramolecular condensation of alicyclic 1,5-di-
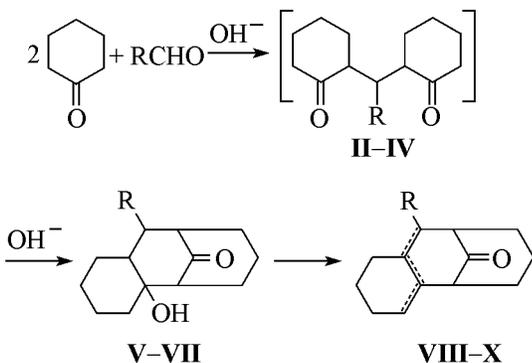
R = H (**II, V, VIII**), CH₃ (**III, VI, IX**), C₆H₅ (**IV, VII, X**).

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ketones **II–IV**, ketols **V–VII**, and the products of dehydration thereof **VIII–X**. The first representatives of these compounds were prepared by condensation of cyclohexanone with aldehydes [2].

Previously it was supposed a priori that the double bond in compounds **VIII–X** was located in *2(7)* position [3].

The problem of the double bond location was first considered in [4], and it was shown that at R = CH₃ the double bond might be both in *2(7)* and *7(8)* positions. It was shown in [5] that the position of he double bond depended on the dehydration agent used in the reaction with ketol. The problem of ketols **V–VII** dehydration was treated in more detail by Cocker and Shannon [6]. They concluded that dehydration by different reagents gave rise to unsaturated ketones with dissimilar location of the double bond. The possibility of the double bond migration in the unsaturated ketones remained unclear.

We found that dehydration of ketols **V–VII** by acidic reagents afforded mixtures of unsaturated ketones with predominant content of some component (Table 1). We carried out dehydration of 2-hydroxy-8-R-tricyclo[7.3.1.0²,⁷]tridecan-13-ones in the presence of phosphoric acid. In this case ketol **V** yielded a single enone **VIIIa** that we separated in a considerably high yield (70%), ketol **VI** afforded a mixture of compounds **IXa** and **IXb** in 7:2 ratio, and ketol **VII** gave rise to a mixture of compounds **Xa** and **Xb**. No migration of double bonds in compounds **VIIIa–Xb** occurred under the condition of synthesis.

At the use as dehydrating agent of a mixture of hydrochloric and acetic acids [3] arise compounds
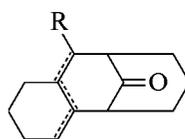
VIIIb–Xb. Unsubstituted ketol **V** afforded compound **VIIIb**; we did not detect its isomer **VIIIc**. In the course of time the double bond in compounds **IXb, Xb** gradually migrated into *7(8)* position providing compounds **IXc, Xc**. In dehydration of ketol **VI** at 60°C in 30 min in the mixture appeared only unsaturated ketone **IXb**, whereas after 3 h the ratio of compounds **IXb : IXc** was 3 : 1. In reaction of ketol **VII** with the mixture HCl–CH$_3$COOH we failed to isolate compound **Xb**, and its presence in the reaction mixture within the initial 3 h of reaction was only detected by GLC and ^{1}H NMR spectroscopy. Besides was obtained a product of hydroxy group replacement by halogen **XI**.
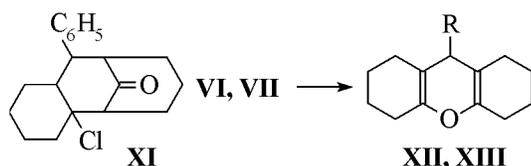
R = CH$_3$ (**XII**), C$_6$H$_5$ (**XIII**).

At the attempt to carry out the dehydration of ketols **VI, VII** by treating with gaseous hydrogen chloride, *p*-toluenesulfonic acid, or iodine in toluene we obtained respectively 9-R-octahydroxanthenes **XII, XIII**. The dehydration products were characterized by IR, ^{1}H and ^{13}C NMR, and mass spectra. When the spectra were registered from mixtures the assignment

Table 1. The ratio of dehydration products **IXa–c**, **Xa–c** from ketols **VI, VII** depending on conditions of the reaction[a]

Reaction time, h	Ketol **VI** in a mixture HCl–CH$_3$COOH			Ketol **VII** in phosphoric acid		
	IXa	**IXb**	**IXc**	**Xa**	**Xb**	**Xc**
0.25	1.0	5.0	0	–	–	–
0.5	1.0	5.0	0	–	–	–
1.0	1.0	4.7	0.4	1.0	0.9	0.9
1.5	1.0	4.3	0.6	1.0	0.8	0.9
2.0	1.0	3.6	0.9	1.0	0.6	0.95
2.5	1.0	3.5	1.0	1.0	0.35	0.97
3.0	–	–	–	1.0	0.15	1.0
3.5	–	–	–	1.0	0.07	0.97
4.0	–	–	–	1.0	0.03	0.98

[a] Intensity of chromatographic peaks of compounds **IXa** and **Xa** were taken equal to unity.

of signals was performed taking into account the GLC data indicating the relative content of compounds in the mixture.

In the IR spectra of compounds **VIII–X** appear the absorption bands of C=O groups at 1711–1713 cm^{-1}. A weak absorption band at 1653 cm^{-1} (C=C) was observed only in the spectra of compounds **VIII, Xa**, in the spectra of compounds with tetrasubstituted double bonds this absorption band was not present.

Table 2. ^{13}C NMR spectra of compounds **VIII–X**

Compd. no.	R	C^1	C^2	C^3	C^4	C^5	C^6	C^7	C^8	C^9	C^{10}	C^{11}	C^{12}	C^{13}	δ_CR
VIIIa	H	48.91	124.45	118.25	28.23	27.90	25.05	42.29	41.90	47.67	35.25	24.77	34.29	213.78	–
IXa	CH$_3$	53.57	137.30	124.76	30.06	28.74	27.36	51.62	36.29	53.40	35.73	26.92	31.49	216.76	17.51
Xa	C$_6$H$_5$	55.07	140.64	125.77	29.45	25.66	22.19	53.89	38.84	58.40	37.25	21.12	30.40	217.26	126.75, 128.10, 128.60, 140.45
VIIIb	H	52.10	128.60	29.00	23.72	23.31	28.80	131.30	41.30	45.50	36.50	19.00	32.00	214.80	–
IXb	CH$_3$	52.50	127.81	28.38	22.76	22.76	27.02	134.62	41.95	50.76	31.38	17.92	29.77	217.19	14.68
IXc	CH$_3$							137.80	122.80					216.44	
Xc	C$_6$H$_5$	53.20	51.07	31.24	27.61	26.60	31.46	140.65	128.50	53.31	36.38	17.40	35.68	214.70	127.9, 128.40, 140.4

The band at 3060 cm^{-1} in the spectrum of compound **VIIIa** may be attributed to the $=C-H$ group; in the spectrum of compound **Xa** the band is overlapped by the absorption of C–H bonds of the benzene ring.

In the ^{1}H NMR spectra the signals of vinyl protons appear at δ 5.27 (compound **VIIIa**, J_1 6.0, J_2 2.0 Hz), 5.46 (compound **IXa**, J_1 6.1, J_2 2.5 Hz), and 5.60 ppm [compound **Xa**, J_1 *6.3, J_2 3.5* Hz). In the spectra of compounds with tetrasubstituted double bonds the signals of vinyl protons are naturally lacking.

The ^{13}C NMR spectra of compounds **VIII–X** are given in Table 2. The signals were assigned taking into account the published data [6, 7].

Apparently the dissimilar dehydration results at the use of different catalysts are due to different reaction mechanisms.

Since we did not study the reaction mechanisms we can only make some suggestions. Note that only at the C^3 carbon close to the C^2–OH group is present an equatorial hydrogen atom. This fact provides a possibility of formation of a cyclic transition state with participation of phosphoric acid hydroxy group or B–F group as occurs under the other conditions [6]. This transition state is a precursor of a compound with a double bond in *2(3)* position. Dehydration effected by hydrochloric acid presumably proceeds through a carbocation at the C^2 atom that stabilizes by proton ejection from the C^7 position (process with thermodynamic control). The compounds formed possess a tetrasubstituted double bond. In compounds **IX, X** the double bond is tetrasubstituted both in position *2(7)* and *7(8)* providing a possibility of its migration. Pyran formation apparently is due to retroaldol cleavage of ketols.

EXPERIMENTAL

^{1}H and ^{13} NMR spectra were recorded on spectrometer Bruker WM 250 from solutions in deuterochloroform, internal reference TMS. The identification and assignment of peaks was carried out with the help of *J*-modulation and off-resonance procedure. IR spectra were registered from thin films or chloroform solutions on Perkin-Elmer Spectrum BX 2 instrument. Chromatograms of substances and their mass spectra were measured on HP 5972 MSD/HP instrument. The *m/z* values for the molecular ions of all compounds synthesized corresponded to the calculated molecular weights. The reactions were monitored by GLC on JanacoG-1800 device equipped with a flame-ionization detector, CPB-5 column, even at 200–250°C,carrier gas helium. The sampling was

performed every 30 min, sample of 0.3 ml was treated with 25% ammonia solution till neutral, then several drops of water were added, the reaction products were extracted into ether, the extract was dried with magnesium sulfate and charged into chromatograph.

Tricyclo[7.3.1.0^{2,7}]tridec-2-en-13-one (VIIIa). A mixture of 5.1 g of ketol **V** and 2 ml of 85% phosphoric acid was stirred at 60°C for 5 h. The viscous reaction mixture was diluted with water and treated with 25% ammonia solution till neutral. The organic compounds were extracted into ether, the extract was dried, and on removing ether the residue was distilled in a vacuum. The fraction boiling at 145–147°C (4 mm Hg) was collected. We obtained 3.3 g (70%) of oily compound **VIIIa** that crystallized on storage. At similar procedure performed with ketol **VI** we obtained a mixture of compounds **IXa** and **IXb** in 7:2 ratio.

Tricyclo[7.3.1.0^{2,7}]tridec-2(7)-en-13-one (VIIIb) [3]. A mixture of 5.7 g of ketol **V**, 3 ml of hydrochloric and 3 ml of acetic acid was stirred at 60°C for 40 min and then poured into 12 ml of 25% water solution of ammonia. The reaction product was extracted into ether, the extract was washed with water, dried on magnesium sulfate, the ether was evaporated, and the residue was distilled in a vacuum at 129–130°C (4 mm Hg). We obtained 4.1 g (78%) of compound **VIIIb**. GLC showed the presence of a single substance.

A similar treatment of ketol **VI** afforded a mixture of compounds **IXa, IXb**, and **IXc** in 1.1:3.5:1 ratio.

8-Phenyltricyclo[7.3.1.0^{2,7}]tridec-2-en-13-one (Xa) and 8-phenyltricyclo[7.3.1.0^{2,7}]tridec-7-en-13-one (Xc). A mixture of 11.5 g of ketol **VII** and 4 ml of 85% phosphoric acid was stirred for 2 h at 100°C. The solid reaction product was separated from the liquid, washed with water, dried, and boiled with hexane. The hot solution was filtered; on cooling separated crystals of compound **Xa**, yield 3.2 g, mp 126–128°C (publ. 127–128.5°C [6]). The mother liquor was evaporated, the viscous residue was ground with ethyl ether to obtain more 0.5 g of crystalline compound **Xa**, overall yield 31%. The ether was evaporated, and the residue was distilled in a vacuum, collecting the fraction of bp 291–203°C (3 mm Hg). We obtained 4.1 g (38%) of compound **Xc**, mp 102–104°C (from petroleum ether).

8-Phenyltricyclo[7.3.1.0^{2,7}]tridec-7(8)-en-13-one (Xc). A mixture of 10 g of ketol **VII**, 10 ml of hydrochloric and 10 ml of acetic acid was stirred at

60°C for 2 h. Then the reaction mixture was neutralized with 25% water solution of ammonia. The solidified organic substances were separated and dissolved in ether. The ether solution was washed with water and stored in refrigerator for 24 h; therewith separated 6 g (56%) of compound **XI**, after recrystallization from ethanol–acetone mixture mp 166–170°C (decomp.) (publ. 166–171°C [3]). The ether filtrate after separation of chloroketone **XI** was dried with magnesium sulfate, the ether was evaporated, and the residue was ground with water. We obtained 4 g (43%) of compound **Xc** with a little chloroketone **XI** impurity. On recrystallization from petroleum ether we obtained 2.9 g of compound **Xc**, mp 102–104°C. IR spectrum: 1711 cm⁻¹ ($C=O$). Found, %: C 85.57, 85.80; H 8.21, 8.55. $C_{19}H_{22}O$. Calculated, %: C 85.66; H 8.32.

9-Methyl-2,3,4,5,6,7,8,9-octahydro-1*H*-xanthene (XII). (a) In a flask equipped with a Dean–Stark trap was mixed 10 g of ketol **VI** and 95 ml of toluene. The mixture was saturated with hydrogen chloride and boiled for 2 h in a constant flow of HCl. On cooling the precipitate of the unreacted ketol was separated, the filtrate was treated with a saturated sodium carbonate solution, the water layer was separated, and it was extracted with toluene. The extract was combined with the organic layer, dried with magnesium sulfate, evaporated, and the residue was subjected to a fractional distillation in a vacuum to collect the fraction of bp 120–128°C (3 mm Hg). We obtained 3.25 g (34%) of compound **XII**.

(b) In a flask equipped with a Dean–Stark trap was boiled for 20 h a mixture of 20 g of ketol **VI**, 60 ml of toluene, and 0.005 g of iodine. On cooling the mixture was filtered to separate the unreacted ketol, toluene was distilled off from the filtrate, and the residue was distilled in a vacuum. We obtained 8.8 g (43%) of compound **XII**, bp 140–145°C (7 mm Hg).

(c) In a flask equipped with a Dean–Stark trap was boiled for 1 h a mixture of 10 g of ketol **VI**, 50 ml of toluene, and 0.7 g of p-toluenesulfonic acid. The amount of separated water was consistent with calculations. On cooling the toluene solution was treated with saturated sodium carbonate solution, dried with magnesium sulfate, toluene was distilled off, and the residue was distilled in a vacuum. We obtained 6.95 g (83%) of compound **XII**, bp 132°C (8 mm Hg), n_D^{20} 1.5261. IR spectrum: 1714, 1675 cm⁻¹ (bands of

moderate intensity, $C=C-O-C=C$). Found, %: C 82.35, 82.39; H 9.59, 9.68. $C_{14}H_{20}O$. Calculated, %: C 82.35; H 9.80.

9-Phenyl-2,3,4,5,6,7,8,9-octahydro-1*H*-xanthene (XIII) was obtained from ketol **VII** along procedure a in 37% yield, mp 94–96°C (96.5–97.5°C [8]).

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