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On the Constituents of *Picrorhiza kurrooa*. (1). The Structure of Picroside I, a Bitter Principle of the Subterranean Part

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A new bitter iridoid glucoside named picroside I has been isolated from the subterranean part of *Picrorhiza kurrooa* Royle ex Benth. (Scrophulariaceae) in addition to mannitol and vanillic acid, and the structure of picroside I has now been established as II(6′-O-*t*-cinnamoyl-catalpol) on the basis of chemical and physicochemical evidences. In addition, the re-examination concerning the stereostructure of catalpol has been performed and the correctness of the proposed structure (IV) has been re-confirmed.

The subterranean part(mostly rhizome) of *Picrorhiza kurrooa* Royle ex Benth. (Scrophulariaceae), which grows in north-west Himalayas from Kashmir to Sikkim at an altitude between 5000 to 10000 ft, has been extensively used in the indigenous system of medicine as a valuable bitter tonic, an antiperiodic and a cholagogue.[2] It has also been described in "Chung Yao Chih" (中葯誌) as a Chinese folk-medicine "hu-huang-lian" (胡黃連).[3]

On the constituents of the plant material, several works have hitherto been made since as early as 1890. It was in 1949 when Rastogi, *et al.* isolated a bitter glucoside kutkin (yield 3.4%) in addition to D-mannitol, vanillic acid and some other unknown substances[4a] and later they put forward a structure 6-cinnamoyl-β-D-glucosidyl vanillate for kutkin.[4b] On the other hand, Yeh reported the isolation of a bitter glucoside picrorhizin(=glucosido-vanilloyl-glucose) together with tripalmitin and phytosterol.[5] Very recently, however, Basu, *et al.* revised the structure of kutkin as I on the basis of the physicochemical examination.[6] As a continuation of our work on the *Scrophulariaceous* plant products,[7] we have investigated the constituents of the subterranean part of *Picrorhiza kurrooa* Royle ex Benth.[8] and isolated a new iridoid glucoside named picroside I in additon to D-mannitol and vanillic acid. The present paper describes the full account elucidating the structure II(6′-O-*t*-cinnamoyl-catalpol) for picroside I.[9]

1) Location: *Toneyama, Toyonaka, Osaka.*
2) *a*) K.R. Kirtikar and B.D. Basu, "Indian Medicinal Plants," Part II, S.N. Basu, Panini Office, Bhuwaneswari Asrama, Bahadurganj, India, 1918, pp. 933—936; *b*) R.N. Chopra, I.C. Chopra, K.L. Handa, and L.D. Kapur, "Indigenous Drug of India," U.N. Dhur & Sons Private Ltd., Calcutta, 1958, p. 181.
3) "Chung Yao Chih" (中葯誌), Vol. I, Peking (北京), 1959, p. 358.
4) *a*) R.P. Rastogi, V.N. Sharma, and S. Siddiqui, *J. Sci. & Ind. Res.* (India), Sect. B, **8**, 173 (1949) [*Chem. Abstr.*, **44**, 3097 (1950)]; *b*) R.P. Rastogi and M.L. Dhar, *J. Sci. & Ind. Res.* (India), Sect. B, **18**, 219 (1959)[*Chem. Abstr.*, **53**, 20294 (1959)] and the literatures cited therein.
5) P.Y. Yeh, *J. Taiwan Pharm. Assoc.*, **4**, 25 (1952) [*Chem. Abstr.*, **48**, 14121 (1954)].
6) K. Basu, B. Dasgupta, and S. Ghosal, *J. Org. Chem.*, **35**, 3159 (1970).
7) *a*) On *Scrophularia buergeriana* Miq.: I. Kitagawa, T. Nishimura, M. Takei, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **15**, 1254 (1967); *b*) On *Rehmannia glutinosa* Libosch. forma *hueichingensis* Hsiao: I. Kitagawa, T. Nishimura, A. Furubayashi, and I. Yosioka, *Yakugaku Zasshi*, **91**, 593 (1971).
8) Commercially available material. *a*) K. Kimura and T. Namba, *Shoyakugaku Zasshi*, **13**, 7 (1959); *b*) T. Namba and M. Togashi, *Journ. Jap. Bot.*, **38**, 161 (1963).
9) Preliminary report on the structure of picroside I: I. Kitagawa, K. Hino, T. Nishimura, E. Mukai, I. Yosioka, H. Inouye, and T. Yoshida, *Tetrahedron Letters*, **1969**, 3837.

Charcoal–Celite column and cellulose powder column chromatography of the aqueous layer [A](*cf.* Chart 1) afforded colorless needles, mp 164—166.5°, which was identified with D-mannitol by mixed mp, infrared(IR) spectrum, and thin-layer chromatographic(TLC) comparison, while the extraction of the *n*-BuOH layer using 1% aq. KOH gave vanillic acid. Further separation of the *n*-BuOH soluble portion as illustrated in Chart 1 furnished picroside I(II) with the approximate yield of 0.84% from the plant material. The chemical constituents of the aqueous layer [B] and $CHCl_3$ soluble portion are now under investigation.

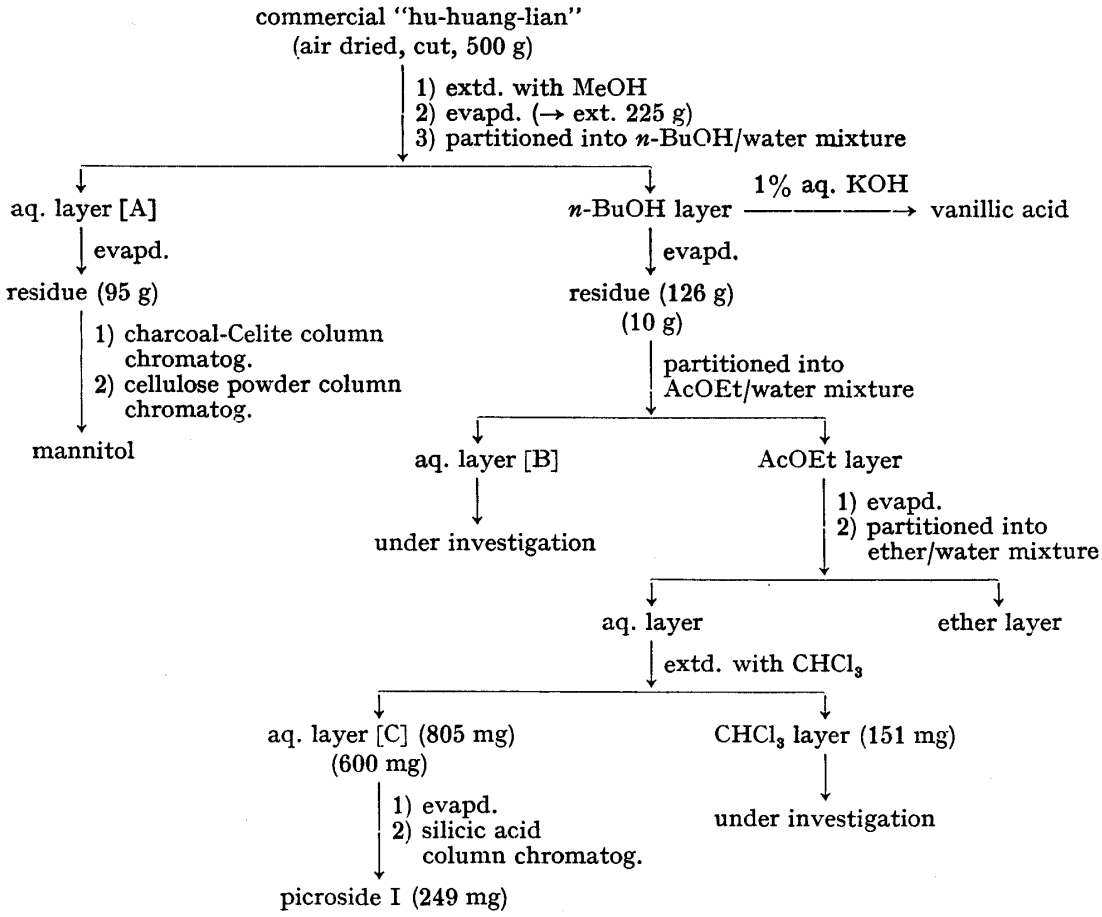
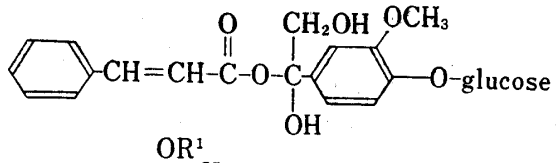


Chart 1. Isolation Procedure of Picroside I

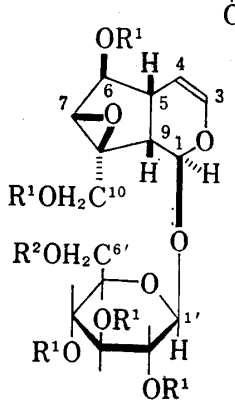
Picroside I (II), $C_{24}H_{28}O_{11}$, $[\alpha]_D$ −82° (MeOH) possesses the extremely bitter taste and slightly hygroscopic property. It darkens gradually upon stand in gin air for a long while and becomes brown on heating with methanolic hydrogen chloride. The IR spectrum(Nujol, cm^{-1}) of picroside I shows the existence of hydroxyl (br. 3400—3200), conjugated ester(1705, 1636), enol ether(1660, shoulder), and aromatic ring(1605, 1580, 1495), while the nuclear magnetic resonance(NMR) spectrum demonstrates the existence of *t*-cinnamoyl ester function by the signals at 2.34 and 3.57 τ (1H each ABq., J=16 Hz) and 2.55 τ (5H br.s., aromatic protons).

On acetylation with acetic anhydride and pyridine, Picroside I afforded a pentaacetate(III), $C_{34}H_{38}O_{16}$, IR(CCl_4, cm^{-1}): 1768, 1750(sh.), 1720(sh.), 1655, 1640, 1240, 1215. Tetrahydropicroside I(VI, hygroscopic), $C_{24}H_{32}O_{11}$, IR(Nujol, cm^{-1}): 3450—3250(hydroxyl), 1725(saturated ester), 1607, 1497(aromatic ring), prepared by catalytic hydrogenation of Picroside I over palladium-carbon, furnished quite hygroscopic pentaacetyl-tetrahydropicroside I(VII), $C_{34}H_{42}O_{16}$, IR(CCl_4, cm^{-1}): 1765, 1750, 1240, 1230(sh.), 1220.

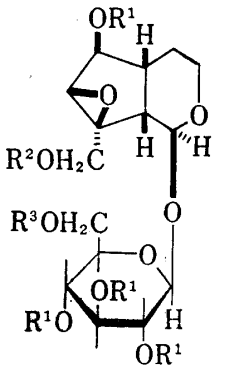
On hydrolysis using $Ba(OH)_2$, picroside I gave a crystalline hexaol, $C_{15}H_{22}O_{10}$, mp 205—206°, $[\alpha]_D$ −110° (90% EtOH), IR(Nujol, cm^{-1}): 3340, 1660 and *t*-cinnamic acid. The NMR



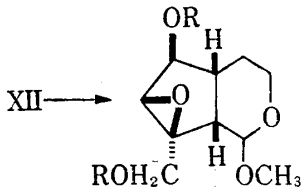
I: kutkin



II: R^1=H, R^2=-OCCH=CH-C_6H_5 (picroside I)
III: R^1=Ac, R^2=-OCCH=CH-C_6H_5
IV: R^1=R^2=H (catalpol)
V: R^1=R^2=Ac



VI: R^1=R^2=H, R^3=-$OCCH_2CH_2$-C_6H_5
VII: R^1=R^2=Ac, R^3=-$OCCH_2CH_2$-C_6H_5
VIII: R^1=R^2=R^3=H
IX: R^1=H, R^2=R^3=Tr
X: R^1=H, R^2=Tr, R^3=-$OCCH_2CH_2$-C_6H_5
XII: R^1=R^2=-OC-C_6H_4·OCH_3(p), R^3=-$OCCH_2CH_2$-C_6H_5
XIX: R^1=R^2=R^3=Ac
XXI: R^1=-OC-C_6H_4·OCH_3 (p), R^2=R^3=Tr
XXVI; R^1=R^2=-OC-C_6H_4·OCH_3 (p), R^3=H



XIII: R=-OC-C_6H_4·OCH_3 (p)

Chart 2

TABLE I.[a] The Decoupling Experiment of Hexaacetyl-catalpol(V)
(τ values at 100 MHz in $CDCl_3$)

Decoupled proton \ Irradiated at [b]	3.69(C_3-H)	5.09(C_4-H)	5.26(C_1-H, C_6-H, C_{10}-H)	5.74($C_{6'}$-H_2)	6.04(C_{10}-H)	6.42(C_7-H, $C_{5'}$-H)[c]	7.44(C_5-H, C_9-H)
C_1-H *ca.* 5.2[d]							deformed
C_3-H 3.69 (d.d.)		broad singlet					doublet
C_4-H *ca* 5.1[d]	deformed						
C_5-H *ca.* 7.4[d]	deformed						
C_7-H 6.33 (br.s.)			sharp singlet				
C_9-H 7.34 (t.)			doublet				
C_{10}-H_2 5.12 (d.)			[d]		singlet		
6.04 (d.)			singlet				
$C_{5'}$-H 6.27 (m.)				deformed			
$C_{6'}$-H_2 5.68, 5.79 (ABX, 12, 4, 2)						deformed	

a) Abbrev. in Tables I—IV: d.=doublet, d.d.=double doublet, m.=multiplet, q.=quartet, s.=singlet, t.=triplet
b) Protons affected are given in the parentheses.
c) An unassigned multiplet at 4.94τ was also deformed by this irradiation.
d) Signal patterns are unclear due to the overlapping.
J values (Hz) clarified: $J_{3,4}$=6, $J_{3,5}$=1—1.5, $J_{6,7}$≒1, $J_{5,9}$=$J_{9,1}$=7, $J_{10,10}$=12, $J_{6'}$,$_{6'}$=12, $J_{5'}$,$_{6'}$=4 & 2

Table II. The NMR Data given in τ Values

	C_1-H	C_3-H(or H_2)	C_4-H(or H_2)	C_5-H	C_6-H
Picroside I(II)[a]	4.8—5.1	3.55 (q., 6 & 2)	4.8—5.1	7.60 (m.)	6.1—6.4
Catalpol (IV)[a]	5.07 (d., 7)	3.53 (q., 6 & 2)	4.78[b] (q., 6 & 5)	7.64 (m.)	5.87[b] (d., 7)
Catalposide (XI)[a]	c)	*ca.* 3.60 (m.)	c)	7.15—7.45 (m.)	c)
Tetrahydro-picroside I(VI)[a]	5.0—5.2	5.4—5.9	7.9—8.3	7.79 (m.)	5.72[b] (d., 9)
Dihydrocatalpol (VIII)[a]	4.8—5.1	5.8—6.4	7.8—8.2	7.73 (m.)	5.50[b] (q., 9 & 1)
Pentaacetyl-Picroside I(III)[d]	4.7—5.3	3.68 (d., 6)	4.7—5.3	*ca.* 7.45 (m.)	4.7—5.3
Hexaacetylcatalpol (V)[e]	*ca.* 5.2[c]	3.69 (d.d., 6 & 1—1.5)	*ca.* 5.1[c]	*ca.* 7.4[c]	*ca.* 5.1[c]
Pentaacetyl-tetrahydro Picroside I(VII)[e]	5.44 (d., 8)	6.3—6.8	8.3—8.7	7.6 —7.8	4.90 (d., 9)
XIII[e]	5.14 (d., 5)	6.3—6.6 (m.)	7.9—8.5 (m.)	7.68 (m.)	4.50 (q., 9.8 & 1.2)
Hexaacetyl-dihydrocatalpol (XIX)[d]	5.43[b] (d., 8)	6.1—6.8	8.2—8.7	7.4 —7.8	4.8—5.1

	C_7-H	C_9-H	C_{10}-H_2	C_6-H_2
Picroside I(II)[a]	6.52 (s., $W_{h/2}$=3.5)	7.22 (q., 9 & 7)	5.62, 6.1—6.4 (d., 13)	5.32 (br., $W_{h/2}$=10)
Catalpol (IV)[a]	6.29[b] (s., $W_{h/2}$=3)	7.31 (q., 9 & 7)	5.67, 6.17 (ABq., 13)	6.11[c] (center, ABX)
Catalposide (XI)[a]	c)	7.15—7.45 (m.)	5.67, *ca.* 6.1[c] (d., 13)	6.1—6.6
Tetrahydro-Picroside I(VI)[a]	6.4—6.5	7.44 (q., 9 & 7)	5.67, 6.28[b] (d., 13)	5.2—5.6[b]
Dihydrocatalpol (VIII)[a]	5.8—6.4	7.39 (q., 9 & 7)	5.56, 6.05 (d., 13)	5.8—6.4[b]
Pentaacetyl-Picroside I(III)[d]	6.35 (s.-like, $W_{h/2}$=3.5)	7.31 (t.-like, 7)	5.10,[b] 6.00 (d., 13)	5.55, 5.67 (ABq., 5.4)
Hexaacetylcatalpol (V)[e]	6.33 (s., $W_{h/2}$=3.5)	7.34 (t., 7)	5.12, 6.04 (d., 12)	5.68, 5.79 (ABX, 12,4,2)
Pentaacetyl-tetrahydro-Picroside I(VII)[e]	6.44 (s., $W_{h/2}$=3.5)	7.6 —7.8	5.27, 6.08 (d., 13)	5.70, 5.84 (ABX, 12,4,2)
XIII[e]	6.24 (s.-like, $W_{h/2}$=3.5)	7.35 (q., 7& 5)	5.07, 5.86 (ABq., 12.5)	—
Hexaacetyl Dihydrocatalpol (XIX)[d]	6.37 (s.-like, $W_{h/2}$=3.5)	7.4 —7.8	5.27, 6.01 (d., 13)	5.76 (m.)

a) measured at 100 MHz in D_2O *b*) tentative assignment *c*) Signal patterns are unclear due to the overlapping. *d*) measured at 60 MHz in $CDCl_3$ *e*) measured at 100 MHz in $CDCl_3$

decoupling experiment(Table I) of the hexaacetyl derivative $C_{27}H_{34}O_{16}$, mp 141—142°, IR (CCl_4, cm^{-1}): 1765, 1755(sh.), 1655, 1240, 1215, obtained from the hexaol, revealed the hexaol being identical with catalpol(IV)[10] and the finding was corroborated by the direct comparison with the authentic sample(mixed mp, TLC, IR, and $[\alpha]_D$). Furthermore, the hexaacetate was also identified with authentic hexaacetyl-catalpol(V) by the direct comparison(TLC, IR, and NMR). Therefore, it follows that picroside I corresponds to a *t*-cinnamoyl ester of catalpol.

10) *a*) J.M. Bobbitt, D.W. Spiggles, S. Mahboob, H. Schmid, and W. von Philipsborn, *J. Org. Chem.*, **31**, 500 (1966); *b*) J.M. Bobbitt, D.E. Kiely, A.Y.-W. Lam, and E.I. Snyder, *J. Org. Chem.*, **32**, 1459 (1967).

The location of *t*-cinnamoyl moiety in picroside I (II) has been elucidated as based on the following evidence. Thus, on treatment with 2.5 molar equivalent trityl chloride in pyridine, dihydrocatalpol(VIII) afforded mainly a ditritylether (IX), $C_{53}H_{52}O_{10}$, NMR($CDCl_3$): 2.68 τ(center, totally 30 H), whereas tetrahydropicroside I(VI) furnished a monotritylether(X), NMR ($CDCl_3$): 2.76 τ (center, totally 20 H) under the same reaction condition, suggesting that *t*-cinnamoyl ester function in tetrahydropicroside I connects with a primary carbinol of either C_{10} or $C_{6'}$. The findings are in good accord with the NMR examination below (Table II).

In picroside I (II), C_5-H is observed at 7.60 τ which would suggest that the hydroxyl function at neighboring C_6 is not esterified, since C_5-H in catalpol(IV) is found similarly at 7.64 τ while that in catalposide(XI) appears between 7.15—7.45 τ. The signals due to the methylene protons of one of two primary alcoholic functions in II and VI appear at the paramagnetically shifted position as compared with corresponding signals in IV, VIII, and XI (Table II). Thus, in II, one of the primary alcoholic methylene protons are observed at 5.32 τ (br., $W_{\frac{1}{2}}^{h}$=10 Hz) and the other at 5.62 and between 6.1—6.4 τ (1H each d., J=13 Hz). The latter could be assigned to the methylene protons at C_{10} on the basis of comparison with the signals of IV (5.67 and 6.17, 1H each ABq., J=13 Hz) and XI (5.67 and *ca.* 6.1, 1H each d., J=13 Hz).

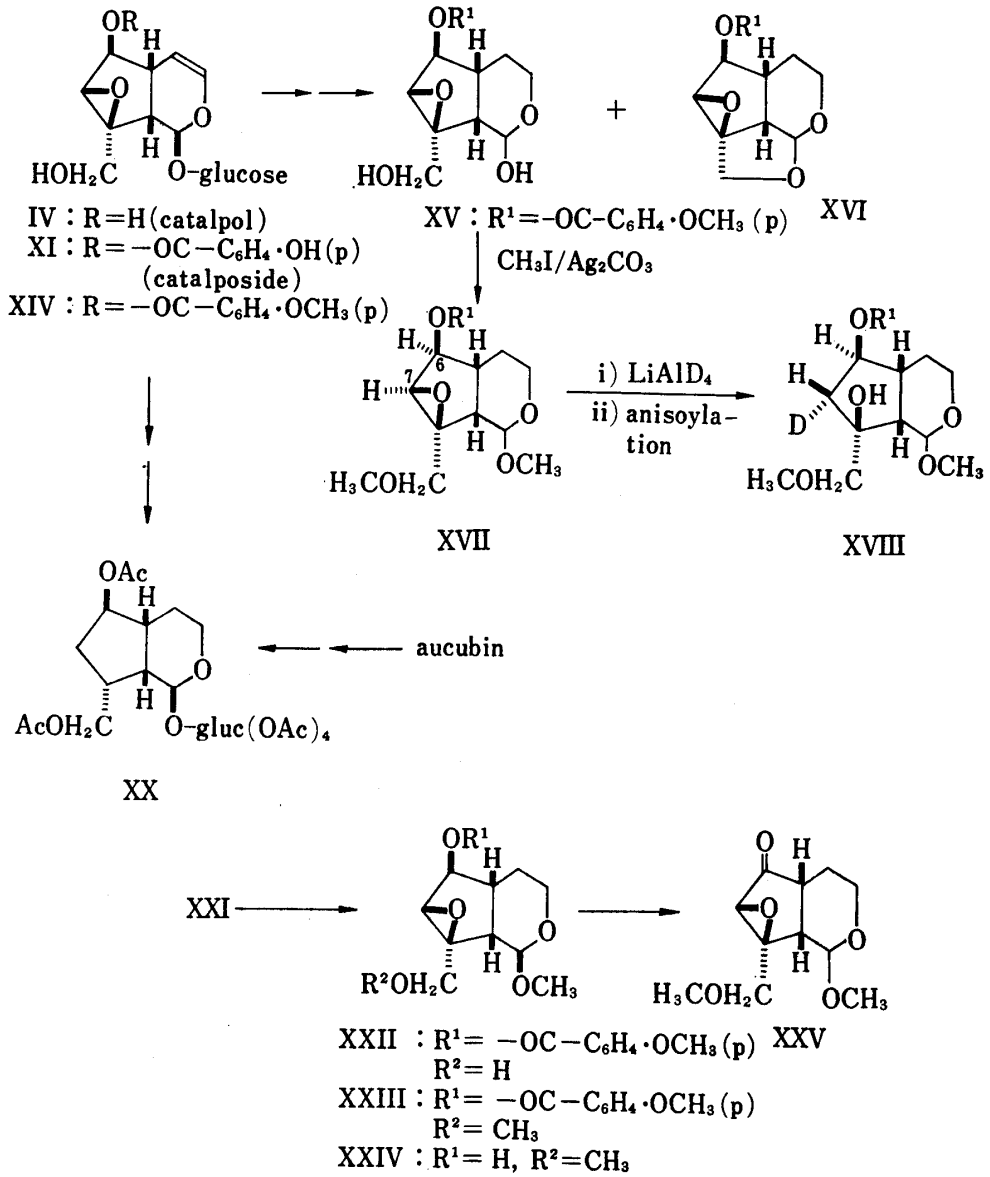


Chart 3

The similar lower field shift of the signals (at 5.2—5.6 τ) due to $C_{6'}$-H_2 is observed in VI as compared with those(at 5.8—6.4 τ) of VIII. These observations reasonably lead to assume that *t*-cinnamoyl function of picroside I attaches at the primary carbinol of $C_{6'}$ rather than C_{10} and the assumption was verified by the following examination.

On treatment with *p*-toluenesulfonic acid in benzene–methanol mixture, the pentaanisoyl derivative(XII), $C_{64}H_{62}O_{21}$, IR(CCl_4,cm^{-1}): 1735, 1725(sh.), 1610, 1510, 1275(sh.), 1255, 1167, 850, prepared from VI, afforded a desglucosyl derivative(XIII),[11] IR(CCl_4,cm^{-1}): 1718, 1608, 1510, 1268, 1252, 1165; NMR ($CDCl_3$, τ): 6.64 (3H s., methoxyl), 6.16 (6H s., methoxyl), 3.10, 2.00 (4H each d., J=9 Hz, aromatic protons). The formulation XIII has been rationalized by the decoupling experiment as tabulated in Table III. Accordingly, the location of dihydrocinnamoyl function in VI has now been elucidated to be $C_{6'}$ of the glucosidyl moiety.

Furthermore, the consumption in the periodate titration[12] of VI as well as VIII was found two moles equivalent each, thus giving the additional evidence for the location of dihydrocinnamoyl group in VI and consequently confirming the structure of picroside I as 6′-O-*t*-cinnamoyl-catalpol(II).

To elucidate the stereostructure of catalpol (IV), Bobbitt, *et al.*[10] took advantage of the following considerations. First, the formation of the cyclic acetal(XVI) rationalizes the β-epoxide moiety in IV. Secondly, based on the fact that C_6-H in XVII and XVIII are observed at 4.58 τ (q., J=9.0 and 1.2 Hz) and 4.83 τ (q., J=3.5 and 2.5 Hz), the coupling constants $J_{6,7}$ and $J_{5,6}$ in XVII are assumed to be 9.0 and 1.2 Hz respectively. Thirdly, the application of the Karplus equation[13] favors C_6-αH rather than C_6-βH in all the possible conformations of XVII and XVIII.

However, as demonstrated by Tori, *et al.*[14] the coupling constant between an epoxidic and an adjacent protons in the five membered ring would not follow the Karplus equation and this was the case in an iridoid glucoside unedoside as presented by Geissman, *et al.*[15] Moreover, as given in Table II and III, the decoupling experiment of the compound XIII disclosed that $J_{5,6}$ is 9.8 Hz whereas $J_{6,7}$ is 1.2 Hz. Since the finding appeared to be inconsistent with the NMR assignment presented by Bobbitt, *et al.* as described above, the detailed NMR examination of III, V, VII, and hexaacetyl-dihydrocatalpol(XIX) has been performed. It has been clarified that the signals due to C_7-H in these compounds are observed as singlet or singlet-like($W_{\frac{h}{2}}$=3.5 Hz). In addition, the decoupling experiment of VII confirmed further that $J_{5,6}$ value in VII is 9 Hz.

Table III. The Decoupling Experiment of XIII
(τ values at 100 MHz in $CDCl_3$ and J values in Hz)

Irradiated proton / Decoupled proton	C_5-H	C_6-H	C_7-H	C_9-H (7.35; q., J=7 & 5)
C_5-H 7.68 (m.)		simplified		
C_6-H 4.50 (q., J=9.8 & 1.2)	s.-like. $W_{h/2}$=2.5		d., J=9	
C_7-H 6.24 (s.-like, $W_{h/2}$=3.5)		s., $W_{h/2}$=2.5		
C_1-H 5.14 (d., J=5)				singlet

Consequently, it has become of importance to re-examine the stereostructure of IV. As presented in our joint paper with Professor Inouye's group,[9] an alternate chemical proof of

11) Monitoring the reaction procedure by TLC disclosed the formation of desdihydrocinnamoyl derivative (XXVI) at the early stage of the reaction, which was proved by the isolation of XXVI as given in the experimental section.
12) J.M. Bobbitt, *Advances in Carbohydrate Chem.*, **11**, 1 (1956).
13) M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963).
14) K. Tori, T. Komeno, and T. Nakagawa, *J. Org. Chem.*, **29**, 1136 (1964).
15) T.A. Geissman, W.F. Knaack, Jr., and J.O. Knight, *Tetrahedron Letters*, **1966**, 1245.

Table IV. The NMR Data of XXII and XXIII
(τ values at 100 MHz and J values in Hz)

	C_1-H	C_6-H	C_7-H	C_9-H	C_{10}-H_2	OCH_3
XXII	5.84 (d., 8.5)[a]	4.66 (q., 9.8 & 1.2)	6.30 (s. -like)[b]	7.66 (t., 8.5)	6.00, 6.40 (ABq., 13.5)	6.17, 6.47 (3H each s.)
XXIII	5.84 (d., 8)	4.66 (q., *ca.* 9 & 1)	6.30 (s. -like)	7.70 (t., 8)	5.29, 5.43 (ABq., 12)	6.17, 6.53, 6.66 (3H each s.)

a) The irradiation at 7.66τ altered the signal to a singlet.
b) Upon irradiation at 4.66τ, the signal was altered to a sharp singlet.

C_6-βOH in IV has been accomplished through the conversion of IV to tetrahydroaucubin-B hexaacetate(XX), the detail of which has been published by the Inouye's group in a separate paper.[16]

Furthermore, we have achieved an additional proof on the β-epoxide configuration in IV. Thus, tetraanisoyl derivative(XXI), $C_{85}H_{82}O_{18}$, prepared from dihydrocatalpol-ditritylether (IX) was treated with *p*-toluenesulfonic acid in methanol–benzene mixture to give XXII, IR(CCl_4): 3540, 1708, 1606, 1510, 1275, 1257 cm^{-1}. Methylation of XXII with CH_3I–Ag_2O in dimethylformamide afforded XXIII, $C_{19}H_{24}O_7$, IR(CCl_4, cm^{-1}): 1715. The coupling constant ($J_{5,6}$ and $J_{6,7}$) in XXII and XXIII are found similar as in XIII, and β-OCH_3 orientation at C_1 in XXII and XXIII are secured by their $J_{1,9}$ values (d., J=8.5 and 8.0 Hz respectively) (Table IV).[17] On oxidation with CrO_3–pyridine, the desanisoyl derivative (XXIV), mp 110—112°, IR (CCl_4, cm^{-1}): 3590, obtained by treatment of XXIII with sodium methoxide in methanol, furnished a fairly unstable epoxy-ketone (XXV), IR (CCl_4, cm^{-1}): 1755.

The epoxyketone exhibited a positive Cotton effect in its CD curve at n→π^* transition ($[\theta]_{308}$+16240 (max))[18] which makes sure of the absolute configuration as depicted by XXV.

The natural occurrence of catalpol has been known fairly wide among the *Scrophulariaceae*,[19] while that of catalposide is rather limited *e.g.* in the genus *Veronica*.[19a] The present paper offers another example of esterified catalpol occurring in the *Scrophulariaceae*.

Experimental[20]

Isolation of Picroside I (II)——Commercial "hu-huang-lian" (500 g, purchased from the Tochimoto–Tenkaido Co., Osaka) was extracted with MeOH under reflux 3 times and filtered while hot. After cooling, uncharacterized precipitates (*ca.* 0.3 g) were removed by filtration and the filtrate was concentrated *in vacuo* to give an extract of 225 g. The extract was then treated as outlined in Chart 1. The *n*-BuOH layer exhibited the significantly bitter taste, while the aqueous layer [A] did not. Although the *n*-BuOH layer showed positive for the Meyer reagent, all the attempts to isolate alkaloid so far were without success.

Methanolic solution of a small portion of the residue obtained from the aqueous layer [A] was passed through a column of 1:1 mixture of active charcoal (Tokusei–Shirasagi, Takeda Chem. Ind.) and Celite

16) H. Inouye and T. Yoshida, *Chem. Pharm. Bull.* (Tokyo), **19**, 1438 (1971).
17) Although the direct comparison was not performed, the compound (XXIII) seems to be identical with XVII prepared by Bobbitt, *et al.*[10b] However, the NMR data of XXIII is correctly assigned as is illustrated in Table IV.
18) *a*) H. Wehrli, C. Lehmann, P. Keller, J.J. Bonnet, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **49**, 2218 (1966); *b*) K. Kuriyama, H. Tada, Y. Sawa, S. Ito, and I. Ito, *Tetrahedron Letters*, **1968**, 2539.
19) *a*) J.M. Bobbitt and K.-P. Segebarth, "Cyclopentanoid Terpene Derivatives," ed. by W.I. Taylor and A.R. Battersby, Marcel Dekker, Inc., New York, 1969, pp. 129—134; *b*) P. Kooiman, *Acta, Bot. Neerl.*, **19**, 329 (1970).
20) Melting points were taken on the Yanagimoto Micro-meltingpoint Apparatus (a hot-stage type) and recorded as read. Specific rotations were measured at room temperature with the Rex Photoelectric Polarimeter NEP-2 (l=1 cm), the IR spectra were taken with the Hitachi EPI-S2 Spectrometer, the NMR spectra with the Hitachi H-60 and the Varian HA-100 Spectrometers (tetramethylsilane as the internal standard in $CDCl_3$ and as the external standard in D_2O), and the Mass spectra with the Hitachi RMU-6D Spectrometer.

535 (Wako Pure Chem. Ind.) developing with MeOH to afford crystalline substance, which was subsequently purified by passing through a column of cellulose powder (200—300 mesh) (Toyo Roshi Kaisha, Ltd.) with the aid of *n*-BuOH saturated with water. Colorless needles thus obtained was then recrystallized with EtOH to give a compound of melting at 164—166.5°, identical with authentic D-mannitol (mp 164—166°) by mixed mp (164—166.5°), IR (Nujol), and TLC (SiO_2, *n*-BuOH–AcOH–water=3–1–1).

At the early stage of the investigation, an experiment gave the following results. The *n*-BuOH layer obtained from 500 g of the plant material was extracted with 1% aq. KOH solution. On subsequent treatment with the organic solvents, the acidic fraction furnished vanillic acid (mp 207°, *ca.* 2.8 g), which was identified with the authentic sample (mp 208°) by mixed mp (207.5°), IR (Nujol), and TLC (SiO_2, $CHCl_3$–MeOH=7–1).

To isolate picroside I, the residue from the *n*-BuOH layer was treated as given in Chart 1. The aqueous layer [C] (600 mg) was chromatographed on a column of silicic acid (Mallinckrodt, 33 g) eluting with $CHCl_3$ andC HCl_3–MeOH mixture to give vanillic acid and then picroside I (II) (249 mg, amorphous[21]) (*ca.* 0.84% from "huhuang-lian"), $[\alpha]_D$ −82° (*c*=1.0, MeOH). *Anal.* Calcd. for $C_{24}H_{28}O_{11}$: C, 58.52; H, 5.73. Found: C, 58.31; H, 5.63. NMR (D_2O, 100 MHz) τ: 3.57, 2.34 (1H, each, ABq., J=16 Hz), 2.55, (5H, br. s.) (*t*-cinnamoyl), and the signals as given in Table II.

Pentaacetyl-picroside I (III) from Picroside I (II)——A solution of picroside I (II) (50 mg) in pyridine (1.5 ml)–acetic anhydride (1 ml) mixture was kept at 35° for 16 hr. The crude product (57 mg) obtained after working up in a usual way was chromatographed over silica gel (Merck, 5 g) developing with benzene and $CHCl_3$ by the gradient elution to give the pentaacetate (III, 29 mg, colorless amorphous). $[\alpha]_D$ −83° (*c*=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{34}H_{38}O_{16}$: C, 58.11; H, 5.45. Found: C, 58.28; H, 5.37. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1768, 1750 (sh.), 1720 (sh.), 1655, 1640, 1240, 1215. NMR ($CDCl_3$, 60 MHz) τ: 7.96 (3H), 7.94 (6H), 7.91, 7.88 (3H each) (all singlets, OAc×5), 3.49, 2.21 (1H each ABq., J=15.6 Hz), 2.55 (center 5H, m.) (*t*-cinnamoyl), and the other signals as given in Table II.

Tetrahydropicroside I (VI) from Picroside I (II)——To a solution of crude picroside I (400 mg) in EtOH (20 ml) was added 5% Pd-C (365 mg) and the mixture was stirred under hydrogen atmosphere at room temperature for 8 hr. After removing the catalyst by filtration, the solvent was evaporated to give a product (380 mg). The analytical sample of VI was obtained by preparative TLC (SiO_2, Camag) as a hygroscopic white powder. $[\alpha]_D$ −80° (*c*=1.1, MeOH). *Anal.* Calcd. for $C_{24}H_{32}O_{11}$: C, 58.05; H, 6.50. Found: C, 57.70; H, 6.60. IR ν_{max}^{Nujol} cm^{-1}: 3450—3250 (br.), 1725, 1607, 1497. NMR (D_2O, 100 MHz) τ: 6.98 (4H center, A_2B_2 type), 2.52 (5H m., $W_{h/2}$=5 Hz) (dihydrocinnamoyl), and the signals as given in Table II.

Pentaacetyl-tetrahydropicroside I (VII) from VI——VI (53 mg) was acetylated with pyridine (1.5 ml)-acetic anhydride (1 ml) mixture by keeping at 35° for 20 hr, followed by the usual work up. The product (65 mg) was then decolorized by passing through a charcoal column to give significantly hygroscopic VII (57 mg, amorphous), $[\alpha]_D$ −61° (*c*=1.0, acetone). *Anal.* Calcd. for $C_{34}H_{42}O_{16}$: C, 57.78; H, 5.99. Found: C, 58.00; H, 6.09. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1765, 1750, 1240, 1230 (sh.), 1220. NMR ($CDCl_3$, 100 MHz) τ: 8.00 (3H), 7.98 (6H), 7.94, 7.90 (3H each) (all singlets, OAc×5), 7.18 (4H center, A_2B_2 type), 2.79 (5H s.) (dihydrocinnamoyl). The assignment given in Table II was substantiated by the decoupling experiments.

Alkaline Hydrolysis of Picroside I (II) giving Catalpol (IV) and *t*-Cinnamic Acid——i) II (250 mg) was dissolved in small amount of MeOH and added with saturated aq. $Ba(OH)_2$ solution (5 ml) and water (5 ml). After stirring for 6 hr at room temperature ,the reaction mixture was left standing overnight and neutralized with 1N H_2SO_4. After removing white precipitates ($BaSO_4$) by filtration, the filtrate was adjusted to pH 3 with 0.1N H_2SO_4 to yield a suspension, which was filtered. The precipitates ($BaSO_4$+*t*-cinnamic acid) were extracted with $CHCl_3$ ($CHCl_3$ extract [A]), and the $CHCl_3$ soluble portion was extracted again with ether giving crude *t*-cinnamic acid (42 mg). Sublimation (4 mmHg, 100—110°) followed by recrystallization with *n*-hexane furnished pure *t*-cinnamic acid (mp 132—134.5°), which was identified with the authentic sample (mp 132—135°) by mixed mp (134—135°), IR (Nujol), and TLC (SiO_2, $CHCl_3$–MeOH=4–1). The aqueous filtrate of pH 3 was washed with $CHCl_3$ to remove additional amount of *t*-cinnamic acid which was combined to the above $CHCl_3$ extract [A]. The aqueous layer was then adjusted to pH 7 with $BaCO_3$ and filtered (to remove $BaSO_4$). The aqueous filtrate was evaporated *in vacuo* to give catalpol (83 mg), which was recrystallized with MeOH and then with MeOH–AcOEt mixture. ii) To an aqueous solution (2 ml) of II (100 mg) was added saturated aq. $Ba(OH)_2$ solution (2 ml). After 10 min, the reaction mixture was neutralized with aq. 1N H_2SO_4 solution and the precipitates were removed by filtration. The filtrate was then adjusted to pH 3 and filtered. Next, the filtrate was neutralized again with $BaCO_3$ and the precipitates ($BaSO_4$) were removed by filtration. The residue obtained by evaporation of the filtrate *in vacuo* was dissolved in MeOH and diluted with AcOEt to remove the insoluble portion. The soluble portion was then crystallized from MeOH–AcOEt affording colorless crystals of catalpol (40 mg, mp 200—205°). Further recrystallization using the same solvent mixture gave a pure sample of mp 205—206°, $[\alpha]_D$ −110° (*c*=0.5, 90% EtOH). *Anal.* Calcd. for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12. Found: C, 50.13; H, 6.06. IR ν_{max}^{Nujol} cm^{-1}:

21) The expression presented as amorphous, powder, or glassy implies that the attempts to crystallize the materials have been failed.

3340, 1660. The sample was identified with authentic catlapol[22] by mixed mp, IR(Nujol and KBr), TLC (SiO_2, *n*-BuOH–AcOH–water=4–1–5, upper layer, detected by the Godin reagent[23]), and $[\alpha]_D$.

Hexaacetyl-catalpol (V) from Catalpol (IV) obtained from Picroside I (II)——A solution of catalpol (IV, 100 mg obtained from picroside I) in pyridine (5 ml)-acetic anhydride (3 ml) mixture was left standing at 27° for 2 days. Working up in the usual manner gave the crude acetate (83 mg), which was purified by preparative TLC (SiO_2, Camag) followed by recrystallization with EtOH to give colorless needles of mp 141—142°. *Anal.* Calcd. for $C_{27}H_{34}O_{16}$: C, 52.77; H, 5.58. Found: C, 53.00; H, 5.37. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1765, 1755 (sh.), 1655, 1240, 1215. $\nu_{max}^{CHCl_3}$ cm^{-1}: 1755—1745 (br.), 1655. NMR ($CDCl_3$, 100 MHz) τ: 7.98 (3H), 7.96 (6H), 7.88 (6H), 7.86 (3H) (all singlets) (OAc×6) and the other signals as given in Table II. The hexaacetate obtained here was identified with authentic hexaacetyl-catalpol (V), by mixed mp, TLC, IR, and NMR.

Dihydrocatalpol (VIII) from Catalpol (IV)——A solution of IV (3 g) in EtOH (30 ml) was hydrogenated over 5% Pd-C (1.5 g) by stirring for 8 hr at room temperature under hydrogen atmosphere. After removing the catalyst by filtration, the filtrate was evaporated to dryness and recrystallized with MeOH–AcOEt mixture to give VIII (2.1 g). Repeated recrystallization using the same solvent mixture raised the mp up to 216—218° (lit.[10a] mp 216—217°).

Hexaacetyl-dihydrocatalpol (XIX) from VIII——Acetylation of VIII (30 mg) using pyridine (1.5 ml)–acetic anhydride (1 ml) mixture at 35° (overnight) followed by the usual work up and preparative TLC purification afforded colorless XIX (16 mg, amorphous). NMR ($CDCl_3$, 60 MHz) τ: 7.99 (3H), 7.96 (6H), 7.88 (9H) (all singlets, OAc×6) and the signals assigned in Table II.

Dihydrocatalpol-ditritylether (IX) from VIII——i) A solution of VIII (100 mg) in pyridine (4 ml) was added with trityl chloride (190 mg, 2.5 molar equivalent of VIII) and heated at 110° for 2.5 hr. After standing overnight at room temperature, the reaction mixture was diluted with water (40 ml), extracted twice with ether (50 ml) giving a crude product (210 mg), which was then chromatographed over Al_2O_3 (Merck standard, 40 g). Elution with CH_2Cl_2–MeOH (100: 8—5: 1) mixture followed by preparative TLC (SiO_2, Camag) afforded IX (pure sample, 34 mg and crude one, 15 mg). White powder, $[\alpha]_D$ −55° (*c*=0.5, MeOH). *Anal.* Calcd. for $C_{53}H_{52}O_{10}$: C, 72.90; H, 6.00. Found: C, 73.30; H, 6.22. NMR ($CDCl_3$, 60 MHz) τ: 2.68 (center 30H, $W_{h/2}$=11 Hz) (aromatic protons). ii) Dihydrocatalpol (VIII) (5.5 g) and trityl chloride (10.45 g, 2.5 mol. eq. of VIII) in pyridine (100 ml) were heated at 110° for 2 hr and treated as above. The crude product (14.25 g) was chromatographed twice over silica gel (Merck, 100 g and 50 g) eluting with CH_2Cl_2–MeOH (100: 1.5—100: 2) to yield IX (5.01 g).

Tetrahydropicroside I-monotritylether (X) from VI——A solution of VI (200 mg) in pyridine (8 ml) was treated with trityl chloride (280 mg, 2.5 molar equivalents of VI) and the total mixture was heated at 110° for 2.5 hr. After working up in the same way as for IX, the crude product was chromatographed over Al_2O_3 (Woelm, grade III, 5g). Elution with CH_2Cl_2-MeOH (10: 1—5: 1) followed by TLC purification afforded X (40 mg, amorphous), $[\alpha]_D$ −46° (*c*=1.0, MeOH). NMR ($CDCl_3$, 60 MHz) τ: 2.76 (center 20 H, m., $W_{h/2}$=12 Hz) (aromatic protons of monotrityl and dihydrocinnamoyl functions), 7.29 (center 4H, A_2B_2 type, dihydrocinnamoyl). Careful examination disclosed that the ratio between aromatic protons and aliphatic protons is 20.1: 26 (calcd. 20: 26).

Pentaanisoyl-tetrahydropicroside I (XII) from VI——A mixture of VI (400 mg) and anisoyl chloride (1 ml, freshly distilled) in pyridine (6 ml) was kept overnight at 34°, poured into water (50 ml) and extracted with ether (40 ml×3). The crude product was then chromatographed twice over silica gel (Merck, 60 g and 35 g) eluting with CH_2Cl_2–MeOH (100:1) to yield XII (690 mg, colorless amorphous), $[\alpha]_D$ −69° (*c*=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{64}H_{62}O_{21}$: C, 65.86; H, 5.35. Found: C, 65.92; H, 5.33. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735, 1725 (sh.) 1610, 1510, 1275 (sh.), 1255, 1167, 1097, 1038, 850, 690. NMR ($CDCl_3$, 60 MHz) τ: *ca.* 8.50 (2H m., $C_{(4)}$ -H_2, *ca.* 7.55 (2H m., $C_{(5)}$, $C_{(9)}$ -H_2), 6.35 (3H), 6.30, 6.22 (6H each) (all singlets), 3.45—3.05 (10 H m.), 2.40—1.90 (10 H m.) (anisoyl×5), 7.32 (center 4H, A_2B_2 type), 2.88 (5H s, -like) (dihydrocinnamoyl).

Acid Treatment of XII giving XIII and XXVI——i) To a solution of pentaanisoyl-tetrahydropicroside I(XII) (400 mg) in anhydrous benzene (10 ml) was added a solution of *p*-TsOH·H_2O (500 mg) in anhydrous MeOH (10 ml) and the total mixture was kept at 45° for 35 hr. After neutralizing with $BaCO_3$, the precipitates were removed by centrifugation. The supernatant was evaporated *in vacuo* and purified by preparative TLC (SiO_2, Camag) to give a pure sample of colorless glassy XIII (40 mg), $[\alpha]_D$ −72° (*c*=1.0, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2940, 1718, 1608, 1510, 1268, 1252, 1165, 1100, 1035, 848. NMR ($CDCl_3$, 100 MHz) τ: 6.64 (3H s.), 6.16 (6H s.), 3.10, 2.00 (4H each d., *J*=9 Hz)(methoxyl and anisoyl×2), and the signals as given in Table II. ii) To a solution of XII (490 mg) in anhydrous benzene (15 ml) was added a solution of *p*-TsOH·H_2O (400 mg) in anhydrous MeOH (15 ml) and the total solution was kept at room temperature for 29 hr. After working up as above, the crude product (496 mg) was purified by column chromatography using silica gel (Merck, 50 g) eluting with CH_2Cl_2–MeOH (100: 1) and then by preparative TLC (SiO_2, Merck HF_{254}) to

22) Kindly provided by Prof. T. Okuda of Okayama University.

23) *a*) P. Godin, *Nature*, **174**, 134 (1954); *b*) A.P. MacLennan, H.M. Randall, W.D. Smith, *Anal. Chem.*, 31, 2020 (1959).

give XXVI (109 mg). The structure was verified by the following data. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3525, 1723, 1715 (sh.), 1608, 1510, 1280, 1254. NMR ($CDCl_3$, 60 MHz) τ: 6.24 (3H s.), 6.18 (6H s.), 6.15, 6.13 (3H each s.), 3.35—2.85 (10 H m.), 2.25—1.75 (10 H m.) (anisoyl×5). No signal due to dihydrocinnamoyl function was observed.

Periodate Oxidation of Tetrahydropicroside I(VI) and Dihydrocatalpol (VIII)——i) VI (24.8 mg=0.05 mmole) and VIII (18.1 mg=0.05 mmole) were dissolved in 0.01 M $NaIO_4$ aq. solution (30 ml=0.3 mmole) separately and let standing at room temperature. As a blank test, 0.01 M $NaIO_4$ aq. solution without addition of sample was also left standing similarly. Aliquots of 3 ml of each three solutions were taken at the definite time intervals and were added quickly with saturated $NaHCO_3$ aq. solution (10 ml), 0.01 M sodium arsenite aq. solution (5.0 ml=0.05 mmole) and 20% aq. KI solution (1 ml) in this order. After keeping 15 min, excess arsenite was titrated with 0.01 M I_2 solution and the differences between sample solution and blank were calculated. The results were as given in Table V.

Table V. The Molar Consumption of $NaIO_4$

Samples \ Period of oxidation (hr)	4	6	8	24	27
Tetrahydropicroside I(VI)	1.29	1.71	1.88	2.32	2.33
Dihydrocatalpol (VIII)	1.29	1.69	1.87	2.02	2.10

ii) The same amount of VI as above was treated with 0.01M aq. $NaIO_4$ solution (30 ml) at room temperature. After 4.5 hr, the titration disclosed the consumption of $NaIO_4$ to be 1.48 mole. The reaction mixture (27 ml) was cooled by adding crushed ice and extracted with ether (30 ml×2). The ether extract, after working up in the usual manner, gave a product exhibiting an ester absorption band at 1735 cm^{-1} but no band due to an acid function in its IR spectrum ($CHCl_3$).

Tetraanisoyl Derivative(XXI) from Dihydrocatalpol-ditritylether(IX)——To a solution of dihydrocatalpol ditritylether (IX) (5.0 g) in pyridine (50 ml) was added freshly distilled anisoyl chloride (7 ml) and the total solution was left standing at 43° for 2 days. The precipitates obtained by pouring the reaction mixture into water were collected by filtration and chromatographed repeatedly over silica gel (Merck). Elution with CH_2Cl_2–MeOH (100: 1) furnished XXI (6.9 g, white powder), $[\alpha]_D$ −110° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{85}H_{82}O_{18}$: C, 73.36; H, 5.94. Found: C, 73.32; H, 5.73. IR (CCl_4, cm^{-1}): 3060, 3025, 1730, 1720 (sh.), 1608, 1511, 1254, 1166, 1090, 1036, 847, 704, 695. NMR ($CDCl_3$, 60 MHz) τ: 6.24, 6.23, 6.20, 6.16 (3H each s., OCH_3×4).

Acid Treatment of XXI yielding XXII——To a solution of XXI (6.48 g) in anhydrous benzene (80 ml) was added a solution of p–TsOH·H_2O(6.0 g) in anhydrous MeOH (80 ml) and the total solution was kept at room temperature for 3 days. After neutralization with $BaCO_3$ followed by filtration with the aid of Hyflo Super-Cel (Wako Pure Chem. Ind.), the filtrate was evaporated to dryness. The $CHCl_3$ soluble portion of the residue was chromatographed three times over silica gel (Merck) eluting with CH_2Cl_2. Crude XXII thus obtained was purified further by preparative TLC twice (SiO_2, Merck HF_{254}), using CH_2Cl_2–MeOH (20: 0.3) mixture and then ether–MeOH (20: 0.1) mixture to afford pure sample of XXII (60 mg, amorphous), $[\alpha]_D$ −170° (c=1.0, $CHCl_3$). Mass Spectrum m/e: 350 (M^+, $C_{18}H_{22}O_7$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3540, 1708, 1606, 1510, 1275, 1257, 1170, 1104, 1069, 854. NMR ($CDCl_3$, 100 MHz) τ : 8.6—8.0 (2H m., $C_{(4)}$ -H_2), 7.8—7.4 (1H m., $C_{(5)}$-H), 7.66(1H t., J=8.5 Hz, $C_{(9)}$-H), 3.10, 2.00 (2H each d., J=9 Hz, aromatic protons), and the signals given in Table IV.

On the above described column chromatography, the elution with CH_2Cl_2 also afforded a compound (140 mg) of mp 158.5—160°(dec.), $[\alpha]_D$+110° (c=1.0, acetone), which is provisionally assigned as a p-toluenesulfonyl-monoanisoyl derivative as based on the following data. *Anal.* Calcd. for $C_{24}H_{26}O_9S$: C, 58.76; H, 5.34. Found: C, 58.63; H, 5.27. Mass Spectrum m/e: 480 (M^+), IR ν_{max}^{Nujol} cm^{-1}: 3470, 1710, 1608, 1510. NMR ($CDCl_3$, 60 MHz) τ: 7.71 (3H s., aromatic CH_3), 6.18 (3H s., OCH_3), 3.20, 2.94 (2H each d., J=9 Hz), 2.36 (4H d., J=9 Hz).

Furthermore, the later eluate afforded a crude product (2.5 g) and a part of which was purified by preparative TLC. Although the physical properties of the product (white powder) suggest it to be a trianisoyl derivative of glucose, further examination is necessary. IR ($CHCl_3$, cm^{-1}): 3600—3450, 1720, 1609, 1512, 1285, 1255, 1168, 1100, 1030, 850. NMR ($CDCl_3$, 60 MHz) τ: 3.45—2.95 (6H m.), 2.25—1.80 (6H m.).

Methylation of XXII yielding XXIII——A mixture of XXII (33 mg), Ag_2O (70 mg), CH_3I (50 mg) and dimethylformamide (0.5 ml) was stirred at room temperature for one day and centrifuged. The supernatant was then evaporated to dryness and purified by preparative TLC (SiO_2, Merck HF_{254}) with the aid of CH_2Cl_2–MeOH (100: 1.8) mixture to afford XXIII (14 mg, colorless glassy), $[\alpha]_D$ −140° (c=1.4 ,$CHCl_3$). *Anal.* Calcd. for $C_{19}H_{24}O_7$: C, 62.69; H, 6.64. Found: C, 62.13; H, 6.69. Mass Spectrum m/e: 363 (M^+−1). IR (CCl_4, cm^{-1}): 1715, 1608, 1510, 1275, 1252, 1165, 848. NMR ($CDCl_3$, 100 MHz) τ: 8.6—8.0 (2H m., $C_{(4)}$-H_2), 7.7—

7.4 (1H m., $C_{(5)}$-H). 7.70 (1H t., $J=8$ Hz, $C_{(9)}$-H), 3.11, 2.01 (2H each d., $J=9$ Hz), and the signals given in Table IV.

Desanisoyl Derivative (XXIV) from XXIII——A solution of XXIII (15 mg) in absolute MeOH (1 ml) was treated with 2N NaOMe (one drop), stirred at room temperature for 3 hr, and neutralized with dil. HCl, and quickly purified by preparative TLC (SiO_2, Camag) using CH_2Cl_2–MeOH (25: 1). Ten mg of XXIII was treated in the same manner. The pure sample of XXIV (totally 11 mg), mp 110—112° (recryst. with CCl_4), was obtained from the both treatments. $[\alpha]_D$ −90° ($c=0.7$, $CHCl_3$). Mass Spectrum *m/e*: 230 (M^+, $C_{11}H_{18}O_5$). IR (CCl_4, cm^{-1}): 3588, 1388, 1122, 1028.

Oxidation of XXIV affording Epoxy-ketone (XXV)——To a solution of XXIV (9 mg) in pyridine (0.5 ml) was added CrO_3 (40 mg) and the total mixture was stirred at room temperature for 3.5 hr. After diluting with ether, the suspension was filtered and the filtrate was evaporated to dryness. The product was then purified by preparative TLC to give an epoxy-ketone (XXV). Repeated TLC purification disclosed that the epoxyketone was fairly unstable and was always accompanied with a trace amount of the concomitants, therefore all the physical data were taken with a little impure sample. $[\alpha]_D$ −23° (isooctane). Mass Spectrum *m/e*: 228 (M^+, $C_{11}H_{16}O_5$). UV $\lambda_{max}^{isooctane}$ mμ (ε): 300 (112). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1755, 1118, 1053. ORD (isooctane)[φ](mμ): +267° (400), +9100° (327) (peak), +3954° (317) (inflex.), −13917° (284) (trough), −11187° (252), −18910° (215), −26700° (205). CD (isooctane)[θ](mμ): 0(360), +11740 (320) (inflex.)[23], +16240 (308) (positive maximum), 0 (245), 0 (215), −8200 (200).

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24) Probably due to the minor concomitants.