THE STRUCTURE OF ACROPTILIN – A SESQUITERPENE LACTONE FROM Acroptilon repens

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UDC 615.256.54.011.5

We have previously [1-5] reported the isolation from the leaves and flower heads of Acroptilon repens L. (DC.) and Centaurea hyrcanica Bornm. of three new sesquiterpene lactones: repin, acroptilin, and hyrcanin.

The present paper gives the results of a study of the structure of acroptilin, which has the composition $C_{19}H_{23}O_7Cl$, mp 196-198°C (from ethanol), $[\alpha]_D^{20}$ +92.3° (c 0.68; ethanol). Initially the composition $C_{21}H_{24}O_9$ was proposed for acroptilin, but it follows from the ^{13}C spectrum taken subsequently (Fig. 1a) that there are 19 carbon atoms in the acroptilin molecule. In addition, acroptilin contains an atom of chlorine, which was shown by a qualitative reaction, by the determination of chlorine using Schoeniger's method, and also by a repeated determination of carbon and hydrogen with the trapping of the halogen by silver.*

Acroptilin forms a monoacetate (II) with the composition $C_{21}H_{25}O_8Cl$, mp 181-182.5°C, and a vitreous diacetate (III), $C_{23}H_{27}O_9Cl$. The hydrogenation of acroptilin over PtO_2 in ethanol and acetic acid takes place with the consumption of 2 and 2.5 moles of hydrogen, respectively.

The reduction of the hydrogenation product (IV) with lithium tetrahydroaluminate led to a glycol $C_{15}H_{28}O_5$ (V), and the dehydrogenation of the latter gave chamazulene (VI).

The alkaline hydrolysis of acroptilin with subsequent acidification by H_2SO_4 formed a lactone with the composition $C_{15}H_{18}O_5$ (VII), giving an acetate $C_{19}H_{22}O_7$ (VIII). The acidic part of the hydrolyzate yielded acetic acid (IX) and an acid (X) with the composition $C_4H_7O_3Cl$, mp 105-106°C (Fig. 1c).

The hydroxylactone (VII) was identical with the dihydroxylactone obtained by the hydrolysis of repin (XI), and their acetates were also identical. Consequently, acroptilin differs from repin only by an acyl residue. The NMR spectra of acroptilin [4] and of repin are similar, but the spectrum of acroptilin lacks a pair of doublets corresponding to the signals of epoxide protons in an acyl group while having a sharp quartet forming the signal of a CH_2Cl group (Table 1).

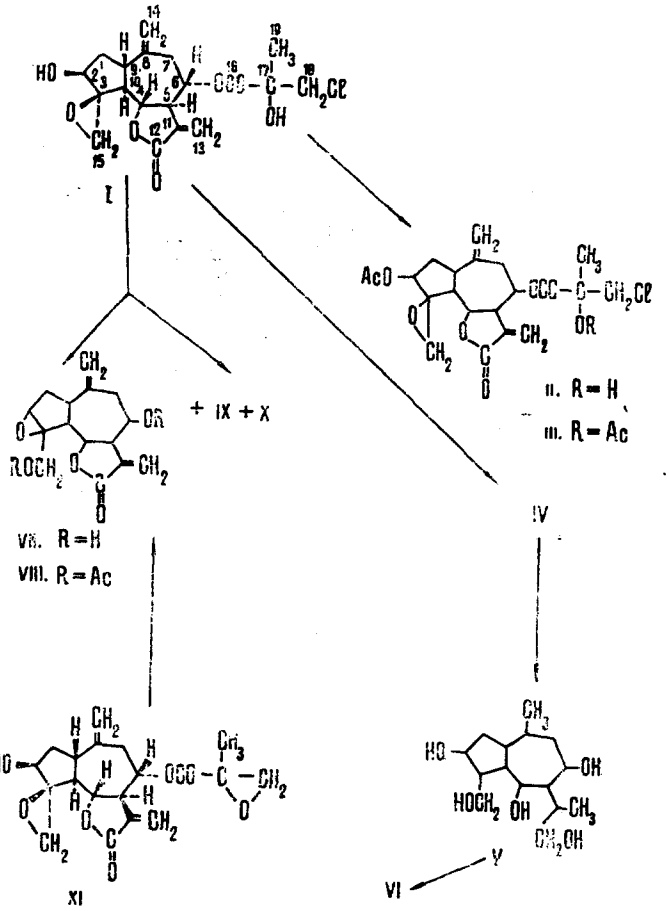
The facts given permit structure (I) to be proposed for acroptilin.

EXPERIMENTAL

The substances isolated were recrystallized to constant melting point and were dried in a vacuum pistol (2-5 mm Hg) over P_2O_5 with heating by ethanol vapor. The melting points were determined on a Kofler instrument. The IR spectra were taken on a UR-10 spectrometer in paraffin oil, the UV spectra on a Hitachi EP-3T instrument in 95% ethanol, the NMR spectra on a Varian HA-100 instrument, the mass spectra on an MKh-1303 spectrometer, and the ^{13}C spectrum on a JNM PS-100 spectrometer with a JNM PFT-100 Fourier transformer.

*The previous results for the carbon and hydrogen contents were obtained without correcting for the halogen, and therefore the carbon content was 2.8-3% too high.

All-Union Scientific-Research Institute of Medicinal Plants. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 161-167, March-April, 1973. Original article submitted June 5, 1972.



Scheme of the reactions of acroptilin

Thin-layer chromatography (TLC) was performed on neutral Al_2O_3 (activity grade IV) in the benzene–methanol (9 : 1) system with a 0.5% solution of $KMnO_4$ in 0.5% H_2SO_4 as the chromogenic reagent. The microanalyses for C, H, and Cl corresponded to the calculated figures.

Acroptilin, $C_{19}H_{23}O_7Cl$, mp 196-198°C (from ethanol), $[\alpha]_D^{20}$ +92.3° (c 0.68; ethanol).

Acetylation of Acroptilin. Preparation of the Monoacetate (II) and the Diacetate (III). A mixture of 0.5 g of acroptilin, 8 ml of pyridine, and 5 ml of acetic anhydride was left at room temperature for 5 h and was then diluted with water (1 : 5) and extracted six times with chloroform. The chlorform extract was washed with a 5% solution of HCl and with water to neutrality, and after the solvent had been driven off 0.2 g of a colorless vitreous substance deposited giving two spots on TLC, with R_f 0.77 and 0.44. The reaction product was chromatographed on neutral Al_2O_3 (activity grade IV), being eluted with benzene, benzene–ether, and ether. The benzene fractions gave 0.03 g of a colorless vitreous substance with the composition $C_{23}H_{27}O_9Cl$ (III), R_f 0.8. IR spectrum, ν_{max}, cm^{-1}: 1780-1740, 1250 (γ-lactone and $-OCOCH_3$), 1660 and 1640 (C=C).

The ethereal fractions yielded 0.05 g of a colorless crystalline substance having the composition $C_{21}H_{25}O_8Cl$ (II) with mp 181-182.5°C; R_f 0.45. IR spectrum, ν_{max}, cm^{-1}: 3550 (OH group), 1775 (C=O of a γ-lactone), 1745 and 1245 ($-OCOCH_3$), 1670 and 1645 (C=C).

Hydrolysis of Acroptilin. Production of the Hydroxylactone (VII) and the Acids (IX) and (X). A. A solution of 2 g of acroptilin in 100 ml of 4% KOH was left at room temperature for a day. The reaction mixture was acidified with 10% H_2SO_4 to pH 1 and was extracted 15 times with ethyl acetate, and the extract was washed with 5% $NaHCO_3$ solution and with water to neutrality. The solvent was evaporated off, and 0.8 g of a crystalline substance deposited which when subjected to TLC on silica gel gave two spots with R_f 0.32 and 0.28 (weak spot). After two recrystallizations from ethyl acetate, colorless prisms were obtained with the composition $C_{15}H_{18}O_5$, mp 162-164°C, R_f 0.35; yield 40%. IR spectrum, ν_{max}, cm^{-1}: 3380, 3440 (OH group), 1770 (γ-lactone), 1650 (C=C).

TABLE 1. Chemical Shifts and Coupling Constants of the Protons of Acroptilin and Its Derivatives, ppm (J in Hz)

Compound	Protons attached to carbon atoms								
	H_2	H_4	H_5	H_6	H_7	$H_{7'}$	H_{10}	H_{13}	$H_{13'}$
I	q 4,23 $J_{1,2} = 4,8$ $J_{1',2} = 7,2$	q 4,96 $J_{4,5} = 8,8$ $J_{4,10} = 11,2$	m 3,14 $J_{5,6} = 9,0$	oct 5,35 $J_{6,7} = 5,8$ $J_{6,7} = 2,8$	q 2,80 $J_{6,7} = 5,8$ $J_{7',7} = 15,0$	q 2,52 $J_{6,7'} = 2,8$ $J_{7',7} = 15$	q 2,19 $J_{4,10} = 11,2$ $J_{9,10} = 8,8$	d 5,79 $J_{13,5} = 3,5$	d 6,20 $J_{13',5} = 4$
II	q 4,91 $J_{2,1} = 4,8$ $J_{2,1'} = 7,2$	q 4,41 $J_{4,10} = 11,5$ $J_{4,5} = 8,5$		m 5,21				d 5,54 $J_{13,5} = 3,5$	d 6,20 $J_{13',5} = 4,0$
III	q 4,81 $J_{2,1} = 4,5$ $J_{2,1'} = 7,5$	q 4,35 $J_{4,10} = 11,5$ $J_{4,4} = 8,5$		m 5,09				d 5,71 $J_{13,5} = 3,5$	d 6,13 $J_{13',5} = 4,0$
VII	s 3,77	t 4,30 $J_{4,10} = 10,0$ $J_{4,5} = 10,0$	m 3,03 $J_{5,4} = 10,0$ $J_{5,6} = 10,0$	m 3,86 $J_{6,7} = 5,5$ $J_{6,7'} = 9,0$ $J_{5,6} = 10,0$	q 2,90 $J_{6,7} = 5,5$ $J_{7,7'} = 12,5$	q 2,23 $J_{6,7'} = 9,0$ $J_{7,7'} = 12,5$	t 2,74 $J_{10,4} = 10,0$ $J_{9,10} = 10,0$	q 6,37 $J_{13,5} = 3,2$ $J_{13,13'} = 1,8$	q 6,59 $J_{13',5} = 3,2$ $J_{13,13'} = 1,8$
VIII	s 3,51	t 4,30 $J_{4,10} = 10$ $J_{4,5} = 10,0$	m 3,07	oct 4,84 $J_{6,7} = 5,5$ $J_{6,7'} = 9,0$ $J_{5,6} = 10,0$	q 2,81 $J_{6,7} = 5,5$ $J_{7,7'} = 12,0$	q 2,14 $J_{6,7'} = 9,0$ $J_{7',7} = 12,0$	t 2,63 $J_{10,4} = 10$ $J_{9,10} = 10$	d 5,74 $J_{13,5} = J_{3,5}$	d 6,25 $J_{13',5} = J_{4,0}$
X									

TABLE 1 (continued)

Compound	Protons attached to carbon atoms							Signals of other groups
	H_{14}	$H_{14'}$	H_{15}	$H_{15'}$	H_{18}	$H_{18'}$	$H_{19, 19', 19''}$	
I	d 5,13 $J_{14,14'} = 1,5$	d 5,18 $J_{14'14} = 1,5$	d 3,21 $J_{15,15'} = 4,5$	d 3,41 $J_{15',15} = 4,5$	d 3,95 $J_{18,18'} = 11,0$	d 4,09 $J_{18,18'} = 11,0$	s 1,70	
II	s 5,09	s 5,17	d 3,03 $J_{15',15} = 4,3$	d 3,27 $J_{15,15'} = 4,3$	d 3,59 $J_{18,18'} = 12,0$	d 3,84 $J_{18,18'} = 12,0$	s 1,50	s 2,0 CH_3COO-
III	s 5,01	s 5,15	d 2,99 $J_{15,15'} = 4,5$	d 3,20 $J_{15',15} = 4,5$	d 3,73 $J_{18,18'} = 12,0$	d 4,01 $J_{18',18} = 12,0$	s 1,62	s 2,05 s 1,99 $2CH_3COO$
VII	br. s 5,01	br. s 5,12	d 4,18 $J_{15,15} = 12,0$	d 4,36 $J_{15',15} = 12,0$				
VIII	br. s 5,13	br. s 5,14	d 4,37 $J = 12,0$	d 4,55 $J = 12,0$				s 2,12 s 2,14 $2CH_3COO$
X					d 3,55 $J = 11,0$	d 3,79 $J = 11,0$	s 1,50	

Notes. The spectra of (I) and (VII) were taken in pyridine and those of (II, III, VIII, and X) in $CDCl_3$ relative to TMS [the spectra of (II) and (III) relative to HMDS]; d – doublet; t – triplet; m – multiplet; oct – octet; sex – sextet; s – singlet; br.s – broadened singlet; q – quartet. The assignment of the signals was made with the aid of double resonance and the INDOR method.

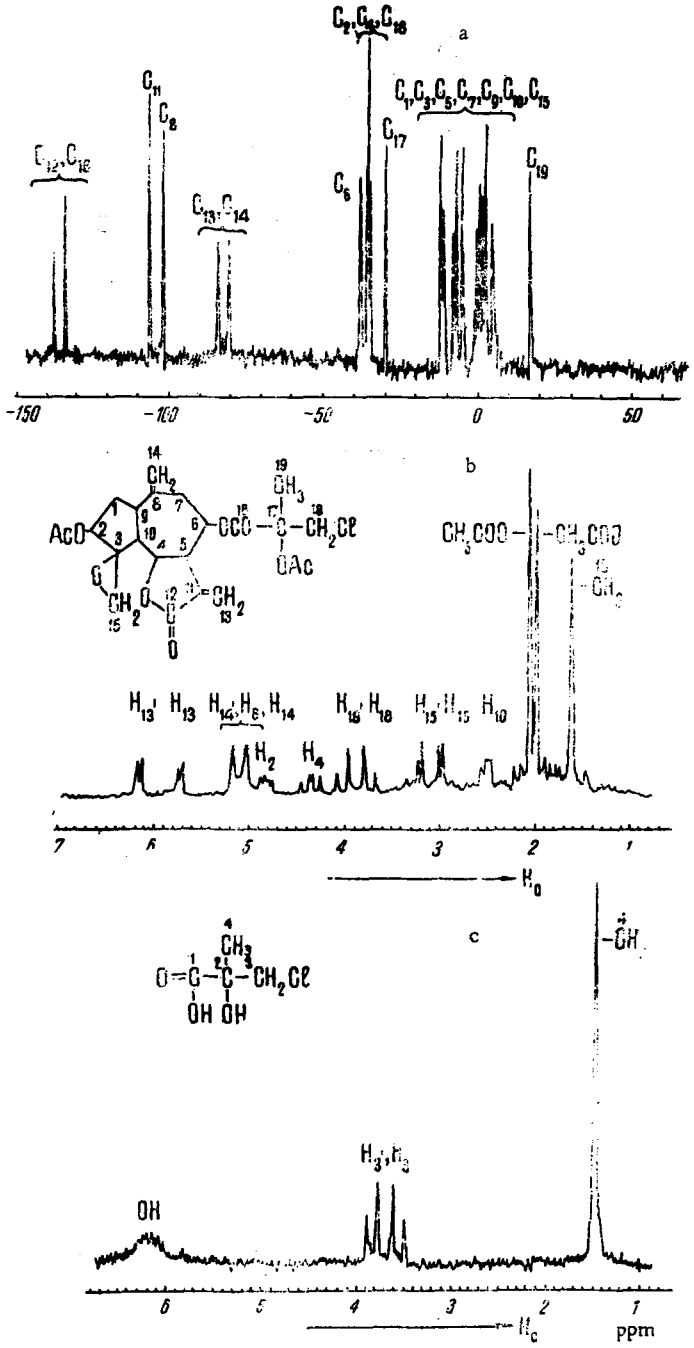


Fig. 1. ^{13}C NMR spectra of acroptilin (I) (DMSO-d_6) (a), of diacetylacroptilin (III) ($CDCl_3$) (b), and of the acid (X) ($CDCl_3$) (c).

B. Production of the Acids. A solution of 1 g of acroptilin in 40 ml of 4% KOH solution was left at room temperature for a day and was then acidified with a 10% solution of HCl to pH 1 and the reaction products were extracted 15 times with ether. The ethereal extract was washed with 5% Na_2CO_3 solution. The sodium carbonate solution was acidified with 10% HCl to pH 1 and was extracted 15 times with ether. The first extract was subjected to gas-liquid chromatography, which showed the presence of acetic acid (IX). The remainder of the ethereal extract was washed with water and the solvent was evaporated at room temperature without vacuum to a viscous slightly yellowish liquid in which, on standing, crystals formed with the composition $C_4H_7O_3Cl$ (X), mp 105-106°C.

Acetylation of the Hydroxylactone (VII). Production of (IX). A mixture of 0.5 g of the hydroxylactone (VII) with mp 162-164°C, 2 ml of acetic anhydride, and 4 ml of pyridine was left at room temperature for

18 h and was then diluted with water (1 : 5) and the reaction product was extracted with chloroform. The chloroform extract was washed with 5% HCl and with water to neutrality, and the solvent was distilled off. The residue consisted of 0.25 g of a substance which, after recrystallization from ethanol, had the composition $C_{19}H_{22}O_7$ (VIII), mp 112-113°C, R_f 0.65. IR spectrum, ν_{max}, cm^{-1}: 1770 (γ-lactone), 1745 and 1250 ($-OCOCH_3$), 1660 and 1650 (C=C).

SUMMARY

Structure (I) is proposed for the new sesquiterpene lactone acroptilin isolated from Acroptilon repens L. (DC.) and Centaurea hyrcanica Bornm. on the basis of the results of reactions performed and an interpretation of IR, UV, NMR, and mass spectra.

LITERATURE CITED

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