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TWO NEW TRITERPENES FROM CAMELLIA SINENSIS AND CAMELLIA SASANQUA

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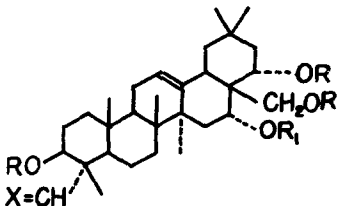
In a general survey on the seed-sapogenins of Camellia species, we have isolated from Camellia japonica L. three sapogenins, camelliagenin A, B, and C and established their structures as Ia, Ib and Ic, respectively (1). On the sapogenins of the other Japanese species of this genus, C. sinensis O. Kuntze (Thea sinensis L.) and C. Sasanqua Thunb., only little was known (2,3) until the recent publications (4) by Yoshioka and his coworkers on the isolation and structure determination of two major sapogenins, theasapogenol A (IIa) and B (IIb) obtained from the seeds of the former plant. This paper prompted us to record the results of our investigation on the seed-sapogenins of both plants mentioned above and to present evidence for the assignment of structures III and XVII for the two new sapogenins, camelliagenin D and E, isolated from both plants.

Ueda's method of isolation (3) followed by a silica gel chromatography afforded eight sapogenins (shown in Table 1) from each plant (5). Five of the sapogenins were found to be identical with Ia, Ib, Ic, IIa and IIb (6), and all of our results from preliminary experiments on the last two are compatible with the structures proposed (4,7).

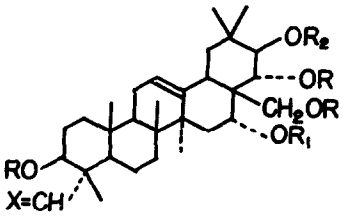
TABLE 1. Sapogenols from C. sinenses and C. Sasanqua

Name of Compd	No.	Mol. formula	m.p.(°C)	$[\alpha]_D$	Rf*	Color†	yield (%)** C.sinenses	yield (%)** C.Sasanqua
Camelliagenin A	Ia	$C_{30}H_{50}O_4$	282-283	+32.6°	1.0	r.v.	4.1	18
Camelliagenin B	Ib	$C_{30}H_{48}O_5$	200-205	+48.0°	0.94	g.b.	0.4	trace§
unidentified					0.88	y.b.	1.8	none
unidentified					0.78	br.	none	0.9
Camelliagenin C (1)	Ic	$C_{30}H_{50}O_5$	262-263	+51.2°	0.70	gr.br.	trace§	trace§
Camelliagenin D	XVII	$C_{30}H_{48}O_6$	250-258	+39.2°	0.59	y.	2.8	4.7
Barringtogenol C (Theasapogenol B)	IIb	$C_{30}H_{50}O_5$	286-289	+0.4°(Py.)	0.58	gr.	7.0	
Camelliagenin E	III	$C_{30}H_{48}O_6$	270-273	+64.0°	0.56	y.	17.4	8.3
Theasapogenol A	IIa	$C_{30}H_{50}O_6$	290-293	+21.3°(Py.)	0.39	r.v.	20.0	5.5

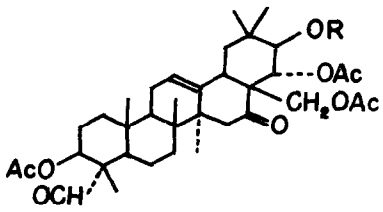
* Relative Rf in silica gel TLC. † Colors developed by sulfuric acid. Abbreviations of colors; r.=red, v.=violet, y.=yellow, g.=green, bl.=blue, br.=brown. ** Based on the crude sapogenin mixture. § not isolated, identified by TLC.



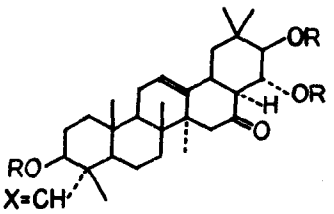
Ia: R=R_1=H, X=H_2
Ib: R=R_1=H, X=O
Ic: R=R_1=H, X=H, OH
VIII: R=R_1=Ac, X=$(OAc)_2$
IX: R=R_1=Ac, X=O
X: R=Ac, R_1=H, X=O



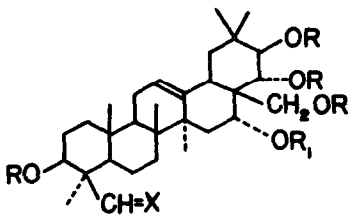
IIa: R=R_1=R_2=H, X=H, OH
IIb: R=R_1=R_2=H, X=H_2
III: R=R_1=R_2=H, X=O
IV: R=R_1=R_2=Ac, X=$(OAc)_2$
V: R=R_1=R_2=Ac, X=O
VI: R=R_2=Ac, R_1=H, X=O
VII: R=Ac, R_1=R_2=H, X=O
XV: R=R_1=R_2=Ac, X=H, OAc
XVI: R=R_1=R_2=Ac, X=H_2



XI: R=Ac
XII: R=H



XIII: R=H, X=O
XIV: R=Ac, X=$(OAc)_2$



XVII: R=R_1=H, X=O
XVIII: R=R_1=Ac, X=$(OAc)_2$
XIX: R=R_1=Ac, X=O
XX: R=R_1=H, X=H, OH
XXI: R=Ac, R_1=H, X=H, OAc
XXII: R=R_1=Ac, X=H, OAc

Camelliagenin E (III) On acetylation with Ac_2O and H_2SO_4, III yielded the heptaacetate IV, $C_{44}H_{64}O_{14}$, m.p. 267-268°, $[\alpha]_D$ 0° ($CHCl_3$) (8) which gave the amorphous pentaacetate V, $C_{40}H_{60}O_{12}$, by mild treatment with $NaHCO_3$; both IV and V exhibit no IR band due to a hydroxyl group. On the other hand, acetylation of III with Ac_2O pyridine afforded the amorphous tetraacetate VI, $C_{38}H_{58}O_{11}$, ν 3450, 3315, 2700, 1735 cm^{-1} and the triacetate VII, $C_{36}H_{54}O_9$, m.p. 212-216°, ν 3515, 3415, 2700, 1745, 1725 cm^{-1} (9). Five of the six oxygens in III are accounted for by hydroxyls, one primary and four secondary from the number of acetoxyl signals (Table 3) and the chemical shift of the carbinyl hydrogens (Table 2) in the acetates. The multiplicity of the carbinyl hydrogens in the spectra of VI and VII discloses the presence in III of an isolated 1,2-glycol system in which both hydroxyl groups are secondary and equatorially oriented. Furthermore, comparison of the spectra of V and VI, and VI and VII reveals that i) the unacetylated hydroxyl group in VI has an axial orientation and is not involved in the glycol system and that ii) the other unacetylated secondary hydroxyl group in VII is part of the 1,2-glycol system.

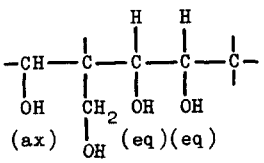
When VI and VII were submitted to CrO_3 oxidation in pyridine, the ketone XI, $C_{38}H_{54}O_{10}$,

TABLE 2. Lower Field Signals of Camelliagenin Derivatives (6)*

Compds	3α-H	16β-H	21α-H	22β-H	28-H_2	23-$H_{(2)}$	24-$H_{(2)}$	12-H
IV	4.83(br.t,8)	5.26	5.32(s)‡	5.32(s)‡	3.73(br.s)	6.78(s)		5.41‡
V	4.99(br.t,8)	5.26	5.33(s)‡	5.33(s)‡	3.75(br.s)	9.30(s)		5.43‡
VI	5.00(br.t,8)	4.20	5.42(d,10)§‡	5.55(d,10)§	3.67(br.s)	9.30(s)		5.38‡
VII	5.00(br.t,8)	4.20	3.99(d,10)	5.23(d,10)	3.66(br.s)	9.30(s)		5.37
VIII	4.85(br.t,8)	5.33‡		5.25(t,9)‡	3.80(br.s)	6.79(s)		5.41‡
IX	4.98(t,8)	5.33‡		5.24(t,9)‡	3.78(br.s)	9.28(s)		5.41‡
X	5.01(br.t,8)	4.28		5.35(q,11,7)‡	3.74(br.s)	9.31(s)		5.41‡
XI	4.97(br.t,8)	=O	5.15(d,10)	5.53(d,10)‡	4.15(d,12) 4.43(d,12)	9.28(s)		5.50‡
XII	4.98‡	=O	4.01(d,10)	4.99(d,10)‡	4.17(d,12) 4.44(d,12)	9.30(s)		5.49
XIII	3.67(br.t,7.5)‡	=O	3.14(d,10)	3.69(t,10)‡	nor	9.29(s)		5.52
XIV	4.80(br.t,8)‡	=O	4.74(d,10)‡	5.28(t,10)	nor	6.77(s)		5.50
XV	4.80(br.t,8)	5.26‡	5.33(s)‡	5.33(s)‡	3.75(br.s)‡	3.75(br.s)‡		5.42‡
XVI	4.51(br.t,8)	5.25‡	5.33(s)‡	5.34(s)‡	3.75(br.s)			5.41‡
XVIII	4.61(q,11,4)	5.24‡	5.33(s)‡	5.33(s)‡	3.73(br.s)		7.42(s)	5.42‡
XIX	~4.6	5.26‡	5.33(s)‡	5.33(s)‡	3.76(br.s)		10.06(s)	5.42‡
XXI	4.60(t,7)	~4.20‡	5.54(d,10)§	5.41(d,10)‡§	3.66(br.s)		4.14(d,12)‡ 4.35(d,12)	5.38‡
XXII	4.58(t,7)	5.24	5.32(s)‡	5.32(s)‡	3.75(br.s)		4.12(d,12.5) 4.34(d,12.5)	5.41‡

* Coupling constants in cps are listed in parentheses together with the signal multiplicities which are abbreviated as s (singlet), br.s (broad singlet), d (doublet), t (triplet) br.t (broad triplet) and q (quartet), and are omitted for multiplets. ‡ Overlaps with the other signals. § Assignment is tentative.

m.p. 216-219°, ν 2705, 1748, 1733, 1715 cm^{-1}, ORD $[\Phi]_{325}^{trough}$ -6298°, $[\Phi]_{279}^{peak}$ +7117°, and the hydroxy-ketone XII, $C_{36}H_{52}O_9$, ν 3450, 2705, 1738 cm^{-1} were formed, respectively; treatment of either X or XII with 0.02 N NaOH at room temperature afforded the hydroxy-norketone XIII, $C_{29}H_{44}O_5$, m.p. 272-275°, $[\alpha]_D$ -45.5°(Py.), ν 3450, 2700, 1723, 1690, 1650 cm^{-1}; pentaacetate XIV, $C_{39}H_{54}O_{10}$, m.p. 266-267°, ORD $[\Phi]_{326}^{trough}$ -6302°, $[\Phi]_{280}^{peak}$ +4070°. Since one of the carbinyl hydrogens of the 1,2-glycol system appears as a triplet in the NMR spectra of XIII and XIV, it is apparent that one end of the glycol is now attached to a tertiary carbon (Table 2)(10). These experimental data establish the presence of the grouping A in III, which accounts for four of the five hydroxyls in III. Furthermore, the chemical shift of the lowest-field methyl signal undergoes characteristic shifts when the axial hydroxyl in part-structure



Grouping A

TABLE 3. Methyl Signals of Camelliagenin Derivatives (6)*

Compds	23, 24, 25		-C(-CH$_3$)- 26	27	29,30		-OCOCH$_3$
IV	0.99	1.02	0.91	1.31	0.91	1.04	1.93, 1.98, 2.04(3), 2.06, 2.23
V	1.09	1.02	0.91	1.31	0.91	1.05	1.94, 1.95, 1.99, 2.04, 2.24
VI	1.09	1.02	0.90	1.47	0.90	1.06	1.98, 2.00(2), 2.05
VII	1.09	1.00	0.91	1.45	1.00	1.00	1.95, 2.03, 2.10
VIII	0.99	1.03	0.93	1.31	0.97	1.03	1.98, 2.05(2), 2.07(2), 2.08
IX	1.09	1.02	0.92	1.33	0.96	1.02	1.95, 1.97, 2.03, 2.08
X	1.09	1.03	0.93	1.46	0.93	1.03	1.95, 2.03(2)
XI	1.09	1.03	1.00	1.26	0.89	1.06	1.95, 1.97, 2.01(2)
XII	1.10	1.03	1.00	1.25	0.95	1.07	1.95, 2.02, 2.06
XIII+	0.86	0.91	0.99	1.08	1.08	1.08	
XIV+	0.85	0.96	0.99	0.99	0.99	1.09	2.02(2), 2.06(3)
XV	0.84	1.00	0.92	1.31	0.92	1.05	1.94, 2.00, 2.02, 2.05(2), 2.24
XVI 0.87	0.87		0.97	0.92	1.31	0.92	1.05	1.94, 1.99, 2.04(2), 2.24
XVIII 0.86			0.98	0.91	1.29	0.91	1.05	1.93, 1.99(2), 2.03(2), 2.09, 2.24
XIX 0.88			1.05	0.91	1.31	0.91	1.05	1.95, 2.00, 2.05(2), 2.25
XXI 0.96			1.03	0.91	1.43	0.91	1.05	2.00(2), 2.02, 2.04(2)
XXII 0.98			1.02	0.91	1.30	0.91	1.05	1.95, 2.01, 2.05(2), 2.08, 2.25

* Numbers in parentheses denote the number of methyl groups overlapped.
+ Assignment is tentative.

A is acetylated or oxidized to a ketone, a behaviour typical of a 1,3-diaxial disposition of the two groups (Me and OH) (1,12): OH (VI, VII)⟶OAc (IV, V), δ_{Me} 1.45, 1.47⟶1.31; OH (VI, VII)⟶=O (XI, XII), δ_{Me} 1.45, 1.47⟶1.25, 1.26.

The remaining oxygen function was revealed to be a formyl group from the presence of IR bands at 2700 and 1720 cm^{-1} in III and of a singlet at around 9.30 ppm in the NMR spectra of all of the compounds described so far (Table 2), except IV and XIV in which the formyl groups were acetylated. The positions of the fifth hydroxyl group and the formyl group were suggested to be at 3β and 23, respectively, from the similarity in chemical shifts of the methyl signals, the hydrogen assignable to a 3α proton and the aldehydic proton, in the compounds mentioned above and camelliagenin B derivatives (Tables 2 and 3). The deduced arrangement of oxygen functions in III is exactly same as in IIa. In fact, most of the NMR signals of the corresponding derivatives in these two series are superimposable (13).

That III is the aldehyde corresponding to IIa was established by $LiAlH_4$ reduction

of III which afforded IIa. Thus III has the structure depicted (14). Huang-Minlon reduction of III yielded IIb.

Camelliagenin D (XVII) XVII is isomeric with III. Acetylation of XVII with Ac_2O and H_2SO_4 afforded the heptaacetate XVIII, $C_{44}H_{64}O_{14}$, m.p. 221.5-222°, $[\alpha]_D$ +2.6°, ν 1748, 1250, 1230 cm^{-1} which, on mild treatment with $NaHCO_3$, yielded the pentaacetate XIX, $C_{40}H_{60}O_{12}$, ν 1735, 1245 cm^{-1}. Both of the acetates showed no IR band due to a hydroxyl group. The presence of a formyl group in XVII was detected by its IR spectrum (ν 2750, 1705 cm^{-1}) and NMR spectra of XVIII and XIX (Tables 2 and 3). The lower field regions of the NMR spectra of XVIII and XIX, are almost superimposable on those of IV and V, respectively, except the signal ascribable to 3α-hydrogen appears in higher field and that due to aldehydic proton (or its acetate) appears in lower field in XVIII and XIX. Four of the methyl signals in XVIII and XIX correspond closely with four methyl signals in the acetates of III, XV and XVI; the two methyl signals which do not match in the two series of acetates can be assigned to the methyl groups on ring A on the basis of the NMR spectra of the derivatives of Ia, Ib, Ic, IIa and IIc (Table 3) (1). These spectral observations suggest that substitution pattern A is also present in camelliagenin D. Appearance of the aldehydic proton of XIX (10.06) at distinctly lower field than in V (9.30) indicated the formyl group to be axially oriented (15). The same tendency was observed also in the shift of the corresponding hydrogen signal in XVIII (7.42) as compared to IV and VIII (6.78, 6.79).

The above evidence suggests XVII to be the aldehyde corresponding to protoaescigenin (4,16). Reduction of XVII with $LiAlH_4$ afforded an alcohol XX, $C_{30}H_{50}O_6$, m.p. 281°, identical with authentic protoaescigenin (6). The NMR spectra of the pentaacetate (XXI) and the hexaacetate (XXII) obtained from XX were also identical with these of protoaescigenin pentaacetate and hexaacetate, respectively (17). Huang-Minlon reduction of XVII yielded IIb. This establishes the structure of XVII and provides a chemical correlation of protoaescigenin and barringtogenol C.

References and Footnotes

1) S. Itô, M. Kodama and M. Konoike, Tetrahedron Letters, 591 (1967). The structures were also established by H. Itokawa, N. Sawada and T. Murakami, ibid., 597 (1967).

2) Cf. J. Simonsen and W. C. J. Ross, the Terpenes, Vol. 4, p. 443, 445. Cambridge Univ. Press, Cambridge (1957).

3) Y. Ueda, Chem. Pharm. Bull., 2, 175 (1954) and the papers cited therein.

4) a. I. Yoshioka, T. Nishimura, A. Matsuda and I. Kitagawa, Tetrahedron Letters, 5973, (1966). b. Idem., ibid., 5979 (1966).

5) The elementary analyses agree with the molecule formulae given. All optical rotations and IR spectra are refered to ethanol solution and KBr, respectively, unless otherwise stated.

6) The identity was established using Rf values in TLC, mixed m.p., and IR spectra as criteria. Our thanks are due to Professor I. Yoshioka and Dr. I. Kitagawa, Osaka University, for their kind comparison of our compounds with authentic IIa and IIb and protoaescigenin.

7) Yoshioka and his coworkers have detected the presence of two other sapogenins, theasapogenol C and D. Their identity with any of our compounds remains to be determined.

8) All the NMR data are listed in Table 2 (for lower field signals) and Table 3 (for methyl signals). NMR spectra (60 Mc and/or 100 Mc) were measured for $CDCl_3$ solution. Chemical shift in these tables are listed in ppm from internal TMS.

9) By similar acetylations, camelliagenin B afforded its hexaacetate VIII, tetraacetate IX, and triacetate X. NMR spectra of the acetates are listed in Tables 2 and 3 for comparison purpose.

10) D/E trans structures were assigned for these compounds because of i) the magnitude (J=10) of the additional coupling constant of C_{22} proton (Table 2), and ii) the disappearance of 1,3-diaxial relationship between C-27 methyl and C-19 methylene [the methyl signals at the lowest field in these compounds (Table 3) appears in higher field than that of olean-12-ene (1.13 ppm)] (11).

11) J. Karliner and C. Djerassi, J. Org. Chem., 31, 1945 (1966).

12) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto and K. Tsuda, Chem. Pharm. Bull., 10, 338 (1962). R. F. Zürcher, Helv. Chim. Acta, 44, 1380 (1961), 46, 2054 (1963).

13) NMR signals of hexaacetate XV (4b) of IIa and pentaacetate XVI (4a) of IIb are listed in Tables 2 and 3 for comparison purpose.

14) Preparation of V from IIa have been described by Yoshioka et al. (4) but no physical constant was given.

15) T. J. King and J. P. Yardley, J. Chem. Soc., 4308 (1961). R. A. Laidlaw and J. W. W. Morgan, ibid., 644 (1963). W. R. Chan, C. Willis, M. P. Cava and R. P. Stein, Chem. Ind., 495 (1963).

16) R. Kuhn and I. Löw, Ann., 669, 183 (1963).

17) Although the NMR spectrum of XXI was identical with that of protoaescigenin pentaacetate (as measured by Yoshioka), the assignments reported for the latter (16) do not correspond to ours (Table 2). The spectra of XXII and protoaescigenin hexaacetate (measured by Kuhn and by Tschesche) are identical, and the IR spectrum reported for protoaescigenin (16) is the same as that of XIX. Our thanks are due to Professor R. Kuhn, Max-Planck Institute, and Professor R. Tschesche, Universität Bonn, for providing the NMR spectra of protoaescigenin acetates.