Chemistry of Natural Compounds, Vol. 41, No. 2, 2005

STRUCTURAL STUDIES AND BIOLOGICAL ACTIVITY OF PLANT TRITERPENOIDS FROM THE *Thalictrum* GENUS

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UDC [547.91+547.4]:543.495.23

Structures and chemical and spectral properties of triterpenoids isolated from plants of the Thalictrum *genus were systematized for the first time. Features of ^{13}C NMR spectra of cycloartane triterpenoids were discussed. Data for the biological activities of certain cycloartane and oleanane triterpenoids were given.*

Key words: *Thalictrum*, triterpenoids, saponins, cycloartane, oleanane, ^{13}C NMR, biological activity.

Triterpenoids are natural isoprenoids, the skeleton of which is constructed of 30 C atoms. They are widely distributed in both terrestrial plants and marine flora and fauna. They occur in the free state and as esters and glycosides called saponins. Triterpenoids are usually classified by the number of rings in the C skeleton. Tetra- and pentacyclic compounds are most widely distributed in nature. This review covers representatives of them.

Plants of the *Thalictrum* (Ranunculaceae) genus produce a large quantity of triterpenoids and other secondary metabolites. The former are interesting because of their chemical structures and practical uses. It should be noted that investigations of secondary metabolites from these plants focused rather successfully and until recently on the alkaloids [1-5]. The first publications devoted to the study of triterpene saponins from plants of the *Thalictrum* genus appeared at the start of the 1981s [6].

There is a reason for the interest in representatives of the broad *Thalictrum* genus. Plants of this genus have been used since long ago by peoples of many nations for medicinal purposes to treat gastrointestinal and gynecological illnesses, various neoplasms, and tuberculosis [7-10]. This, in turn, stimulated studies of the chemical composition of the plants, the isolation of biologically active compounds, and investigations of their pharmacologic activity.

We have for the first time systematized and generalized information on triterpenoids from plants of the *Thalictrum* genus (from 1981 to 2003), features of their spectral and chemical properties, and their biological activity. Individual representatives of these compounds were included in reviews on triterpenoids [11, 12] and cycloartanes [13,14]. However, the complete picture will be given for the first time.

TRITERPENOID GENINS AND THEIR GLYCOSIDES

Triterpenoid saponins from plants of the *Thalictrum* genus were first isolated and characterized in 1981-1983 from *T. minus* and *T. foetidum* collected in eastern Siberia [6, 15, 16]. Compounds of this type were not observed in the same species from Middle Asia and Europe. Based on this, which indicates that the chemical composition of a species is dependent on the ecological and geographical habitat, it was proposed [17, 18] to separate the species growing in eastern Siberia into a Siberian chemorace. Then, the triterpenoid compounds were isolated only from species growing in the east (Japan, China, Korea). Now it is probably possible to generalize and view the Siberian chemorace as the "eastern Asian" one.

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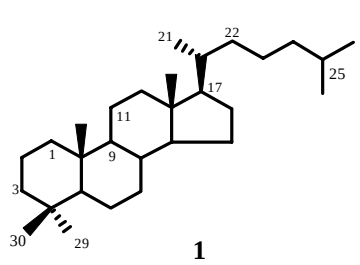
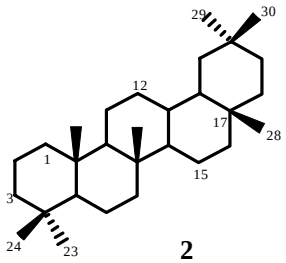
0009-3130/05/4102-0117

Plants of the *Thalictrum* genus produce both tetracyclic (lanostane **1** type) and pentacyclic (oleanane **2** type) triterpenoids [19]. Lanostane derivatives containing a 9,19-cyclopropane ring (CPR) are called cycloartanes (**3**) and are separated into an independent group.



1



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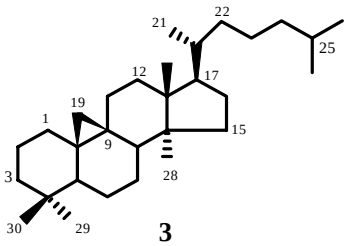


3

More than 50 triterpenoid saponins were isolated from 9 species of the genus, more than half of which contain new genins belonging to cycloartane triterpenoids.

Glycosides with pentacyclic genins have unique structures for the carbohydrate chain. However, we will not discuss these compounds in more detail.

CYCLOARTANE COMPOUNDS

Triterpenoids isolated from plants of the *Thalictrum* genus have various structures. In our opinion, they are conveniently combined into several groups:

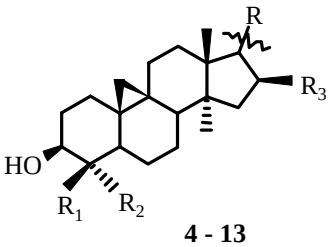
a) cycloartanes with an open sidechain on C-17;

b) cycloartanes with a tetrahydrofuran (THF) ring on C-17;

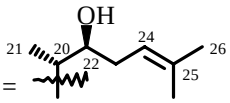
c) cycloartanes with a THF-ring on C-20;

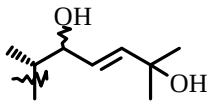
d) cycloartanes with a cyclopentane ring on C-17.

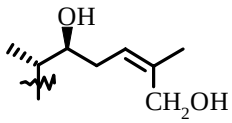
Cycloartanes with an open sidechain (on C-17), type "a," have been isolated from various *Thalictrum* species. Table 1 gives the structures for **4-13** (Table 1, in this table and henceforth the physicochemical constants are given only for the genins obtained by cleaving the glycosides; the remaining genins were not isolated). Table 2 lists glycosides **14**-**30** corresponding to them.

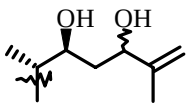


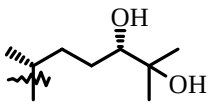
4 - 13

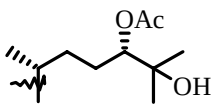
4: R = 

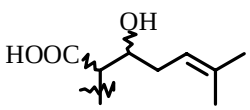
5: R = 

6, 11: R = 

7, 8: R = 

9, 10: R = 

12: R = 

13: R = 

4, 5, 6, 7, 8: $R_1 = CH_3$, $R_2 = CH_2OH$, $R_3 = OH$; **9:** $R_1 = CH_3$, $R_2 = CH_3$, $R_3 = OH$; **10:** $R_1 = CH_2OH$, $R_2 = CH_3$, $R_3 = OH$; **11:** $R_1 = CH_3$, $R_2 = CH_3$, $R_3 = H$; **12:** $R_1 = CH_3$, $R_2 = COOH$, $R_3 = OH$; **13:** $R_1 = CH_2OH$, $R_2 = CH_3$, $R_3 = H$

TABLE 1. Structures of Cycloartanes with Open Side Chains

Compound	Empirical formula, mp, $[\alpha]_D$	Ref.
Thalicogenin (**4**)	$C_{30}H_{50}O_4$; 201-202° (EtAc); +34.5° (c 1.0; Py)	[22]
22(*ξ*)-3*β*,16*β*,22,25,29-Pentahydroxycycloart-23-ene (**5**)		[25]
22(*S*)-3*β*,16*β*,22,26,29-Pentahydroxycycloart-24(*Z*)-ene (**6**)		[26]
22(*S*),24(*S*)-3*β*,16*β*,22,24,29-Pentahydroxycycloart-25-ene (**7**)		[26]
22(*S*),24(*R*)-3*β*,16*β*,22,24,29-Pentahydroxycycloart-25-ene (**8**)		[89]
Cyclofoetigenin A (**9**)	$C_{30}H_{52}O_4$; 182-184° (MeOH); +68.2° (c 1.32; MeOH)	[30]
Cyclofoetigenin B (**10**)	$C_{30}H_{52}O_5$; 240-242° (Me_2O); +72.0° (c 0.5; MeOH)	[31]
Thalictogenin a (**11**)	$C_{30}H_{50}O_3$; 202-204°; +30.2° (c 0.5; Py)	[36]
	190-192°; (Me_2O)	[35]
24(*S*)-Cycloart-3*β*,24-diacetyl-16,25-diol-29-carboxy (**12**)		[40]
22(*ξ*)-Cycloart-24-en-21(*ξ*)-carboxy-3*β*,22,30-triol (**13**)		[41]

TABLE 2. Triterpenoid Saponins from Plants of the *Thalictrum* Genus

Compound	Saponin, mol. formula, mp, $[\alpha]_D$, spectra[a]	Chemical structure	Plant species[b]	Ref.
	Glycosides of cycloartanes **4-13** with an acyclic sidechain on C-17			
14	Thalicoside A, $C_{42}H_{70}O_{14}$, 255-258° (MeOH), +8.9° (c 2.0; Py), ^1H, ^{13}C NMR, FAB-MS	3-O-*β*-D-Gal*p*, 29-O-*β*-D-Glc*p* of thalicogenin (**4**)	*T. minus*	[20]
15	Thalicoside C, $C_{48}H_{80}O_{19}$, 205-207°, +50.0° (c 1.0; Py), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Gal*p*, 22-O-*β*-D-Glc*p*, 29-O-*β*-D-Glc*p* of thalicogenin (**4**)	*T. minus*	[23]
16	Thalicoside A2, $C_{41}H_{68}O_{13}$, 272-274°, +10.6° (c 0.9; MeOH-$CHCl_3$, 1:1) ^1H, ^{13}C NMR, 2D MNR, HR-FAB-MS	*3*-O-*α*-L-Ara*p*, 29-O-*β*-D-Glc*p* of thalicogenin (**4**)	*T. minus*	[24]
17	Thalicoside E, $C_{42}H_{70}O_{15}$, 249-251°, +4.7° (c 0.85; Py), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Gal*p*, 29-O-*β*-D-Glc*p* of triterpenoid (**5**)	*T. minus*	[25]
18	Thalicoside G1, $C_{42}H_{70}O_{15}$, 296-298°, +11.1° (c 0.18; Py), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Gal*p*, 29-O-*β*-D-Glc*p* of triterpenoid (**6**)	*T. minus*	[26]
19	Thalicoside G2, $C_{42}H_{70}O_{15}$, 292-294°, +12.3° (c 0.41; Py), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Gal*p*, 29-O-*β*-D-Glc*p* of triterpenoid (**7**)	*T. minus*	[26]
20	Thalicoside H2, $C_{42}H_{70}O_{15}$, ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Gal*p*, 29-O-*β*-D-Glc*p* of triterpenoid (**8**)	*T. minus*	[89]
21	Cyclofoetoside A, $C_{47}H_{80}O_{17}$, 265-266°, +22.0°(c 1.32; Py), ^1H, ^{13}C NMR, FAB-MS	3-O-*α*-L-Ara*p*, 16-O-[*α*-L-Rha*p*-(1→6)-*β*-D-Glc*p*] of cyclofoetigenin A (**9**)	*T. foetidum*	[29]
22	Cyclofoetoside B, $C_{47}H_{80}O_{18}$, 194-197°, +15.7° (c 0.88; Py), ^1H, ^{13}C NMR, FAB-MS	3-O-*α*-L-Ara*p*, 16-O-[*α*-L-Rha*p*-(1→6)-*β*-D-Glc*p*] of cyclofoetigenin B (**10**)	*T. foetidum*	[32]
23	Glycoside, $C_{40}H_{68}O_{13}$, 211-213°, ^1H, ^{13}C NMR, FAB-MS	3-O-*β*-D-Xyl*p*-(1→2)-*β*-D-Xyl*p* of cyclofoetigenin B (**10**)	*T. smithii*	[33]
24	Thalifoenoside A, $C_{50}H_{82}O_{30}$, dec. 245° (MeOH), +12.5° (c 1.99; MeOH), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Qui*p*-(1→2)-*α*-L-Rha*p*-(1→6)-*β*-D-4-O-acetyl-Glc*p* of thalictogenin a (**11**)	*T. foeniculaceum* (roots)	[35]
25	Thalictoside A, -1.3° (c 0.25; Py), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Qui*p*-(1→6)-*β*-D-Glc*p*-(1→4)-*β*-D-Fuc*p* of thalictogenin a (**11**)	*T. thunbergii*	[36]
26	Thalictoside C, -23.5° (c 0.48; Py), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Glc*p*-(1→6)-[*α*-L-Rha*p*-(1→2)-*β*-D-Glc*p*-(1→4)-*β*-D-Fuc*p* of thalictogenin a (**11**)	*T. thunbergii;* *T. squarrosum*	[36] [39]

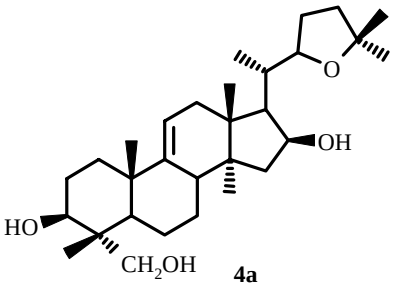
TABLE 2. (Continued)

Compound	Saponin, mol. formula, mp, $[\alpha]_D$, spectra[a]	Chemical structure	Plant species[b]	Ref.
27	Squarroside I, -2.7° (c 0.9; MeOH) ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-β-D-Glc*p*-(1→4)-[α-L-Rha*p*-(1→2)]-β-D-Fuc*p* of thalictogenin a (**11**)	*T. squarrosum*	[39]
28	Glycoside, $C_{51}H_{82}O_{21}$, 220-222°, ^1H, ^{13}C NMR, FAB-MS	29-O-α-L-Rha*p*-(1→2)-[β-D-Xyl*f*-(1→6)]-β-D-Glc*p* of triterpenoid (**12**)	*T. uchiyamai*	[40]
29	Thalictoside V, -16.5° (c 0.23; MeOH), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-α-L-Rha*p*-(1→2)-[α-L-Rha*p*-(1→6)]-β-D-Glc*p* of triterpenoid (**13**)	*T. Herba*	[41]
30	Thalictoside IX, $C_{59}H_{96}O_{27}$, -14.0° (c 1.0; MeOH), ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-α-L-Rha*p*-(1→2)-[α-L-Rha*p*-(1→6)]-β-D-Glc*p*, 21-O-β-D-Xyl*p*-(1→6)-β-D-Glc*p* of triterpenoid (**13**)	*T. Herba*	[41]
	Glycosides of cycloartanes **31-38** with a THF ring on C-17			
39	Squarroside A1, $C_{37}H_{60}O_{10}$, ^1H, ^{13}C NMR, FAB-MS	3-O-β-D-Glc*p* of squarrogenin 1 (**31**)	*T. squarrosum*	[43]
40	Squarroside B1, $C_{43}H_{70}O_{14}$, ^1H, ^{13}C NMR, FAB-MS	3-O-[α-L-Rha*p*-(1→6)-β-D-Glc*p*] of squarrogenin 1 (**31**)	*T. squarrosum*	[43]
41	Squarroside A2, $C_{37}H_{60}O_{10}$, ^1H, ^{13}C NMR, FAB-MS	3-O-β-D-Glc*p* of squarrogenin 2 (**32**)	*T .squarrosum*	[43]
42	Squarroside B2, $C_{43}H_{70}O_{14}$, ^1H, ^{13}C NMR, FAB-MS	3-O-[α-L-Rha*p*-(1→6)-β-D-Glc*p*] of squarrogenin 2 (**32**)	*T. squarrosum*	[43]
43	Squarroside B3, $C_{42}H_{68}O_{14}$, ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-[α-L-Rha*p*-(1→6)-β-D-Glc*p*] of squarrogenin 3 (**33**)	*T. squarrosum*	[44]
44	Squarroside B4, $C_{42}H_{68}O_{14}$, ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-[α-L-Rha*p*-(1→6)-β-D-Glc*p*] of squarrogenin 4 (**34**)	*T. squarrosum*	[44]
45	Squarroside C, $C_{48}H_{78}O_{19}$, 211-213°, -46.9° (c 1.1; MeOH), ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-[α-L-Rha*p*-(1→6)-β-D-Glc*p*], 21-O-β-D-Glc*p* of squarrogenin 3 (**33**)	*T. squarrosum*	[45]
46	Thalictoside I, +10.3° (MeOH), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-α-L-Rha*p*-(1→2)-β-D-Glc*p* of triterpenoid (**35**)	*T. Herba*	[46]
47	Thalictoside II, -32.2° (MeOH), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-α-L-Rha*p*-(1→2)-β-D-Glc*p* of triterpenoid (**36**)	*T. Herba*	[46]
48	Thalictoside III, $C_{49}H_{80}O_{18}$, +4.5° (c 0.51; MeOH), ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-α-L-Rha*p*-(1→2)-[α-L-Rha*p*-(1→6)]-β-D-Glc*p* of triterpenoid (**35**)	*T. Herba*	[47]
49	Thalictoside IV, $C_{49}H_{80}O_{18}$, -40.8° (c 0.63; MeOH), ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-α-L-Rha*p*-(1→2)-[α-L-Rha*p*-(1→6)]-β-D-Glc*p* of triterpenoid (**36**)	*T. Herba*	[47]
50	Thalictoside XII, -2.4° (c 1.0; MeOH), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-α-L-Rha*p*-(1→2)-[α-L-Rha*p*-(1→6)]-β-D-Glc*p* of triterpenoid (**37**)	*T. Herba*	[48]
51	Thalictoside XIII, +3.9° (c 1.0; MeOH), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-α-L-Rha*p*-(1→2)-[α-L-Rha*p*-(1→6)]-β-D-Glc*p* of triterpenoid (**38**)	*T. Herba*	[48]
	Glycosides of cycloartanes **52-54** with a THF ring on C-20			
55	Thalicoside A1, $C_{42}H_{70}O_{14}$, 300-301°, +3.6° (c 0.66; Py), ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-β-D-Gal*p*, 29-O-β-D-Glc*p* of thalicogenin A1 (**52**)	*T. minus*	[24]
56	Thalicoside A3, $C_{41}H_{68}O_{13}$, 253-255°, +1.1° (c 0.57; MeOH-$CHC1_3$, 1:1) ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-α-L-Ara*p*, 29-O-β-D-Glc*p* of thalicogenin A1 (**52**)	*T. minus*	[24]
57	Thalicoside H1, $C_{42}H_{70}O_{15}$, 260-262°, +10.3° (c 0.34; Py), ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-β-D-Gal*p*, 29-O-β-D-Glc*p* of triterpenoid (**53**)	*T. minus*	[51]
58	Thalicoside H3, $C_{42}H_{70}O_{15}$, ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-β-D-Gal*p*, 29-O-β-D-Glc*p* of triterpenoid (**54**)	*T. minus*	[89]

Table 2. (Continued)

Compound	Saponin, mol. formula, mp, $[\alpha]_D$, spectra[a]	Chemical structure	Plant species[b]	Ref.
	Glycosides of cycloartanes **60** and **61** with a cyclopentane on C-17			
62	Thalictoside D, $C_{60}H_{100}O_{28}$, -28.9° (MeOH), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*α*-L-Rha*p*-(1→2)-[*α*-L-Rha*p*-(1→6)]-*β*-D-Glc*p*, 22-O-*β*-D-Glc*p*-(1→2)-*β*-D-Glc*p* of triterpenoid (**60**)	*T. thunbergii*	[52]
63	Thalictoside E, $C_{65}H_{108}O_{32}$, -29.6° (MeOH), ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*α*-L-Rha*p*-(1→2)-[*α*-L-Rha*p*-(1→6)]-*β*-D-Glc*p*, 22-O-*β*-D-Glc*p*-(1→2)-[*β*-D-Xyl*p*-(1→6)]-*β*-D- Glc*p* of triterpenoid (**60**)	*T. thunbergii*	[52]
64	Thalictoside F, $C_{65}H_{108}O_{32}$, ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*α*-L-Rha*p*-(1→2)-[*α*-L-Rha*p*-(1→6)]-*β*-D-Glc*p*, 22-O-*β*-D-Glc*p*-(1→2)-[*β*-D-Xyl*p*-(1→6)]-*β*-D-Glc*p* of triterpenoid (**61**)	*T. thunbergii*	[53]
	Glycosides of pentacyclic triterpenoids **70**-**84**			
70	Thalicoside B, $C_{53}H_{84}O_{20}$, 213-216°, +10.49° (c 3.58; Py), ^1H, ^{13}C NMR	3-O-[*α*-L-Rha*p*-(1→2)-*β*-D-Glc*p*(1→3)*α*-L-Ara*p*]-28-O-*β*-D-Glc*p* of oleanolic acid (**65**)	*T. minus*	[57]
71	Thalicoside D, $C_{59}H_{96}O_{26}$, 218-220°, -0.8° (c 5.0; H_2O), ^1H, ^{13}C NMR, 2D NMR, SIMS	3-O-[*β*-D-Glc*p*-(1→2)-*β*-D-Glc*p*-(1→4)*α*-L-Ara*p*]-28-O-[*β*-D-Glc*p*-(1→6)-*β*-D-Glc*p* of oleanolic acid (**65**)	*T. minus*	[58]
72	Foetoside C, $C_{58}H_{94}O_{25}$, 212-214°, -23.5° (c 1.36; MeOH) ^1H, ^{13}C NMR, FAB-MS	3-O-[*β*-D-Xylp-(1→3)-*α*-L-Rha*p*-(1→2)-*α*-L-Ara*p*], 28-O-[*β*-D-Glc*p*-(1→6)-*β*-D-Glc*p* of oleanolic acid (**65**)	*T. foetidum*	[59]
73	Thalictoside VII, $C_{59}H_{96}O_{25}$, -18.6° (c 0.58; MeOH), ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-*α*-L-Rha*p*-(1→3)-*β*-D-Glc*p*-(1→3)-*α*-L-Rha*p*-(1→4)-*β*-D-Xyl*p*, 28-O-*β*-D-Glc*p* of oleanolic acid (**65**)	*T. Herba*	[47]
74	Squarroside II, -4.8° (c 0.9; MeOH) ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Glc*p*-(1→4)-[*α*-L-Rha*p*-(1→2)]-*β*-D-Xyl*p*, 28-O-*β*-D-Glc*p* of oleanolic acid (**65**)	*T. squarrosum*	[47]
75	Squarroside III, -14.1° (c 0.55; MeOH) ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Glc*p*-(1→4)-[*α*-L-Rha*p*-(1→2)]-*β*-D-Xylp,28-O-*β*-D-Glc*p*-(1→6)-*β*-D-Glc*p* of oleanolic acid (**65**)	*T. squarrosum*	[47]
76	Squarroside IV, -4.2° (c 0.85; MeOH) ^1H, ^{13}C NMR, 2D NMR, FAB-MS	3-O-*β*-D-Glc*p*-(1→4)-[*β*-D-Glc*p*-(1→3)-*α*-L-Rha*p*-(1→2)]-*β*-D-Xylp, 28-O-*β*-D-Glc*p* of oleanolic acid (**65**)	*T. squarrosum*	[47]
77	Thalictoside VI, $C_{53}H_{86}O_{22}$, +0.41° (c 0.51; MeOH), ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-*β*-D-Glc*p*-(1→3)-*α*-L-Rha*p*-(1→4)-*β*-D-Xylp, 28-O-*β*-D-Glc*p* of hederagenin (**67**)	*T. Herba*	[47]
78	Thalictoside VIII, $C_{59}H_{96}O_{26}$, -11.6° (c 0.5; MeOH), ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3-O-*α*-L-Rha*p*-(1→3)-*β*-D-Glc*p*-(1→3)-*α*-L-Rha*p*-(1→4)-*β*-D-Xylp, 28-O-*β*-D-Glc*p* of hederagenin (**67**)	*T. Herba*	[47]
79	Glycoside, $C_{35}H_{56}O_7$, 243-246°	3-O-*α*-L-Ara*p* of oleanolic acid (**65**)	*T. minus*	[55]
80	Glycoside, $C_{41}H_{66}O_{12}$, 262-264° (MeOH), ^{13}C NMR, FAB-MS	3-O-*β*-D-Glc*p*-(1→3) *α*-L-Ara*p* of oleanolic acid (**65**)	*T. minus*	[55]
81	Glycoside, $C_{47}H_{76}O_{16}$, 249-250° (MeOH), ^{13}C NMR, FAB-MS	3-O-*α*-L-Rha*p*-(1→2)-*β*-D-Glc*p*(1→3)*α*-L-Ara*p* of oleanolic acid (**65**)	*T. minus*	[55]
82	Glycoside, $C_{47}H_{76}O_{17}$, 219-220° (MeOH), ^{13}C NMR, FAB-MS	3-O-[*β*-D-Glc*p*-(1→3)*α*-L-Ara*p*]-28-O-*β*-D-Glc*p* of oleanolic acid (**65**)	*T. minus*	[55]
83	Aquilegifoline, $C_{46}H_{72}O_{16}$, 195-197°, -5.88° (c 0.13, MeOH), ^{13}C NMR, FAB-MS	28-O-[*α*-L-Rha*p*-(1→2)-*β*-D-Glc*p*] of triterpenoid (**66**)	*T. aquilegfolium*	[60]
84	Thalicoside F, $C_{47}H_{74}O_{17}$, 268-270°, ^1H, ^{13}C NMR, 2D NMR, HR-FAB-MS	3- O-[*α*-L-Rha*p*-(1→2)-*β*-D-Glc*p*(1→4)*α*-L-Ara*p*] of triterpenoid (**69**)	*T. minus*	[61]

Thalicoside A (**14**) was the first triterpenoid glycoside isolated from *T. minus* [20]. Strong acid hydrolysis produced artifact **4a**, the structure of which was established by x-ray structure analysis (XSA) [21]. The native genin, thalicogenin (**4**), was obtained from **14** by periodate oxidation with subsequent alkaline destruction of the oxidation products [22].



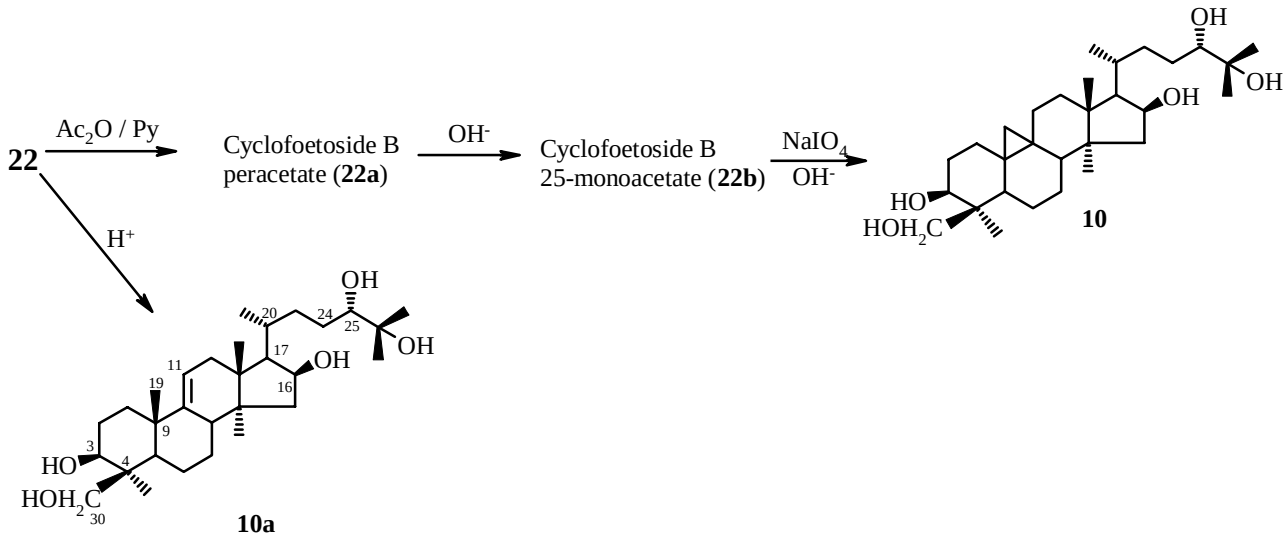
4a

Later another two saponins containing genin **4** were isolated from *T. minus*: thalicoside C (**15**) [23] and thalicoside A2 (**16**) [24]. The first of these was a trisdesmoside; the second, a bisdesmoside. The carbohydrate components of these glycosides contained galactose, two glucoses (in **15**), arabinose, and glucose (in **16**).

A glycoside from this plant, thalicoside E (**17**) [25], contained a polycyclic genin and a carbohydrate part like in thalicoside A. However, the sidechain of the new genin (**5**) had a different structure.

Thalicosides G1 (**18**) [26], G2 (**19**) [26], and H2 (**20**) [27] are genins with isomers in the sidechain. The genins of G2 and H2, corresponding to **7** and **8**, are epimeric at C-24. The *S*-configuration of asymmetric C-22 was found for **18**-**20** by the literature method [28]. This enabled the stereochemistry of the hydroxyls in the chiral secondary alcohols to be established using the glycosylation effect in the ^{13}C NMR spectra.

During a study of the structures of cycloartane saponins from another Siberian species *T. foetidum*, a problem similar to that for production of the native genin from low meadowrue. Whereas acid hydrolysis of cyclofoetoside A (**21**) gave in low yield native genin **9** [29, 30], cyclofoetoside B (**22**) was not hydrolyzed by enzymes (gastric juice of the grape snail) or under usual acid-hydrolysis conditions [31, 32]. Stronger acid-hydrolysis conditions produced an artifact (**10a**). Native genin **10**, cyclofoetigenin B, was obtained as usual in several steps: glycoside **22** was acetylated and the peracetate of the glycoside (**22a**) was hydrolyzed by KOH under mild conditions in order to retain the sterically hindered acetate on C-25. Then native genin **10** was isolated by periodate oxidation of cyclofoetoside B 25-monoacetate (**22b**) with subsequent alkaline hydrolysis of the resulting products [31].



Roots of *T. smithii* [33, 34] yielded the new glycoside **23**, which also contained cyclofoetigenin B (**10**).

Genin **11** of three new glycosides isolated from *T. foeniculaceum*, *T. thunbergii*, and *T. squarrosum* turned out to be the same cycloartane.

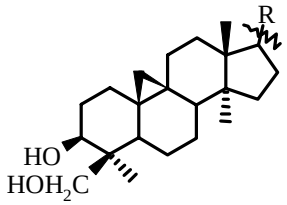
Roots of *T. foeniculaceum* [35] yielded the trioside thalifoenoside A (**24**) with the new genin 3*β*,22(*S*),27-trihydroxycycloart-24-ene (**11**) and a carbohydrate chain with quinovose and acylated glucose. Later new trioside and tetraoside saponins, thalictosides A (**25**) and C (**26**) with the same genin thalictogenin a (**11**), were observed in the aerial part of *T. thunbergii* [36]. The PMR and ^{13}C NMR spectra indicate that thalictogenin a has the same structure as the genin thalifoenoside A (**24**). The difference in melting points [202-204°C and 190-192°C (Table 1)] is probably explained by the different crystallization conditions and the different purities of the isolated compounds. In both instances **11** was prepared by acid hydrolysis of the corresponding glycosides and studied by spectral methods. The *Z*-configuration of the double bond was established using the nuclear Overhauser effect (NOE). The *S*-configuration of C-22 was determined [36] using the Moscher method [37] after acetylation of the primary alcohol on C-26. In this instance, ^{13}C chemical shifts (CSs) of **11** [35] and the corresponding values for 22*S*- and 22*R*-hydroxycholestanols [38] were compared.

The aerial part of *T. squarrosum* [39] collected in China afforded the new trioside **27** with the same genin **11**.

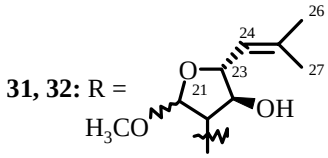
The new glycoside **28** containing genin **12** acylated at the C-3 and C-24 positions and a carbohydrate chain of three sugars bonded through an ester bond to the C-29 carboxyl was observed in *T. uchiyamai* [40].

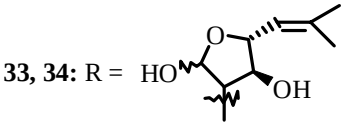
Saponins **29** and **30** were isolated from *T. Herba*. The cycloartane genin **13** of these had an acyclic sidechain with a C-21 COOH group. It should be noted that selective cleavage with LiI and 2,6-lutidine in anhydrous CH_3OH was used to cleave the ester bond.

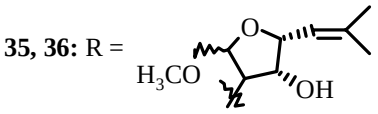
Type "b" cycloartanes with a THF ring on C-17 include triterpenoids **31-38** (Table 3) and were isolated from *T. squarrosum* collected in the trans-Baikal region of Russia and *T. Herba* growing in Japan. Table 2 lists the glycosides **39-51** corresponding to these triterpenoids.

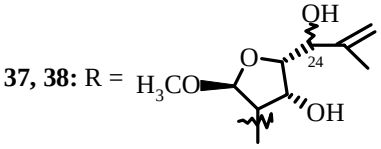


31 - 38









Saponins containing a tetrasubstituted THF ring in the sidechains and exhibiting stereoisomerism at the asymmetric centers of this ring were isolated from *T. squarrosum*. Enzymatic hydrolysis (gastric juice of *Helix pomatia*) of the total saponins produced two cycloartane genins, squarrogenins 1 (**31**) and 2 (**32**), which are the OCH_3-21*R*- and 21*S*-isomers, respectively [42]. The relative configuration of the THF substituents was determined using the NOE. These compounds were genins of four new glycosides [43]: squarrosides A1 (**39**) and B1 (**40**) (squarrogenin 1) and squarrosides A2 (**41**) and B2 (**42**) (squarrogenin 2), which differ in the number of carbohydrate units.

Later another pair of biosides, squarrosides B3 (**43**) and B4 (**44**) [44] were isolated from this same species. The genins of these had hydroxyls in the 21*R* and 21*S* positions.

Genin **33** of another saponin, trioside **45** [45], is a 21*S*-epimer and has a carbohydrate chain on the C-21 hydroxyl. It should be noted that its 21*R* isomer was not isolated. The authenticity of **39**-**42** was confirmed by isolating these compounds under conditions that excluded methylation, namely, in the absence of methanol. The 21-O-ethylated derivatives of **43** and **44** were isolated along with **39**-**44** using ethanol. This is indicative of the ease with which the hemiacetal hydroxyl is acylated.

TABLE 3. Structures of Triterpenoids with a THF Ring on C-17

Compound, empirical formula, MW, mp, $[\alpha]_{546}$	Ref.
Squarrogenin 1 (**31**), $C_{31}H_{50}O_5$; 502; 169-171° (C_6H_{12}-Me_2O); -11.1°(c 4.5; Py)	[42]
Squarrogenin 2 (**32**), $C_{31}H_{50}O_5$; 502; 190-193° (C_6H_{12}-Me_2O); +106.6°(c 0.3; Py)	[42]
Squarrogenin 3 (**33**)	[44]
Squarrogenin 4 (**34**)	[44]
21(*S*),22(*R*),23(*R*)-3β,22α,30-Trihydroxy-21β-methoxy-21,23-epoxycycloart-24-ene (**35**)	[46]
21(*R*),22(*R*),23(*R*)-3β,22α,30-Trihydroxy-21β-methoxy-21,23-epoxycycloart-24-ene (**36**)	[46]
21(*S*),22(*R*),23(*R*),24(*S*)-3β,22α,24,30-Tetrahydroxy-21β-methoxy-21,23-epoxycycloart-25-ene (**37**)	[48]
21(*S*),22(*R*),23(*R*),24(*R*)-3β,22α,24,30-Tetrahydroxy-21β-methoxy-21,23-epoxycycloart-25-ene (**38**)	[48]

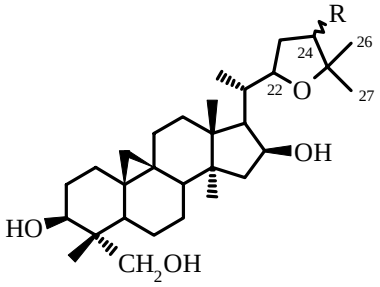
TABLE 4. Structures of Triterpenoids with a THF Ring on C-20

Compound, empirical formula, MW, mp, $[\alpha]_{546}$	Ref.
22(*S*)-3β,16β,29-Trihydroxy-22,25-epoxycycloartane (thalicogenin A1) (**52**), $C_{30}H_{50}O_4$; HR-MS 474.371; 332-333°; $[\alpha]_D$ +7.1° (c 2.0; MeOH-$CHCl_3$)	[24]
22(*S*),24(*S*)-3β,16β,24α,29-Tetrahydroxy-22,25-epoxycycloartane (**53**)	[51]
22(*S*),24(*R*)-3β,16β,24β,29-Tetrahydroxy-22,25-epoxycycloartane (**54**)	[89]

Two biosides [thalictosides I (**46**) and II (**47**)] [46] and two triosides [thalictosides III (**48**) and IV (**49**)] [47] were found in *T. Herba* (Takatogusa). Glycosides **46**, **48**, and **47**, **49** contain cycloartane genins (**35** and **36**, respectively) with a C-21—C-23 epoxide ring and are epimeric at the C-21 methoxyl. It is interesting that **35** and **36** differ from the 21 (*R* and *S*)-OCH_3 isomers of **31** and **32** only by the configuration of the 22-OH in the THF ring of the genin.

The new glycosides thalictoside XII (**50**) and XIII (**51**) were isolated from *T. Herba* [48]. They differ in the absolute configuration of the C-24 hydroxyl of the genins (**37** and **38**). This was established by comparing the CSs of these compounds in the ^{13}C NMR spectra and the CSs of 24*R* and 24*S* dammarane compounds that have the same sidechain.

Type "c" cycloartanes with a THF ring on C-20 are limited to cycloartane genins **52-54** (Table 4) of four glycosides isolated from *T. minus* (glycosides **55-58** in Table 2).

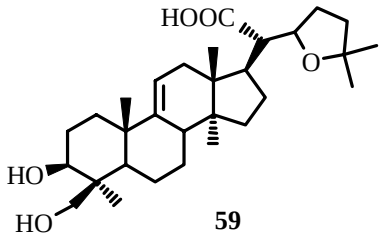


52: R = H
53, 54: R = OH

Thalicosides A1 (**55**) and A3 (**56**) [24] contain the same new genin thalicogenin A1 (**52**). The structure and stereochemistry of the asymmetric center in the sidechain (22*S*) of this group of compounds were determined by spectral methods using the NMR spectrum of artifact **4a** [23] and squarrofuric acid (**59**) [49] and their XSA [21, 50].

Thalicosides H1 (**57**) [51] and H3 (**58**) [27] differ from glycosides **55** and **56** by the presence of an additional hydroxyl on C-24. The *S*-configuration of chiral center C-22 in both genins (**53** and **54**, respectively) was determined using the literature method [28]. The configuration of the C-24 hydroxyl was determined as *S* in **57** and *R* in **58** using the NOE in ^{13}C NMR spectra and Drieding models.

Acid hydrolysis of the methanol extract of the aerial part of *T. squarrosum* produced squarrofuric acid (**59**) [49], which contains a CH_3-19, a 9(11)-double bond, a sidechain with a disubstituted THF ring, which is analogous to the same ring in the genins mentioned above, and a C-21 carboxyl. Apparently this compound is an artifact formed during hydrolysis by the action of mineral acid on squarrogenins 1-4. However, the pathways of these conversions were not discussed.



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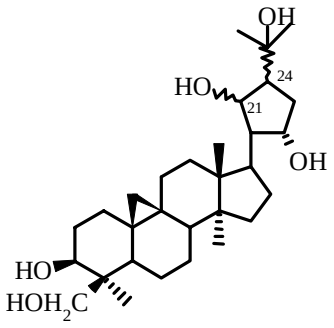
Type "d" cycloartanes with a cyclopentane ring on C-17 include two stereoisomeric genins **60** and **61**, which were observed in glycosides (**62-64**) (Table 2).



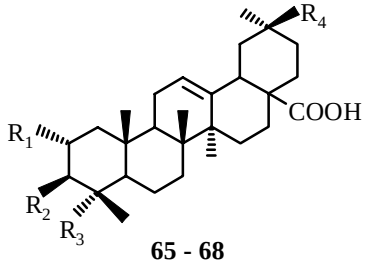
60, 61

60: 21(R),22(S),24(R)-3β,21β,22α,25,30-pentahydroxy-21,24-cycloartane [52]
61: 21(S),22(S),24(S)-3β,21β,22α,25,30-pentahydroxy-21,24-cycloartane [53]

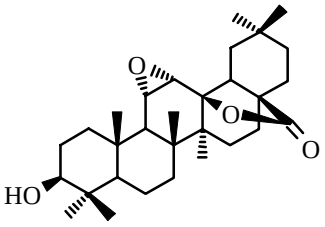
Two bisdesmosides (**62** and **63**, thalictosides D and E, respectively) with the same genin **60** were isolated from the aerial part of *T. thunbergii* [52]. The relative and absolute configurations of the asymmetric centers of the sidechain of **60** were determined spectrally using NOESY correlation methods. The glycoside thalictoside F (**64**) [53] with genin **61**, which is stereoisomeric with genin **60** and has the opposite configuration at C-21 and C-24, was also isolated.

PENTACYCLIC TRITERPENOIDS AND SAPONINS

Pentacyclic saponins isolated from plants of the *Thalictrum* genus contain oleanane (**2**) derivatives as the genins. There are five of these genins: oleanolic acid (**65**), 2α,3β-diacetoxy-30-hydroxyolean-12-en--28-oic acid (**66**), hederagenin (**67**), olive acid (**68**), and 11α,12α-epoxyolean-28,13β-olide (**69**).



65 - 68



69

	R_1	R_2	R_3	R_4
65:	H	OH	CH_3	CH_3
66:	OAc	OAc	CH_3	CH_2OH

	R_1	R_2	R_3	R_4
67:	H	OH	CH_2OH	CH_3
68:	OH	OH	CH_3	CH_3

Free pentacyclic genins were found in two *Thalictrum* species. These are oleanolic and olive acids in *T. aquilegifolium* [54] and oleanolic acid in *T. minus* [55].

STRUCTURAL STUDIES OF CYCLOARTANE TRITERPENOIDS USING ^{13}C NMR SPECTROSCOPY

The rapid development of NMR spectroscopy had an important role in progress on the chemistry of triterpenoids. The capabililties of two-dimensional NMR spectroscopy were widely applied and the elegance of correlation methods was demonstrated in studies of natural triterpenoids and saponins [62-65]. In addition, a large amount of experimental data on ^{13}C NMR spectra was accumulated and used to follow trends and features of ^{13}C NMR spectra on going from one structure to another and to establish structures of new compounds. A necessary condition for this is a sufficient set of spectra for structurally similar model compounds. In the present review, we attempted to generalize ^{13}C NMR data for cycloartane triterpenoids isolated from representatives of the *Thalictrum* genus.

All signals for ^{13}C nuclei of cycloartanol were assigned unambiguously by Kamisako [66], who studied the ^{13}C-labelled compound. The signals of the CPR in the ^{13}C NMR spectrum are very characteristic, especially for the strong-field signals of quaternary C-9 near 20 ppm, C-10 near 26 ppm, and CH_2-19 near 29-30 ppm.

Hydroxyls occur at positions 3, 16, 29, and 30 in the polycyclic fragment of the structural types given in the review and at positions 21, 22, 24, 25, and 26 of the sidechain.

Known cycloartanes from plants of the *Thalictrum* genus have a substituent on C-3 in the β-orientation relative to the plane of the molecule. The ^{13}C NMR spectra are a great help in determining this [67].

The ^{13}C CSs of C-29 or C-30 can be used to determine the location of the primary hydroxyl. Thus, the signal of C-29 with an equatorial hydroxyl is found at weaker field (66.9-68.5 ppm for **4** and **52**) than for C-30 with an axial hydroxyl (~64.5 ppm, **10**, **31**, and **32**). A methyl located geminal to any CH_2OH group is shielded by 3.4-3.9 ppm. The signal for an equatorial methyl (CH_3-29) occurs at weaker field (18.4-21.7 ppm, **10**, **31**, and **32**) than that of an axial CH_3-30 (11.1-11.4 ppm, **4** and **52**). The signal for C-4 in any of the aforementioned instances undergoes a weak-field shift by 2.8-3.8 ppm that does not depend on the configuration of the CH_2OH group. The γ-effect of this hydroxyl is evident in the change of the CSs of C-3 and C-5. For a 29-CH_2OH, the γ-effect for C-3 and C-5 is 3.2-4.6 ppm and 5.3-6.4 ppm (**4** and **52**), respectively. For a 30-CH_2OH, this is a weak-field effect and less evident: +0.1-0.4 ppm for C-5 and ~2.2 ppm for C-3 (**10**, **31**, **32**) (Table 5).

The data examined above are very characteristic and unambiguously determine the type of substitution in ring A. Thus, atoms C-29, C-30, C-3, and C-5 in thalicogenin (**4**) with a 29-CH_2OH have ^{13}C CSs of 68.5, 11.4, 74.8, and 42.3 ppm; in cyclofoetigenin B (**10**) with a 30-CH_2OH, 21.7, 64.6, 80.3, and 48.0 ppm. According to the literature, two compounds with a 30-CH_2OH are found only in *Mangifera indica* besides in plants of the *Thalictrum* genus [68].

The ^{13}C CSs of C-16 and C-17 of cycloartanes are characteristic. For compounds with 16-OH in the α-configuration {aquilegioside I (**85**) from *Aquilegia vulgarus* as an example [69]}, C-16 and C-17 resonate at weaker field than for compounds with a 16-β-OH (Table 6). It should be noted that most cycloartanes have a 16-OH in the β-orientation.

Acetylation of the hydroxyl produces a further weak-field shift of the α-C atom. Among compounds isolated from plants of the *Thalictrum* genus, only **28** and its genin **12** have native acetates. Like for the β-effect upon introducing a hydroxyl, the β- and γ-effects of acetylation depend on the degree of substitution of the C atom and increase with the number of protons on this atom [70].

Any of the triterpenoid hydroxyls can be glycosylated. The magnitude of the effects from glycosylating secondary hydroxyls ranges from 8.9 to 14.0 ppm. Thus, the CS of C-3 varies from 78.0-80.1 ppm to 88.7-89.1 ppm; of C-16, from 72.1 to 82.7; of C-22, from 72.7-75.8 to 85.3-86.7. If a 3-OH is glycosylated, the signal for C-2 shifts to strong field by 0.7-1.5 ppm whereas the signal for quaternary C-4 either does not change position (**11**, **24**, and **26**) or shifts to weak field ($\Delta\delta$ +~1.1 ppm for **31** and **39**, **10** and **22**). Changes in the CSs for β-C atoms C-15 and C-17 upon glycosylation of the 16-OH are analogous to those of the corresponding atoms C-2 and C-4 (Tables 5a-5f).

The shift of the NMR signal for an α-C atom upon glycosylation of a primary alcohol is much less than upon glycosylation of a secondary alcohol and lies in the range 2.6-4.7 ppm. The resonance of the β-C atom shifts to weak field by 0.2-1.0 ppm. The given values of $\Delta\delta$ refer to an equatorial 29-CH_2OH (**14** and **15** compared with their genin **4** and **55** and **56** compared with the corresponding genin **52**). An axial 30-CH_2OH is sterically hindered toward glycosylation so that glycosides at this position are not observed. Glycosylation of the carboxyl (**12** and its glycoside **28**) causes a strong-field shift of the carbonyl C atom by 6.4 ppm.

TABLE 5a. ^{13}C Chemical Shifts of Cycloartane Genins (**4**, **9**-**11**, **31**, **32**, **52**)

C atom	**4** [22]	**9** [30]	**10** [31]	**11a** [35]	**11** [36]	**31** [42]	**32** [42]	**52** [24]
1	32.6	32.5	32.4	32.4	32.4	32.4	32.4	32.0
2	31.0	31.3	30.7[d]	31.1	31.3	31.7	31.7	30.6
3	74.8	78.0	80.3	78.0	80.0	80.1	80.2	73.4
4	44.9	41.1	43.9	41.0	41.1	43.8	43.8	44.4
5	42.3	47.6[d]	48.0	47.4	47.5	48.6	48.7	41.2
6	21.4	21.5	21.9	21.5	21.5	21.8	21.9	20.8
7	26.9	26.5	26.5[e]	26.7	28.0	27.0	26.9	26.1
8	48.6	48.4[d]	48.5	48.2	48.2	47.7	47.8	48.2
9	20.3	20.0	21.3	20.0	20.0	21.7	21.8	19.5
10	26.0	26.8	26.4	26.6	26.6	26.0	26.0	25.8
11	26.5	26.5	26.9[e]	26.2	26.3	26.7	26.5	26.0
12	33.7	33.3[e]	33.4	33.3	35.9	36.1	35.9	33.2
13	46.3	45.8	45.8	45.4	45.4	45.3	45.6	45.7
14	47.6	47.1	47.1	47.0	49.1	48.4	48.5	46.6
15	49.0	48.8	48.8	35.8	33.4	30.6	30.5	47.9
16	72.1	72.0	72.1	27.9	26.7	30.0	27.8	71.3
17	53.5	57.5	57.5	49.0	49.1	40.7	44.8	52.4
18	20.7	18.3	18.2	18.2	19.6	26.3	26.4	19.1
19	30.5	30.3	31.7[d]	30.0	30.0	31.3	30.7	30.0
20	36.2	28.7	28.8	41.6	41.7	52.5	55.6	32.7
21	14.8	19.4	19.5	12.0	12.1	104.9	108.7	14.6
22	75.8	33.1[e]	33.1	72.7	72.7	75.0	76.7	82.2
23	34.0	27.9	28.1	34.7	34.8	80.7	79.0	27.0
24	123.9	77.2	77.3	125.1	125.2	f	-	38.2
25	132.4	72.5	72.6	137.6	137.7	-	-	80.1
26	26.2	26.2	26.5	22.2	61.1	21.3	21.3	28.3
27	18.2	26.5	25.6	61.0	22.2	19.8	19.8	27.4
28	19.7	20.3	20.4	19.6	18.4	19.8	18.9	20.1
29	68.5	25.6	21.7	26.1	26.2	18.4	18.6	66.9
30	11.4	14.8	64.6	14.7	14.9	64.5	64.6	11.1
OMe						54.5	54.8	

[a]Spectrum taken in $CDCl_3$, [b]in DMSO-d_6, [c]in MeOH-d_4, all others in C_5D_5N.
[d,e]Assignment of signals is equally probable within columns.
[f]Signal overlaps with solvent.

TABLE 5b. ^{13}C Chemical Shifts of Glycosides (**14**-**20**)

C atom	**14** [20]	**15** [23]	**16** [24]	**17** [25]	**18** [26]	**19** [26]	**20** [89]
1	32.6	32.1	32.1	32.2	32.1	32.4	32.1
2	29.7	29.5	29.5	29.5	29.4	29.8	29.4
3	82.1	81.7	81.1	81.9	81.7	81.6	81.6
4	45.3	45.1	45.9	45.1	45.0	44.9	44.9
5	41.2	40.7	40.7	40.9	40.7	40.7	40.7
6	21.1	20.8	20.7	20.8	20.7	20.7	20.7
7	26.8	26.6	26.4	26.6	26.5	26.5	26.5
8	48.8	48.5	46.6	48.4	48.4	48.4	48.4
9	20.3	19.8	19.6	20.0	19.8	19.8	19.7
10	26.3	26.0	25.7	26.1	25.9	25.9	25.9

TABLE 5b. (Continued)

C atom	**14** [20]	**15** [23]	**16** [24]	**17** [25]	**18** [26]	**19** [26]	**20** [89]
11	26.6	26.0	26.4	26.3	26.3	26.3	26.3
12	33.8	33.5	33.6	37.8	33.6	33.6	33.5
13	46.3	46.0	45.0	46.2	46.0	46.0	45.9
14	47.7	47.3	47.2	47.5	47.3	47.3	47.3
15	49.1	49.7	48.8	48.5	48.7	48.4	48.4
16	72.1	71.9	71.7	72.0	71.7	71.9	71.9
17	53.3	51.9	53.0	53.3	53.0	53.2	52.9
18	21.0	20.6	19.7	20.5	20.6	20.6	20.5
19	31.9	30.5	30.6	30.4	30.5	30.5	30.4
20	36.3	34.5	36.0	36.8	36.0	36.5	35.5
21	14.9	13.1	14.6	15.5	14.7	15.0	14.3
22	75.6	85.3	75.2	76.3	75.1	72.5	71.8[d]
23	34.0	33.4	33.5	128.5	33.0	39.6	39.3
24	123.8	123.1	123.9	139.8	125.5	72.9	74.8[d]
25	131.9	131.5	132.0	70.0	137.5	f	-
26	26.2	25.9	18.1	30.9	61.2	110.0	110.0
27	18.4	18.2	26.0	30.9	22.5	18.8	19.4
28	19.9	19.7	20.6	19.6	19.5	19.8	19.5
29	71.5	71.4	71.1	71.2	71.1	71.0	71.0
30	12.1	11.8	11.7	11.8	11.7	11.7	11.7
	3-O-Gal*p*		3-O-Ara*p*	3-O-Gal*p*			
1′	106.2	106.4	106.4	106.2	106.5	106.1	106.1
2′	75.9	75.6	73.2	73.5	73.3	73.3	73.3
3′	73.8	73.4	74.9	75.6	75.5	75.4	75.4
4′	70.8	70.5	70.0	70.5	70.4	70.4	70.4
5′	76.5	76.3	67.0	76.3	76.2	76.1	76.1
6′	63.5	62.5		63.3	63.0	63.0	63.0
	29-O-Glc*p*						
1″	105.2	106.6	105.1	105.0	105.0	104.9	104.9
2″	75.9	75.4	75.4	75.3	75.3	75.2	75.2
3″	79.0	78.9	78.7	78.8	78.4	78.5	78.6
4″	72.5	72.0	71.8	72.3	72.1	72.0	71.9
5″	78.2	78.0	78.4	78.0	78.0	77.9	78.0
6″	62.9	63.1[d]	62.8	62.6	62.5	62.4	62.4
		29-O-Glc*p*					
1‴		105.3					
2‴		75.6					
3‴		78.7					
4‴		72.0					
5‴		78.2					
6‴		63.2[d]					

[a]Spectrum taken in $CDCl_3$, [b]in DMSO-d_6, [c]in MeOH-d_4, all others in C_5D_5N.
[d,e]Assignment of signals is equally probable within columns.
[f]Signal overlaps with solvent.

TABLE 5c. ^{13}C Chemical Shifts of Glycosides (**21**-**27**)

C atom	**21** [29]	**22** [32]	**23** [33][b]	**24** [35]	**25** [36]	**26** [36]	**27** [39]
1	32.3	32.2	31.3	32.1	32.2	32.0	32.3
2	29.9	30.0	28.9	29.6	30.0	29.7	30.0
3	88.7	89.6	88.6	88.7	88.6	89.1	88.4
4	41.3	45.0	43.9	41.0	41.3	41.1	41.2
5	47.8	48.0	47.4	47.6	47.7	47.5	47.9
6	21.2	21.9	21.3	21.3	21.2	20.6	21.1
7	26.4	26.5[d]	26.1	26.2	28.0	27.8	26.1
8	48.2	48.6	47.8	47.9	48.0	47.8	47.7
9	20.1	21.3	20.2	20.2	20.1	19.8	19.9
10	26.4	26.2[d]	24.9	26.7	26.3	26.1	26.3
11	26.4	25.7[d]	25.5	26.1	26.2	26.0	26.7
12	33.6	33.6	32.4	33.3	35.9	35.6	33.4
13	45.8	45.8	44.7	45.4	45.4	45.2	45.4
14	47.1	47.0	46.0	47.0	49.1	48.9	49.1
15	48.2	48.1	48.1	35.9	33.4	33.2	35.8
16	82.7	82.7	70.5	28.0	26.7	26.5	28.0
17	57.8	57.8	56.2	49.0	49.1	48.9	49.0
18	17.5	17.5	17.6	18.2	19.6	19.4	18.2
19	30.2	30.0	29.2	29.6	29.7	29.5	29.6
20	29.7	29.6	28.3	41.0	41.7	41.4	41.7
21	19.5	19.7	17.6	12.0	12.1	11.9	12.1
22	33.1	33.2	32.3	72.8	72.7	72.6	72.7
23	28.9	28.9	27.1	34.7	34.9	34.6	34.8
24	78.1	77.1	76.6	125.0	125.2	124.9	125.2
25	72.8	72.7	71.5	137.7	137.7	137.4	137.7
26	26.3	26.2[d]	25.9	61.0	61.1	60.8	61.1
27	25.8	25.7	24.8	22.1	22.3	22.0	22.7
28	20.5	20.6	19.8	19.6	18.4	18.1	19.5
29	25.6	21.3	19.7	25.4	25.8	25.6	25.6
30	15.4	63.5	65.3	15.1	15.4	15.1	15.5
	3-O-Ara*p*		3-O-Xyl*p*	3-O-Glc*p*	3-O-Fuc*p*		
1′	106.9	106.1	103.6	104.9	106.9	107.0	105.1
2′	72.7[e]	72.7	79.7	75.2	73.5	74.9	76.5
3′	74.4	74.0	75.8	75.2	75.7	75.6	77.1
4′	69.1	68.7	69.2	73.5	82.9	77.8	84.8
5′	66.2	65.7	65.1	77.2	70.4	72.7	70.3
6′				69.7	17.9	17.8	17.4
	16-O-Glc*p*		Xyl*p*	Rha*p*	Glc*p*		Rha*p*
1″	106.5	106.5	103.8	103.4	106.6	102.7	101.9
2″	75.5	75.6	74.1	83.1	75.8	78.5	72.3
3″	78.4	78.4	75.8	72.8	78.9	78.2	72.4
4″	71.9[e]	71.9	69.2	74.5	71.4	71.4	74.1
5″	76.6	76.7	65.6	70.5	77.4	76.6	69.5
6″	68.4	68.4		18.4	69.9	69.8	18.7

TABLE 5c. (Continued)

C atom	**21** [29]	**22** [32]	**23** [33][b]	**24** [35]	**25** [36]	**26** [36]	**27** [39]
	Rha*p*			Qui*p*		Glc*p*	
1‴	102.2	102.2		106.3	105.3	105.3	107.0
2‴	72.7[e]	72.3		76.7	75.4	75.6	75.7
3‴	72.2[e]	72.7		78.5	77.9	78.2	78.7
4‴	74.0	74.0		71.2	76.9	71.7	71.5
5‴	69.5	69.5		77.6	72.9	78.2	78.5
6‴	18.6	18.6		17.6	18.6	62.5	62.8
				Ac		Rha*p*	
1⁗				21.2; 170.0		101.7	
2⁗						72.1	
3⁗						72.3	
4⁗						74.1	
5⁗						70.4	
6⁗						18.5	

[a]Spectrum taken in $CDCl_3$, [b]in DMSO-d_6, [c]in MeOH-d_4, all others in C_5D_5N.
[d,e]Assignment of signals is equally probable within columns.
[f]Signal overlaps with solvent.

TABLE 5 d. ^{13}C Chemical Shifts of Glycosides (**28**-**30**, **39**-**44**)

C atom	**28** [40][c]	**29** [41]	**30** [41]	**39** [43]	**40**, **42** [43]	**41** [43]	**43**, **44** [44]
1	32.3	30.5	30.7	32.0	33.2	32.0	33.2
2	28.0	30.0	30.5	30.5	31.1	30.5	32.0
3	81.3	89.4	89.7	89.1	90.9	89.1	89.8
4	51.5	45.2	45.4	44.9	46.1	44.9	45.5
5	49.3	47.9	48.4	48.5	49.9	48.5	48.1
6	23.2	22.6	22.8	21.9	22.6	21.9	22.1
7	27.6	26.7	26.3	26.6	27.9; 27.3	26.6	26.7
8	50.0	48.2	48.4	47.7	49.1	47.7	48.8
9	22.1	19.8	19.9	21.2	22.2	21.2	21.6
10	26.8	26.2	26.4	25.7	26.9	25.7	27.2
11	27.5	26.2	26.7	25.9	28.8; 27.9	25.9	26.9
12	33.8	36.2	35.9	35.9	37.2; 37.1	35.9	36.1; 36.3
13	46.5	45.2	45.6	45.3	46.6; 46.7	45.3	45.8
14	47.7	48.8	48.7	48.5	49.9	48.5	48.9
15	49.6	32.0	32.1	29.9	31.1	29.9	30.4
16	72.9	26.9	27.0	29.9	31.1	27.6	30.2
17	57.8	45.9	45.4	40.6	41.9; 45.8	44.3	41.3; 45.1
18	20.6	19.6	19.7	25.7	27.3	25.7	25.9
19	30.2	29.8	30.0	29.9	32.6; 32.0	29.9	31.0
20	31.1	52.3	53.1	52.3	53.6; 55.5	55.5	52.6; 56.7
21	18.2	-	173.5	104.8	106.1; 109.6	108.5	98.8; 101.6
22	34.1	72.2	72.3	74.8	76.1; 76.4	76.5	77.0; 77.5
23	27.3	35.2	35.5	80.6	79.9; 81.9	78.8	78.6; 80.5
24	81.4	122.2	122.4	f	-	-	-
25	72.9	132.8	133.2	-	-	-	-

TABLE 5 d. (Continued)

C atom	**28** [40][c]	**29** [41]	**30** [41]	**39** [43]	**40**, **42** [43]	**41** [43]	**43**, **44** [44]
26	25.9	25.8	26.0	21.2	20.9	21.2	21.3
27	25.8	18.0	18.3	19.7	19.7	19.7	19.9
28	20.0	18.5	18.7	18.6	19.5	18.6	18.8
29	172.9	19.7	19.9	18.4	19.5	18.4	18.5
30	21.9	60.5	60.6	63.2	64.6	63.2	63.5
	Ac		OMe	OMe	OMe		
	21.2; 172.7		54.5	55.9	54.7		
	21.4; 173.4			56.4			
				3-O-Glc*p*			
1′	94.6	105.2	105.4	106.0	106.9	106.0	106.2
2′	77.6	80.0	80.1	75.4	75.0	75.4	75.6
3′	79.2	76.1	76.2	78.5	79.5	78.5	79.5
4′	70.8	72.6	72.8	71.6	70.4	71.6	72.1
5′	77.0	76.4	76.2	78.2	77.8	78.2	78.7
6′	69.7	68.1	68.4	62.7	68.2	62.7	68.3
	Xyl_f	Rha*p*			Rha*p*		Rha*p*
1″	105.6	100.7	100.9		103.1		103.0
2″	74.9	71.9	72.0		72.9		72.4
3″	77.5	72.0	72.3		73.1		72.9
4″	71.0	74.3	74.5		73.7		74.2
5″	66.8	69.1	69.1		69.2		69.6
6″		18.5	18.6		19.5		18.6
		Rha*p*					
1‴	101.5	102.3	102.6				
2‴	-	71.9	72.3				
3‴	72.1	72.2	72.4				
4‴	73.8	73.8	74.0				
5‴	70.0	69.6	69.8				
6‴	18.4	18.3	18.5				
			21-O-Glc*p*				
1⁗			96.1				
2⁗			73.8				
3⁗			78.5				
4⁗			71.2				
5⁗			77.7				
6⁗			69.6				
			Xyl*p*				
1⁗′			105.7				
2⁗′			74.8				
3⁗′			78.1				
4⁗′			71.0				
5⁗′			66.8				

[a]Spectrum taken in $CDCl_3$, [b]in DMSO-d_6, [c]in MeOH-d_4, all others in C_5D_5N.
[d,e]Assignment of signals is equally probable within columns.
[f]Signal overlaps with solvent.

TABLE 5e. ^{13}C Chemical Shifts of Glycosides (**45**-**51**)

C atom	**45** [45]	**46** [46]	**47** [46]	**48** [47]	**49** [47]	**50** [48]	**51** [48]
1	32.3	30.8	31.5	30.8	31.4	30.7	30.7
2	30.7	29.9	29.9	30.3	30.5	30.3	30.3
3	89.8	89.3	89.3	89.7	89.6	89.6	89.7
4	45.4	45.3	45.3	45.4	45.4	45.4	45.4
5	48.1	47.6	47.4	48.2	48.2	48.2	48.2
6	22.4	22.6	22.5	22.9	22.8	22.8	22.9
7	27.2	27.7	27.0	27.7	27.0	27.6	27.5
8	49.0	48.2	48.2	48.5	48.3	48.4	48.5
9	21.6	20.1	20.1	20.1	20.1	20.1	20.1
10	26.1	26.4	26.5	26.4	26.5	26.5	26.5
11	27.8	26.6	26.6	26.5	26.7	26.4	26.4
12	36.6	35.7	35.8	35.8	36.0	35.8	35.8
13	45.7	45.5	45.3	45.5	45.4	45.4	45.4
14	49.0	48.8	48.8	48.8	48.8	48.8	48.8
15	26.7	32.2	32.2	32.3	32.3	32.3	32.3
16	31.7	26.7	26.9	27.0	26.9	27.0	27.0
17	41.0	44.7	40.7	44.8	40.7	44.6	44.5
18	20.4	18.6	19.5	18.7	19.7	18.8	18.7
19	30.5	29.8	29.7	30.1	30.1	30.1	30.1
20	53.2	54.8	52.5	54.8	52.5	54.3	54.9
21	99.1	108.7	104.9	108.7	104.9	109.2	109.0
22	75.7	76.7	75.0	76.7	75.0	73.3	74.8
23	81.7	79.0	80.6	79.0	80.6	82.8	83.1
24	123.8	122.7	123.7	122.6	123.8	75.0	75.9
25	136.3	136.1	135.9	136.1	135.8	147.9	146.7
26	18.7	26.0	26.0	26.0	26.0	112.3	112.7
27	26.4	19.7	19.6	19.8	19.8	19.8	19.7
28	20.2	18.6	18.6	18.8	18.7	18.7	19.1
29	21.7	19.9	19.9	19.9	19.9	19.9	19.9
30	63.8	60.7	60.7	60.7	60.7	60.6	60.6
		OMe	OMe	OMe	OMe	OMe	OMe
		55.5	54.6	55.6	54.6	55.5	55.7
				3-O-Glc*p*			
1′	106.6	105.4	105.4	105.4	105.3	105.4	105.4
2′	75.9	80.3	80.3	80.1	80.1	80.2	80.2
3′	79.2	76.3	76.3	76.3	76.3	76.2	76.2
4′	72.4	72.4	72.4	72.8	72.8	72.8	72.8
5′	77.5	78.2	78.2	76.6	76.6	76.5	76.5
6′	68.6	62.8	62.8	68.2	68.2	68.2	68.2
				Rha*p*			
1″	102.9	100.2	100.9	100.9	101.0	100.9	100.9
2″	72.8	71.9	72.0	72.2	72.1	72.0	72.0
3″	73.3	72.1	72.1	72.3	72.3	72.3	72.3
4″	74.4	74.5	74.4	74.4	74.5	74.5	74.5
5″	70.1	69.1	69.1	69.2	69.2	69.1	69.1
6″	19.1	18.5	18.4	18.5	18.5	18.7	18.7

TABLE 5e. (Continued)

C atom	**45** [45]	**46** [46]	**47** [46]	**48** [47]	**49** [47]	**50** [48]	**51** [48]
	21-O-Glc*p*		Rha*p*				
1‴	96.9			102.5	102.5	102.5	102.5
2‴	75.3			72.2	72.1	72.1	72.2
3‴	79.1			72.3	72.3	72.3	72.3
4‴	72.4			74.0	74.0	74.0	74.0
5‴	79.2			69.8	69.8	69.8	69.8
6‴	63.3			18.5	18.4	18.5	18.5

[a]Spectrum taken in $CDCl_3$, [b]in DMSO-d_6, [c]in MeOH-d_4, all others in C_5D_5N.
[d,e]Assignment of signals is equally probable within columns.
[f]Signal overlaps with solvent.

TABLE 5f. ^{13}C Chemical Shifts of Glycosides (**55**-**58**, **62**, **63**)

C atom	**55** [24]	**56** [24]	**57** [51]	**58** [89]	**62** [52]	**63** [52]
1	32.3	32.4	32.1	32.1	32.4	32.5
2	29.8	29.9	29.4	29.4	30.0	30.0
3	81.8	81.4	81.7	81.6	90.0	90.0
4	45.3	45.3	44.9	44.9	45.4	45.4
5	40.9	41.0	40.7	40.7	48.7	48.7
6	21.0	21.0	20.7	20.7	22.9	22.9
7	26.6	26.7	26.5	26.5	27.4	27.4
8	48.5	48.8	48.3	48.4	48.8	48.8
9	19.8	19.9	19.7	19.7	19.9	19.9
10	25.9	26.0	25.9	25.9	26.5	26.5
11	26.7	26.7	26.3	26.3	26.7	26.7
12	33.7	33.8	33.6	33.5	30.8	30.8
13	46.3	46.3	46.1	45.9	45.7	45.8
14	47.3	47.3	47.0	47.0	48.8	48.8
15	48.5	48.6	47.9	48.4	36.1	36.1
16	71.9	72.0	71.7	71.9	28.1	28.1
17	53.1	53.1	52.5	52.5	45.7	45.8
18	19.7	19.8	20.5	20.5	18.7	18.9
19	30.8	30.9	30.4	30.4	31.2	31.2
20	33.4	33.4	32.7	33.2	57.3	57.2
21	15.2	15.2	15.4	14.3	77.4	77.5
22	82.8	82.9	79.7	79.8	86.7	86.8
23	27.7	27.7	36.7	39.3	34.5	34.7
24	38.9	38.9	77.6	77.6	60.7	60.4
25	80.8	80.8	82.8	82.8	71.1	71.2
26	29.0	29.0	26.3	27.6[d]	29.2	29.2
27	28.0	28.0	23.4	29.9[d]	29.8	29.8
28	20.8	20.9	19.4	19.5	21.2	21.2
29	71.6	71.4	71.1	71.0	20.1	20.1
30	11.6	12.0	11.7	11.7	60.8	60.9

TABLE 5f. (Continued)

C atom	**55** [24]	**56** [24]	**57** [51]	**58** [89]	**62** [52]	**63** [52]
	3-O-Gal*p*	3-O-Ara*p*	3-O-Gal*p*		3-O-Glc*p*	
1′	106.8	106.8	106.1	106.1	105.4	105.4
2′	73.6	73.6	73.3	73.3	76.3	76.4
3′	75.9	75.3	75.5	75.4	80.2	80.2
4′	70.8	70.4	70.4	70.4	72.1	72.1
5′	76.7	67.4	76.2	76.1	76.6	76.6
6′	63.2		63.0	63.0	68.6	68.6
	29-O-Glc*p*				Rha*p*	
1″	105.7	105.7	105.0	104.9	101.0	101.0
2″	75.8	75.7	75.3	75.2	72.3	72.3
3″	79.0	79.1	78.6	78.6	72.4	72.4
4″	72.1	72.2	72.0	71.9	74.5	74.5
5″	78.7	78.8	78.0	78.0	69.2	69.2
6″	62.7	63.2	62.4	62.4	18.5	18.5
					Rha*p*	
1‴					102.7	102.7
2‴					72.2	72.3
3‴					72.9	72.9
4‴					73.9	73.9
5‴					69.8	69.8
6‴					18.7	18.7
					22-O-Glc*p*	
1⁗					103.1	103.1
2⁗					81.5	81.3
3⁗					78.6	78.6
4⁗					71.6	71.2
5⁗					78.6	77.3
6⁗					63.0	68.9
					Glc*p*	
1′′′′′					105.4	105.4
2′′′′′					75.5	75.5
3′′′′′					78.7	78.2
4′′′′′					71.9	71.9
5′′′′′					79.8	79.8
6′′′′′					63.9	63.9
						Xyl*p*
1′′′′′′						105.9
2′′′′′′						75.0
3′′′′′′						78.2
4′′′′′′						71.2
5′′′′′′						67.2

[a]Spectrum taken in $CDCl_3$, [b]in DMSO-d_6, [c]in MeOH-d_4, all others in C_5D_5N.
[d,e]Assignment of signals is equally probable within columns.
[f]Signal overlaps with solvent.

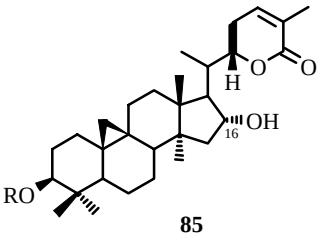
TABLE 6. ^{13}C Chemical Shifts of C-15, C-16, and C-17 of 16-Hydroxy-Epimers **55** [24] and **85** [69]

Compound	C-15	C-16	C-17
Aquilegioside I (**85**) (16α-OH)	48.7	77.2	57.5
Thalicoside A1 (**55**) (16β-OH)	48.5	71.9	53.1

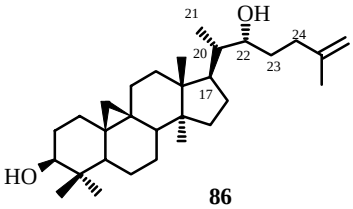
TABLE 7. ^{13}C Chemical Shifts of C-17 and Sidechain C Atoms for 22-Hydroxy-Epimers of Cycloartanes **11** [35] and **86** [71] Compared with Cycloartanol (**3a**) [66] and Hydroxycholestanols (**87**, **88**) Compared with Cholestanol (**89**) [72]

Compound	C-17	C-20	C-21	C-22	C-23
3a 3β-Hydroxycycloartane	52.4	35.9	18.3	36.4	25.0
11 (22S)	49.0	41.6	12.0	72.7	34.7
86 (22R)	52.3	36.0	18.4	76.8	28.1
87 (3β-OH, R=H)	56.3	35.8	18.8	36.3	23.9
88 (22S) R=OH	52.6	40.3	11.6	73.8	33.3
89 (22R) R=OH	53.2	42.6	12.5	74.0	27.5

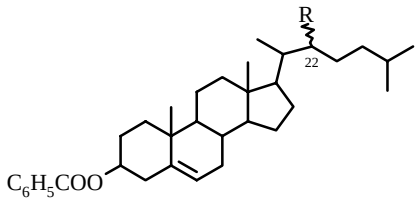
Most examined *Thalictrum* triterpenoids with an acyclic sidechain contain a C-22 hydroxyl. It has the *S*-configuration in compounds for which the configuration has been determined. The CSs of the neighboring C atoms are sensitive to epimerization of C-22. CSs were compared using the ^{13}C NMR spectrum for cycloartane **86**, which was isolated from *Amberboa ramose* [71] and has a 22*R*-OH in the acyclic sidechain.



85



86



87 - 89

R = β-D-Glc*p*(1→6)-β-D-Glc*p*(1→2)-α-L-Ara*p*

Table 7 shows that the CSs of C-22 depend on its configuration. The value $\Delta\delta$ is +4.1 ppm on going from the *S*-isomer to the *R*-isomer. The signal for C-23 shifts more clearly by +9.7 ppm for the *S*-isomers and +3.1 ppm for the *R*-isomers. It should be mentioned that an analogous picture was observed for 22(*R*,*S*)-hydroxycholestanols (**87** and **88**) [72]. However, atoms C-17 ($\Delta\delta$ 3.1-3.7 ppm) and C-21 ($\Delta\delta$ 6.3-7.2) are somewhat shielded in these compounds whereas C-20 ($\Delta\delta$ +4.5-6.8 ppm) is substantially deshielded (the $\Delta\delta$ in parentheses are given for the *R*- and *S*-isomers, respectively, compared with cholestanol **89**). These changes in the reviewed cycloartanes are not so unambiguous and are examined only for C-22 and C-23. The explanation for these phenomena should probably be sought in structural differences of the sidechains of cycloartane triterpenoids and hydroxycholestanols.

The conformation of the sidechains in cycloartane triterpenoids is difficult to study. Only single instances of reports of this endeavor have appeared. Thus, the structure of artifact **4a** was established using XSA [21]. It showed that the sidechain is stabilized through an intramolecular H-bond (IHB) between the 16-OH and the O atom of the THF ring. Figure 1a shows this conformation of the sidechain in **4a** as a Newman projection along the C-20—C-17 axis. The presence of an IHB is also evident in the ^{13}C NMR spectra. The signal for C-21 in the ^{13}C NMR spectrum of thalicoside A peracetate (**14a**) shifts by 2.2 ppm to strong field compared with its position in the spectrum of glycoside **14**. This cannot be explained by effects of acylating the OH groups on C-16 and C-22. An analogous shift in the position of the signal for C-21 occurred in the spectrum of the methyl ester of thalicoside A (**14b**) and the acetate artifact (**4d**) (Table 8). It was assumed that the sidechains in **4** and **14** are stabilized by IHBs between the OH groups on C-16 and C-22 and have a different conformation than in **14a**, **14b**, and **4d**, where an IHB is impossible. An analogous trend in the changes of CSs for C-20 and C-21 was observed for other derivatives of **14** upon establishing its structure [20].

TABLE 8. ^{13}C Chemical Shifts of C-20 and C-21 for Thalicogenin 4 [22], its Artifact (**4a**) [23], Artifact Peracetate (**4d**), Thalicoside A (**14**), its Peracetate (**14a**) and Methyl Ester (**14b**) [20]

C Atom	**4**	**14**	**4a**	**14a**	**14b**	**4d**
2021	36.2	36.3	35.2	32.5	34.4	38.7
	14.8	14.9	15.3	12.7	13.1	11.6

TABLE 9. ^{13}C Chemical Shifts of C-17 and Sidechain C Atoms of C-23-Epimers **44** [44] and **90** [75]

Compound	C-17	C-20	C-21	C-22	C-23
44 (23R)[a]	45.1	56.7	101.6	77.5	80.5
90 (23S)[b]	45.2	58.8	101.4	78.0	80.3

[a]Solvent C_5D_5N; [b]solvent $CDCl_3$.

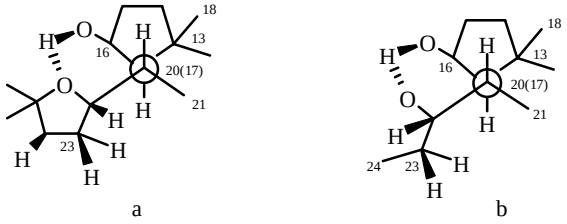
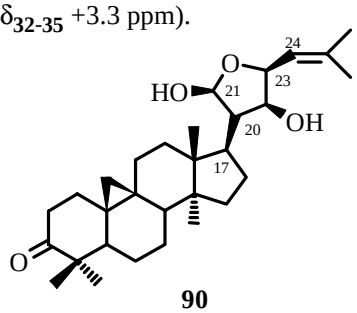


Fig. 1

A study of the conformations of sidechains in the aforementioned compounds that do and do not have IHBs using Dreiding molecular models and the good agreement of experimental values for the CSs of C-20, C-21, and C-22 with those calculated using the Beierbeck and Saunders method [73] confirmed that the sidechain of **4** has the conformation shown in Fig. 1b that is stabilized by an IHB between the OH groups on C-16 and C-22.

Compounds **31** and **32**, like genins **35** and **36**, are pairs of diastereomers with the opposite configuration at C-21. Analogously to the methylfuranosides [74] in **31** and **36** with 1,2-*cis*-substituents, the CSs of C-1 and C-2 are found at stronger field (C-21 104.9 ppm and C-20 52.5 ppm) compared with the 1,2-*trans*-substituents in **32** and **35** (C-21 108.7 ppm in **32** and **35** and C-20 54.8 and 55.6 ppm in **32** and **35**, respectively). Coupling of *syn*-1,3 H-21-α and H-17-α produces a weak-field shift by 4.1 ppm for C-17 in squarrogenin 2 (**32**) compared with squarrogenin 1 (**31**). C-22 and C-23 are less sensitive to the spatial location of substituents on C-21. The change of their CSs is 1.6-1.7 ppm to weak field for C-22 and to strong field for C-23 on going from the *R*-isomer to the *S*-isomer. The pair of compounds **33** and **34** differs from **31** and **32** by the nature of the C-21 substituent. It should be expected that the methoxyl (**31** and **32**) causes a larger shift of the signal for a C-α atom than for a OH (**33** and **34**). The signals for C-21 occur at weaker field by 6.1 and 7.1 ppm in **31** and **32** than the corresponding signals in the other stereoisomeric pair (Table 5).

The next two pairs of diastereomers are **31** and **36** and **32** and **35** with the opposite configuration at C-22. The CSs of the C atoms in the sidechain were weakly sensitive to the spatial location of the C-22 substituents. Even the position of the signal for this atom does not change. Insignificant changes are observed for C-20 ($\Delta\delta_{\mathbf{32\text{-}35}}$ +0.8 ppm) and the C atoms of the double bond (C-24 $\Delta\delta_{\mathbf{32\text{-}35}}$ -3.6 ppm; C-25 $\Delta\delta_{\mathbf{32\text{-}35}}$ +3.3 ppm).



90

Yet another pair of stereoisomers consists of compounds with the opposite orientation of C-23 substituents. It was stated that only one component of this pair was isolated from a plant of the *Thalictrum* genus (**44**); the other component (argenteanone A **90**), from *Aglaia argentea* [75]. Table 9 shows that the absolute configuration of C-23 has little effect on the CSs of the surrounding C atoms.

BIOLOGICAL ACTIVITY OF TRITERPENOID GLYCOSIDES FROM PLANTS OF THE *Thalictrum* GENUS

Natural triterpenoid glycosides have a broad spectrum of biological activity. It should be noted also that they have fungicidal and antibacterial, anti-inflammatory and antitumor, and antiallergic and immunostimulating activites [76]. Saponins have a significant influence on metabolism and the cardiovascular system of mammals [11, 77, 78]. The effects of triterpenoid glycosides on fertility of animals have been reported [86, 88].

The basis of such a variety of medical and biological activities of triterpenoid glycosides is assumed to be their ability, on one hand, to affect biochemical processes occurring in the cell and, on the other, to modify structural and functional properties of biological membranes and, therefore, to act as bioregulators [81, 82].

Japanese researchers have studied the biological activity of triterpenoid saponins from plants of the *Thalictrum* genus and authored many publications on the isolation of triterpenoid glycosides from them. They indicate that *Thalictrum* species are used in traditional Japanese medicine to treat stomach illnesses. Among the glycosides isolated by them are several cycloartane compounds with a THF ring on C-17 that have strong activity in the lymphocyte transformation test (LTT) [10].

The total triterpenoid glycosides from *T. foetidum* [cyclofoetosides A (**21**) and B (**22**) and foetoside C (**72**)] and pure foetoside C (**72**) were studied in animals with experimental endogenous hypercholesterinemia. Regular administration (7 days at a dose of 50 mg/kg) of total foetosides and pure foetoside C showed that both preparations have a positive effect on lipid and cholesterol exchange. The sum of compounds **21**, **22**, and **72** lowers the cholesterol level in blood serum by 25.5 mg%; **72**, by 60.0 mg% relative to controls [83, 84].

Certain dominant pure glycosides isolated from *T. minus* and *T. foetidum* were studied for antitumor activity in animals [85]. The most interesting results were found for foetoside C (**72**), thalicoside A (**14**), and cyclofoetoside B (**22**). Thus, oleanane pentaoside **72** at a dose of 30 mg/kg inhibited the growth of grafted tumor strains as follows: sarcoma 45-91%, RMC-1 breast cancer 85%, and Pliss lymphosarcoma and Walker carcinosarcoma 84-86%. Cycloartane bioside **14** moderately inhibited growth of Pliss lymphosarcoma, sarcoma 45, and RMC-1 (73-77%). Sarcoma 45 is rather sensitive to **22** (87% tumor-growth inhibition).

From the applied viewpoint, **72** was significantly effective in experiments on rats with grafted medically resistant tumor strains. In particular, growth of sarcoma 45, which is resistant to sarcolysine used in cancer clinics, was inhibited by **72** by up to 90%. The remaining two compounds exhibited moderate (**14**) or weak (**22**) activities [85].

The contraceptive activity of triterpenoid glycosides from *T. minus*, *T. foetidum*, and *T. squarrosum* has been thoroughly studied [86]. As it turned out, subcutaneous administration *post coitum* of total triterpenoid glycosides from *T. minus* was most active. Total glycosides from *T. foetidum* and *T. squarrosum* showed less contraceptive activity.

Mildly toxic (LD_{50} 1800 mg/kg) **14** from *T.minus* showed high (80-100%) *post coitum* activity at low doses (0.001-0.1 mg/kg) [86]. A study of the mechanism of the contraceptive activity of thalicoside A established that the achieved effect was explained by the influence of this compound on the formation of endometrium and the transport rate of ova [87].

The effect of **14** on ovulation and gonadotropin level in blood serum of laboratory animals has been studied [88]. It was found that 5-day oral administration of **14** to rabbits at a dose of 1 mg/kg stimulates ovulation. It was also determined that **14** changes the level of gonadotropin production. Enteral administration over five days at a dose of 1 mg/kg to rats lowered the content of lutenizing hormone and increased the content of follicle-stimulating hormone in active stages of the cycle (proestrus-estrus). The observed effect of dysrhythmia in incretion of gonadotropins caused by thalicoside A can apparently be used to treat various forms of ovarian polycystosis in women that is accompanied by hormone unbalance.

Thus, investigation of the biological activity of *Thalictrum* triterpenoid saponins revealed the most promising directions for their use. The compounds have signficiant antitumor activity and are nonhormonal. At low doses they have significant effects on the reproductive system of mammals.

REFERENCES

1. P. L. Shiff, in: *Alkaloids: Chemical and Biological Perspectives*, Pergamon, New York (1987), p. 271; *Chem. Abstr.*, **107**, 228242u (1988).
2. P. L. Shiff, in: *Alkaloids: Chemical and Biological Perspectives*, Pergamon, New York (1996), Vol. 11, p. 376.
3. S. Yu. Yunusov, *Alkaloids* [in Russian], Fan, Tashkent (1981).
4. R. Djurkovic, O. Gasic, and Y. Popovic, *Hem. Pregl.*, **32**, 86 (1991); *Chem. Abstr.*, **118**, 22445f (1993).
5. B. Kuzmanov and H. Dutschewska, *J. Nat. Prod.*, **45**, 766 (1982).
6. A. S. Gromova, V. I. Lutskii, E. V. Kostyleva, N. N. Dedkova, and A. A. Semenov, *Izv. Sib. Otd. Akad. Nauk SSSR*, 129 (1981).
7. V. V. Telyat′ev, *Useful Plants of Central Siberia* [in Russian], Irkutsk (1985).
8. A. I. Shreter, *Medicinal Flora of the Soviet Far East* [in Russian], Meditsina, Moscow (1975).
9. A. A. Fedorov, ed., *Plant Resources of the USSR* [in Russian], Nauka, Leningrad (1984), p. 90.
10. T. Nohara, S. Yahara, and J. Kinjo, in: *Advances in Experimental Medicine and Biology*, **404**: *Saponins Used in Traditional and Modern Medicine*, G. R. Waller and K. Yamasaki, eds., Plenum Press, New York and London (1996), p. 263.
11. S. B. Mahato and A. K. Nandy, *Phytochemistry*, **30**, 1357 (1991).
12. S. B. Mahato, A. K. Nandy, and G. Roy, *Phytochemistry*, **31**, 2199 (1992).
13. M. I. Isaev, M. B. Gorovits, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 431 (1985).
14. M. I. Isaev, M. B. Gorovits, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 156 (1989).
15. A. A. Semenov, V. I. Lutsky, A. S. Gromova, E. V. Slavyanov, and V. N. Biyushkin, in: *Abstracts of the First International Conference on Chemistry and Biotechnology of Biologically Active Natural Products*, Varna, Bulgaria (1981), Vol. 3-1, p. 135.
16. A. S. Gromova, V. I. Lutsky, A. A. Semenov, V. Denisenko, and V. Isakov, in: *Abstracts of the Second International Conference on Chemistry and Biotechnology of Biologically Active Natural Products*, Budapest, Hungary (1983), p. 160.
17. A. A. Semenov, V. I. Lutsky, A. S. Gromova, T. V. Ganenko, E. A. Khamidullina, and N. N. Trofimova, in: *Advances in Experimental Medicine and Biology*, 405: *Saponins Used in Food and Agriculture*, G. R. Waller and K. Yamasaki, eds., Plenum Press, New York and London (1996), p. 193.
18. E. A. Khamidullina, N. N. Trofimova, A. S. Gromova, and V. I. Lutskii, *Khim. Interesakh Ustoich. Razvit.*, 195 (1999).
19. A. A. Semenov, in: *Abstracts of Third International Conference on Chemistry and Biology of Biologically Active Natural Products*, 4, Sofia, Bulgaria (1985), p. 315.
20. A. S. Gromova, V. I. Lutskii, A. A. Semenov, V. A. Denisenko, and V. V. Isakov, *Khim. Prir. Soedin.*, 213 (1984).
21. A. S. Gromova, V. I. Lutskii, A. A. Semenov, E. V. Slavyanov, V. N. Biyushkin, and G. I. Malinovskii, *Khim. Prir. Soedin.*, 718 (1982).
22. A. S. Gromova, V. I. Lutskii, A. A. Semenov, V. A. Denisenko, and V. V. Isakov, *Khim. Prir. Soedin.*, 207 (1984).
23. A. S. Gromova, V. I. Lutskii, S. V. Zinchenko, N. N. Trofimova, A. A. Semenov, and N. A. Nakhova, *Khim. Prir. Soedin.*, 103 (1993).
24. A. S Gromova, V. I. Lutsky, D. Li, S. G. Wood, N. L. Owen, A. A. Semenov, and D. M. Grant, *J. Nat. Prod.*, **63**, 911 (2000).
25. A. S. Gromova, V. I. Lutskii, S. V. Zinchenko, T. V. Ganenko, and A. A. Semenov, *Khim. Prir. Soedin.*, 567 (1993).
26. N. N. Trofimova, A. S. Gromova, V. I. Lutskii, A. A. Semenov, S. A. Avilov, A. I. Kalinovskii, D. Li, and N. Owen, *Izv. Akad. Nauk, Ser. Khim.*, 103 (1998).
27. N. N. Trofimova, A. S. Gromova, V. I. Lutsky, and A. A. Semenov, in: *Medicinal Raw Material and Phytopreparations for Medicine and Agriculture (Abstracts of International Conference)*, Karaganda (1999), p. 91.
28. S. Seo, J. Tomita, K. Tori, and J. Yashimura, *J. Am. Chem. Soc.*, **100**, 3331 (1978).
29. T. V. Ganenko, M. I. Isaev, V. I. Lutskii, A. A. Semenov, N. D. Abdullaev, M. B. Gorovits, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 66 (1986).

30. T. V. Ganenko, M. I. Isaev, N. D. Abdullaev, V. I. Lutskii, A. A. Semenov, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 370 (1985).
31. T. V. Ganenko, M. I. Isaev, A. S. Gromova, N. D. Abdullaev, V. I. Lutskii, M. F. Larin, A. A. Semenov, M. B. Gorovits, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 312 (1986).
32. T. V. Ganenko, M. I. Isaev, A. S. Gromova, N. D. Abdullaev, A. A. Semenov, M. B. Gorovits, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 341 (1986).
33. S. C. Yu, Q. L. Wu, L. W. Wang, and P. G. Xiao, *Chin. Chem. Lett.*, **10**, 485 (1999).
34. S. C. Yu, Q. L. Wu, L. W. Wang, and P. G. Xiao, *Zhongoaoyao*, **30**, 321 (1999).
35. Y. Yijun and W. Zhixing, *J. Chin. Pharm. Univ.*, **22**, 270 (1991).
36. H. Yoshimitsu, K Hayashi, K. Shingu, J. Kinjo, S. Yahara, K. Nakano, K. Murakami, T. Tomimatsu, and T. Nohara, *Chem. Pharm. Bull.*, **40**, 2465 (1992).
37. J. A. Dale and H. S. Moscher, *J. Am. Chem. Soc.*, **95**, 512 (1973).
38. Y. Letourneux, Q. Khuong-Huu, and M. Gut, *J. Org. Chem.*, **40**, 1674 (1975).
39. H. Yoshimitsu, M. Nishida, Z.-Z. Qian, Z.-H. Lei, and T. Nohara, *Chem. Pharm. Bull.*, **48**, 828 (2000).
40. Y.-H. Choi, N. G. Kim, and I. R. Lee, *Arch. Pharmacol Res.*, **19**, 429 (1996).
41. H. Yoshimitsu, K. Hayashi, M. Kumabe, and T. Nohara, *Phytochemistry*, **38**, 939 (1995).
42. V. I. Lutskii, E. A. Khamidullina, A. S. Gromova, and A. A. Semenov, *Khim. Prir. Soedin.*, 510 (1989).
43. E. A. Khamidullina, A. S. Gromova, V. I. Lutskii, A. L. Vereshchagin, A. A. Semenov, and M. F. Larin, *Khim. Prir. Soedin.*, 516 (1989).
44. E. A. Khamidullina, A. S. Gromova, V. I. Lutskii, S. V. Zinchenko, and A. A. Semenov, *Izv. Akad. Nauk, Ser. Khim.*, 1547 (1996).
45. E. A. Khamidullina, A. S. Gromova, V. I. Lutsky, D. Li, and N. L. Owen, *J. Nat. Prod.*, **62**, 1586 (1999).
46. H. Yoshimitsu, K. Hayashi, M. Kumabe, and T. Nohara, *Chem. Pharm. Bull.*, **41**, 786 (1993).
47. H. Yoshimitsu, K. Hayashi, M. Kumabe, and T. Nohara, *Chem. Pharm. Bull.*, **42**, 101 (1994).
48. H. Yoshimitsu, K. Hayashi, M. Kumabe, and T. Nohara, *Nat. Med.*, **51**, 131 (1997).
49. A. S. Gromova, V. I. Lutskii, A. A. Semenov, M. F. Larin, and R. B. Valeev, *Khim. Prir. Soedin.*, 376 (1987).
50. Yu. V. Gatilov, I. Yu. Bagryanskaya, V. I. Lutskii, A. S. Gromova, and A. A. Semenov, *Khim. Prir. Soedin.*, 533 (1987).
51. N. N. Trofimova, A. S. Gromova, V. I. Lutskii, A. A. Semenov, S. A. Avilov, D. Li, and N. L. Owen, *Izv. Akad. Nauk, Ser. Khim.*, 602 (1999).
52. H. Yoshimitsu, M. Nishida, S. Yahara, and T. Nohara, *Tetrahedron Lett.*, **39**, 6919 (1998).
53. H. Yoshimitsu, M. Nishida, and T. Nohara, *Tetrahedron*, **57**, 10247 (2001).
54. H. Ina and H. Iida, *Chem. Pharm. Bull.*, **34**, 726 (1986).
55. A. S. Gromova, V. I. Lutskii, A. L. Vereshchagin, and A. A. Semenov, *Khim. Prir. Soedin.*, 107 (1987).
56. T. V. Ganenko, A. S. Gromova, V. I. Lutskii, and A. A. Semenov, *Khim. Prir. Soedin.*, 262 (1982).
57. A. S. Gromova, V. I. Lutskii, A. A. Semenov, R. B. Valeev, G. A. Kalabin, and Yu. N. El′kin, *Khim. Prir. Soedin.*, 670 (1985).
58. A. S. Gromova, A. A. Semenov, V. I. Lutskii, S. V. Zinchenko, N. N. Trofimova, and Ya. V. Rashkes, *Khim. Prir. Soedin.*, 398 (1994).
59. T. V. Ganenko, M. I. Isaev, T. T. Gorovits, A. S. Gromova, V. I. Lutskii, A. A. Semenov, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 458 (1984).
60. H. Ina, Y. Ohta, and H. Iida, *Phytochemistry*, **24**, 2655 (1985).
61. A. S. Gromova, V. I. Lutsky, A. A. Semenov, D. Li, and N. L. Owen, *Phytochemistry*, **47**, 437 (1998).
62. R. A. Komoroski, E. C. Gregg, J. P. Shockcor, and J. M. Geckle, *Magn. Res. Chem.*, **24**, 534 (1986).
63. H. Schroder and E. Haslinger, *Magn. Res. Chem.*, **32**, 12 (1994).
64. H. Schroder and E. Haslinger, *Liebigs Ann. Chem.*, 751 (1993).
65. H. Schroder and E. Haslinger, *Liebigs Ann. Chem.*, 959 (1993).
66. W. Kamisako, C. Honda, K. Suwa, and K. Isoi, *Magn. Res. Chem.*, **25**, 683 (1987).
67. L.-J. Lin and M.-S. Shiao, *J. Nat. Prod.*, **52**, 595 (1989).
68. M. A. Khan, S. S. Nizami, M. N. I. Khan, S. W. Azeem, and Z. Ahmed, *J. Nat. Prod.*, **57**, 988 (1994).

69. M. Nishida, H. Yoshimitsu, M. Okawa, and T. Nohara, *Chem. Pharm. Bull.*, **51**, 956 (2003).
70. V. A. Denisenko, Candidate Dissertation in Chemical Sciences, PIBOC, FED, RAS, Vladivostok (1984).
71. N. Akhtar, A. Malik, N. Afza, and Y. Badar, *J. Nat. Prod.*, **56**, 295 (1993).
72. F. W. Wehrli and T. Nishida, in: *Progress in the Chemistry of Organic Natural Products*, Springer-Verlag, Vienna and New York (1979), Vol. 36, p. 114.
73. H. Beierbeck, J. K. Saunders, and J. W. ApSimon, *Can. J. Chem.*, **55**, 2813 (1977).
74. A. S. Shashkov and O. S. Chizhov, *Bioorg. Khim.*, **2**, 437 (1976).
75. O. R. Omobuwajo, M.-T. Martin, G. Perromat, T. Sevenet, K. Awang, and M. Pais, *Phytochemistry*, **41**, 1325 (1996).
76. M. F. Balandrin, in: *Advances in Experimental Medicine and Biology*, 404, *Saponins Used in Traditional and Modern Medicine*, G. R. Waller and K. Yamasaki, eds., Plenum Press, New York and London (1996), p. 1.
77. S. B. Mahato, S. K. Sarkar, and G. Poddar, *Phytochemistry*, **27**, 3037 (1988).
78. M. M. Anisimov and V. Ya. Chirva, *Usp. Sovrem. Biol.*, **90**, 351 (1980).
79. N. M. Pirozhkova, M. N. Mats, and V. K. Gorshkova, in: *Problems in Developing Medicinal Resources of Siberia and the Far East* [in Russian], Novosibirsk (1983), p. 261.
80. Jpn. Pat. No. 59073600 (1984); *Chem. Abstr.*, **101**, 123902g (1984).
81. M. M. Anisimov, L. I. Strigina, P. G. Gorovoi, D. L. Aminin, and I. G. Agafonova, *Rastit. Resur.*, **1**, 107 (2000).
82. B. A. Salakhutdinov, D. N. Dalimov, T. F. Aripov, I. I. Tukfatullina, R. Kh. Ziyatdinova, A. Zh. Dzhuraev, F. G. Kamaev, L. Yu. Izotova, B. T. Ibragimov, I. Mavridis, and P. Giastas, *Khim. Prir. Soedin.*, 209 (2002).
83. T. V. Ganenko, Candidate Dissertation in Chemical Sciences, IrIOC, SD, RAS, Irkutsk (1986).
84. T. V. Ganenko, A. S. Gromova, V. I. Lutsky, A. A. Semenov, and M. I. Isaev, in: *Abstracts of Third International Conference on Chemistry and Biotechnology of Biologically Active Natural Products*, Sofia, Bulgaria (1985), p. 330.
85. K. D. Rakhimov, S. M. Vermenichev, V. I. Lutskii, A. S. Gromova, T. V. Ganenko, and A. S. Semenov, *Khim.-Farm. Zh.*, 1434 (1987).
86. M. N. Mats, V. V. Korkhov, V. I. Lutskii, A. S. Gromova, T. V. Ganenko, and A. A. Semenov, *Rastit. Resur.*, 570 (1988).
87. USSR Pat. No. 1748321; *Byull. Izobret.*, 26 (1992) DSP.
88. V. V. Korkhov, V. V. Boikova, and E. A. Lesik, *Eksp. Klin. Farmakol.*, **58**, 43 (1995).
89. N. N. Trofimova, Candidate Dissertation in Chemical Sciences, ISU, Irkutsk (1999).