SUMMARY

Simple conditions have been developed for the effective synthesis of 7-hydroxy- and 5,7-dihydroxyisoflavones and also of 3-aryloxy-7-hydroxychromones. The advantages and disadvantages of alternative pathways of the synthesis of the compounds are discussed. A method is proposed for the synthesis of isoflavones and 3-aryloxychromones which permits a considerable simplification of the preparation of compounds of these series in the necessary amounts.

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NATURAL ANTIOXIDANTS.

FURANOEREMOPHILANES FROM Cacalia ROOTS

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Sesquiterpene compounds of the furanoeremophilane series have been isolated from extracts of the roots of Cacalia sp. growing in the Soviet Far East. The presence of antioxidant and antiradical activities in two representatives of the series has been established.

The present paper, which continues a cycle of investigations directed to the search and characterization of antioxidants from plants of the Far East [1-5] reports the results of the isolation of nonpolar antioxidants and the determination of their structures.

Wide screening among herbaceous plants has revealed a number of taxons producing such compounds. Included among them were several species belonging to the genus Cacalia, family Asteraceae.

Plants of the genus Cacalia have been studied chemically very thoroughly. Romo et al. [6, 7] were first to isolate from the roots of the shrub C. decomposita A. Gray a group of sesquiterpene compounds of the furanoeremophilane series which they called cacalol, cacalone, and decompostin. Later, British and Japanese investigators studying seven representatives of the genus Cacalia isolated from the roots more than 30 compounds that were derivatives of cacalol, cacalone, and decompostin [8-15].

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TABLE 1. Chemical Composition of the Roots of Cacalia sp., %

Compound	C. auriculata	C. robusta	C. hastata	C. aconitifolia
o-Methylcacaloene	—	0,020	0,018	—
Cacalol acetate	—	0,006	0,016	—
Cacalol	0,005	—	—	—
6β-Propionyloxy-1,10-furanoeremophil-9-one	0,079	0,038	0,017	—
Cacalone	0,002	—	—	—
β -Sitosterol	—	—	—	0,047
Oleanolic acid acetate	—	—	—	0,035
Ethyl caffeate*	0,036	0,002	0,017	0,002
Caffeic acid*	0,009	0,002	0,027	0,003
Caffeoyl β-glucopyranoside*	0,019	0,012	0,050	0,007

*Isolated from an ethyl acetate extract.

We have studied extracts of the roots of four species of Cacalia growing in the Far East: C. auriculata DC., C. hastata L., C. robusta Tolm., and C. aconitifolia Bunge. From hexane extracts of C. auriculata (Table 1) we have isolated cacalol, cacalone, and 6β-propionyloxy-1,10-furanoeremophil-9-one, which has been detected previously in the roots of C. decomposita [6, 7] and C. adenostyloides [15].

Hexane extracts from C. robusta and C. hastata proved to be qualitatively identical.

A hexane extract of Cacalia aconitifolia proved to be completely different. No compounds of the furanoeremophilane series were detected in it. Column and preparative chromatography with subsequent mass spectroscopy of the fractions showed only the presence of β-sitosterol and of oleanolic acid acetate, which were identified by comparison (TLC, melting points) with authentic samples.

Thus, the hypotheses put forward previously that from their botanical characteristics the species C. aconitifolia cannot be assigned to the genus Cacalia [16, 17] are confirmed by the chemical facts given above, although ethyl acetate extracts of all the plants studied proved to be identical in qualitative composition and contained among the main phenolic components caffeic acid and its derivatives.

Below, we give the activities of the furanoeremophilanes isolated from the roots of Cacalia sp. (a – at an inhibitor concentration of 0.03 mg/ml; b – 0.10 mg/ml):

Compound	Antioxidant activity (in comparison with Ionol)	Antiradical activity (in comparison with α-tocopherol)
Cacalol	0.28[a], 0.31[b]	0.27
Cacalone	0.02[a], 0.03[b]	0.02
Cacalol acetate	None	None
6β-Propionyloxy-1,10-furanoeremophil-9-one	None	None
O-Methylcacaloene	None	None

As we see, cacalol possesses a fairly high antioxidant and antiradical activity while cacalone is only slightly active.

We have characterized the activities of the caffeic acid derivatives previously [4].

EXPERIMENTAL

For TLC we used Silufol plates, while column chromatography was carried out on KSK silica gel. Chromatograms were run in the toluene–acetone (95:5) and benzene–methanol (4:1) systems; melting points were determined on a Boetius stage (and are uncorrected); optical rotations were measured on a Perkin-Elmer 141 polarimeter; NMR spectra were taken on a Bruker WM-250 spectrometer with working frequencies of 250 MHz for ^{1}H and 62.9 MHz for ^{13}C. Mass spectra were obtained on a LKB-9000S spectrometer by the direct introduction of the sample into the ion source at energies of 15 and 70 eV. UV spectra were taken on a Cary-Varian 219, in methanol. GLC was conducted on a GC-5AP instrument (Shimadzu) with a flame-ionization detector (3% of OV-1, program 80-300°C at 6°C/min).

Antioxidant activities were determined on the model of the autooxidation of methyl oleate at 50°C [18] and were evaluated by the ratio of the induction periods in experiments with the addition of the compounds under investigation and of an equal amount of a standard antioxidant – Ionol.

Antiradical activity was established spectrophotometrically from the decoloration by the compounds under investigation of a methanolic solution of diphenylpicrylhydrazyl (DPPH) [19]. The titer of the DPPH solution was determined with respect to standard α-tocopherol (Sigma), and the activities were expressed as the number of moles of α-tocopherol equivalent to 1 mmole of the substance being tested.

The plants were collected in the flowering phase: C. auriculata in the environs of Vladivostok; C. hastata – in the Khasan region of the Maritime Territory; C. aconitifolia (Syneilesis aconitifolia Maxim) – in the Oktyabr'skii region of the Maritime Territory; and C. robusta on the island of Sakhalin.*

The fresh roots were extracted with ethanol. The ethanolic extracts were separated and the residue was diluted with water and was re-extracted with hexane and ethyl acetate.

Cacalia auriculata (550 g). Hexane Fraction (2.9 g). The fractions were eluted from the column by hexane with increasing concentrations of toluene.

Cacalol, $C_{15}H_{18}O_2$, mp 92°C (hexane), $[\alpha]_D^{20}$ +10° (c 1.0; ethanol). IR spectrum: ν 3550 (OH), 1635 (C=C), 1590 (furan). Cacalol acetate was obtained by the acetylation of cacalol with a mixture of pyridine and acetic anhydride (1:1) at room temperature, $C_{17}H_{20}O_3$, mp 103°C, $[\alpha]_D^{20}$ –9.2° (c 1.0; ethanol). Mass spectrum: m/z 272, 245, 230 (100%). PMR spectrum (ppm): 1.1 (d, J = 7, 3H), 2.22 (s, 3H), 5.1 (m), 6.83 (s, 1H), 2.32 (s, 3H).

6β-Propionyloxy-1,10-dehydrofuranoeremophil-9-one, $C_{18}H_{22}O_4$, mp 94°C (heptane), $[\alpha]_D^{20}$ +22° (c 1.0; ethanol). IR spectrum: ν 1720 (C=O), 1660 (C=O), 1585 (furan). PMR spectrum (ppm): 0.98 (d, J = 7, 3H), 1.12 (s, 3H), 1.12 (d, J = 7, 1H), 1.27 (t, J = 7.5, 3H), 1.95 (s, 3H), 2.50 (q, J = 7.5, 2H).

Cacalone, $C_{15}H_{22}O_3$, mp 140°C (heptane), $[\alpha]_D^{20}$ +80° (c 1.0; ethanol). IR spectrum: ν 3550 (OH), 1660 (C=O), 1590 (furan). PMR spectrum (ppm): 1.26 (d, J = 7, 3H), 1.66 (s, 1H), 2.21 (d, J = 1, 3H).

Ethyl Acetate Fraction (5.5 g). The fractions were eluted from the column by benzene with increasing concentrations of ethyl acetate.

Ethyl caffeate, $C_{11}H_{12}H_4$, mp 144.5°C (chloroform). UV spectrum, $\lambda_{max}^{methanol}$: 218, 241, 312 (sh.), 330.

Caffeic acid, $C_9H_8O_4$, mp 196-197°C. UV spectrum, $\lambda_{max}^{methanol}$: 217, 238, 290 (sh.), 333.

Caffeoyl β-D-glucopyranoside, $C_{15}H_{18}O_9$, mp 176°C (acetone). UV spectrum, $\lambda_{max}^{methanol}$: 218, 241, 301 (sh.), 333.

Cacalia robusta (520.0 g). Hexane Fraction (33.2 g). The main mass of the hexane fraction consisted of steam-volatile oily substances with an intense persistent odor. Information on the composition of the volatile components will be reported later.

O-Methylcacaloene, $C_{16}H_{18}O_2$, mp 85°C (hexane). UV spectrum, $\lambda_{max}^{methanol}$: 223, 250 (br), 285, 294. Mass spectrum, m/z: 242, 277 (100%), 212. PMR spectrum (ppm): 1.02 (d, J = 7, 3H), 2.3 (d, J = 1, 3H), 2.42 (s, 3H), 3.98 (s, 3H).

Cacalol acetate.

6β-Propionyloxy-1,10-dehydrofuranoeremophil-9-one.

Ethyl Acetate Fraction (0.4 g). Ethyl caffeate; caffeic acid; caffeoyl β-D-glucopyranoside.

Cacalia hastata (55 g). Hexane Fraction (0.4 g). O-Methylcacaloene; cacalol acetate; 6β-propionyloxy-1,10-dehydrofuranoeremophil-9-one.

*The authors are grateful to workers of the chemotaxonomy laboratory for assistance in the collection of the material.

Ethyl Acetate Fraction (0.3 g). Ethyl caffeate; caffeic acid; caffeoyl β-D-glucopyranoside.

Cacalia aconitifolia (420 g). Hexane Fraction (0.64 g). Oleanolic acid acetate, $C_{32}H_{50}O_4$, mp 258°C (ethanol). Mass spectrum, m/z: 498, 456 (100%).

β-Sitosterol, $C_{29}H_{50}O$, mp 139°C (benzene). Mass spectrum, m/z: 414, 302.

Ethyl Acetate Fraction (0.17 g). Ethyl caffeate; caffeic acid; caffeoyl β-D-glucopyranoside.

SUMMARY

1. Compounds of the furanoeremophilane series and caffeic acid derivatives have been found in extracts of the roots of three Far Eastern representatives of the genus Cacalia (C. auriculata DV, C. hastata, and C. robusta Tolm.).

2. Cacalol and, to a smaller degree cacalone, have revealed antioxidant and antiradical activity.

3. The roots of C. aconitifolia did not contain derivatives of the furanoeremophilane series, which, together with morphological characteristics, has confirmed the necessity for excluding this species from the genus Cacalia.

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