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Isolation and structure of monochaetin, a metabolite of the fungus *Monochaetia compta*[1,2]

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A new metabolite has been isolated from the fungus *Monochaetia compta*. The properties and reactions of the metabolite suggest that it is 6,8*a*-dihydro-4-acetyl-8-methyl-6-oxo-7(3-methyl-2-oxo)-pentyl-1*H*-2-benzopyran-1-one (**2***a*).

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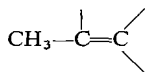
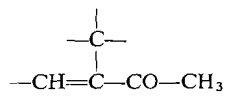
A fungus (PRL 1754) was isolated from wild rose hips (*Rosa acicularis* Lindl.) and identified as *Monochaetia compta* (or possibly *Cryptostictis cynosbati* (Fckl) Sacc. (Melanconiales) (1)). The only member of the Melanconiales for which a metabolite has been reported (2) is *Gloeosporum musarum* (Cke et Mass.) which produced the carotenoid canthaxanthin (4,4′-diketo-β-carotene) (3). The present fungus deposited white crystals m.p. 202.5–203.5° in potato dextrose agar cultures. Constancy of m.p., t.l.c. and p.m.r. spectroscopy, and mass spectral analysis attested to the homogeneity of the new metabolite, which analyzed for $C_{18}H_{20}O_5$. We propose the name monochaetin for this compound and describe work which suggests that its structure is represented by **2***a*.

The p.m.r. spectrum of monochaetin in deuterochloroform solution (Fig. 1) was interpreted as follows: τ 9.03 (3H), a triplet (J = 7 Hz), CH_3CH_2—; 8.3 (2H), a multiplet CH_3CH_2-CH—; 6.81 (1H), a sextet $CH_3CH_2CHCH_3$; 8.87 (3H), a doublet (J = 6 Hz) CH_3CH_2-$CHCH_3$. Double irradiation experiments confirmed the appropriate mutual couplings of this group. Since the methine sextet occurred at a low field position it follows that the next carbon atom was not substituted by hydrogen but by an electronegative atom or group. In view of the i.r. spectrum (see below) a carbonyl group seemed the most probable. A singlet τ 8.67 (3H) was assigned as



and a singlet at τ 7.87 (3H) was interpreted as being due either to a methyl ketone or to an *O*-acetyl group. Chemical tests confirmed that this was a methyl ketone; no acetic acid could be detected after monochaetin was hydrolyzed with sulfuric acid but iodoform was generated by an alkaline solution of iodine and potassium iodide. The remaining peaks were at τ 6.25 (1H), double-doublet (J's = 2 and 13 Hz); 5.90 (1H), a doublet (J = 13 Hz); 4.72 (1H), doublet (J = 0.5 Hz); 4.00 (1H), singlet —CH=C<, a very small coupling to the methyl group at τ 7.87 was revealed by a sharpening of this peak on double irradiation at the frequency of the methyl group, so that the substitution of this double bond could be written



τ 3.20 (1H), double doublet (J's = 0.5 and 2 Hz).

The i.r. spectrum of monochaetin (chloroform) had two sharp bands at 1788 and 1718 cm^{-1} (Fig. 2), which could be assigned to an enol-lactone (or vinyl ester) and a saturated ketone, respectively. A third broad band at 1650–1640 cm^{-1}, together with the bands at 1605 and 1532 cm^{-1} were interpreted as an α,β-α′,β′-dienone and an α,β-unsaturated ketone. The broad

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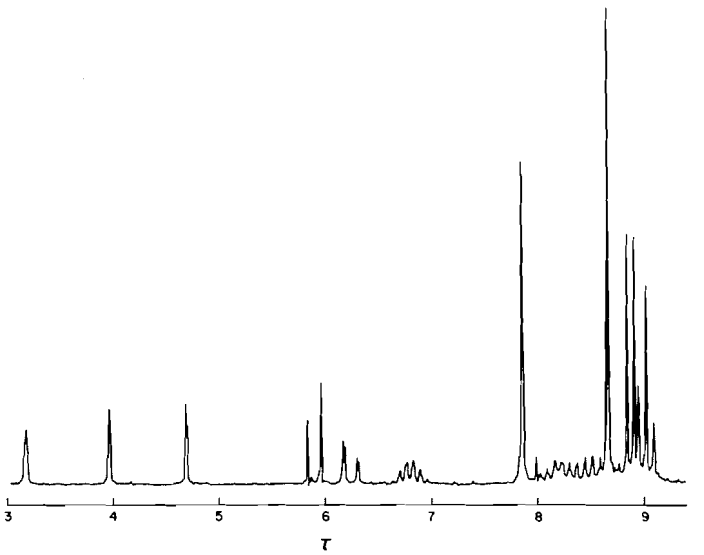


FIG. 1. The p.m.r. spectrum of monochaetin in deuterochloroform solution.

carbonyl band was at lower frequency than is usually suggested for these groups (4), however, this is probably due to the extended conjugation in monochaetin. Additional support for these assignments was provided by the u.v. spectrum (ethanol–water) which had two maxima at 248 (ε 5.83 × 10^3) and 343 nm (ε 2.53 × 10^4). The high extinction coefficients of these absorptions suggested that they were associated with a conjugated unsaturated ketone rather than with an aromatic chromophore. Since an α,β-α′,β′-dienone absorbs close to 244 nm (5) at least one more double bond and several substituents are needed to extend the absorption to the observed maximum at 343 nm.

Treatment of monochaetin with sodium borohydride gave a product, $C_{18}H_{22}O_5$ (**10**), whose i.r. spectrum (KBr) had bands at 3555 and 3380 cm^{-1} (OH) and 1760 cm^{-1} (enol lactone). The band at 1718 cm^{-1} was missing, showing that only the saturated carbonyl group was reduced. The u.v. absorption spectrum was identical to that of monochaetin, confirming that the dienone and α,β-unsaturated ketone functions were not affected. The p.m.r. spectrum of the acetylated reduction product (**11**, $C_{20}H_{24}O_6$) in deuterochloroform, was similar to that of monochaetin but with the following differences. The three protons of the acetate group gave rise to a singlet at τ 7.98. The proton attached to the same carbon atom as the *O*-acetyl appeared as a quartet at τ 4.79. There was a single two proton doublet at τ 6.68 in place of the two separate one proton signals which in monochaetin were at τ 6.25 and 5.9. The signal due to the methine proton in the *sec*-butyl chain had moved upfield. Double irradiation experiments showed that it was located at τ 8.1 and was coupled to the quartet at τ 4.79 as also was the doublet at τ 6.68. Irradiation at the frequency of the quartet caused the doublet to collapse to a singlet at τ 6.68. This spectrum was consistent only with the presence of the group $—CH_2CH(OAc)CH(CH_3)CH_2CH_3$ in this derivative which would have been formed from the $—CH_2COCH(CH_3)CH_2CH_3$ side chain in monochaetin.

Hydrogenation of monochaetin over Adam's catalyst at atmospheric pressure resulted in the rapid uptake of 3 moles of hydrogen with the formation of a crystalline hexahydro derivative **12**. Yields of this crystalline derivative were low but the mother liquors, from which the crystalline hexahydro compound had been isolated, could be further hydrogenated with a slow absorption of hydrogen to give a crystalline octahydromonochaetin **13** in good yield. Neither of the hydrogenated derivatives showed any absorption in the u.v. region. In its i.r. spectrum hexahydromonochaetin did not show any hydroxyl peaks so that it was formed from monochaetin by reduction of three carbon–carbon double bonds. The i.r. spectrum of octahydromonochaetin did have an O—H stretching band at 3390 cm^{-1} and differs from the hexahydro derivative in that a

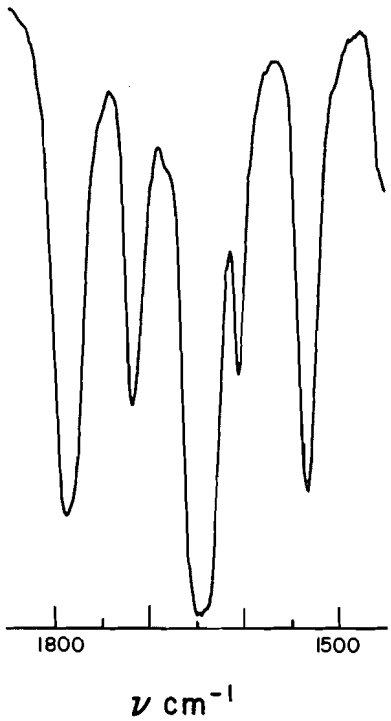
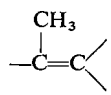
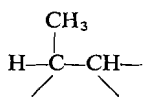


FIG. 2. Part of the i.r. spectrum of monochaetin (chloroform solution).

carbonyl group had been reduced. The p.m.r. spectra of both hydrogenated derivatives, in pyridine-d_5, were too complicated to permit a full analysis but one point is significant. Both spectra contained two high field, three proton, doublets. In octahydromonochaetin these were at τ 8.75 (J = 7 Hz) and 8.9 (J = 6 Hz). Double irradiation experiments showed that the lower field one was coupling to a sextet at τ 7.10 and hence was due to the methyl group in the *sec*-butyl chain. The upper field one was coupling to a multiplet at τ 6.82. Neither of the hydrogenated products had a three proton singlet near τ 8.67 which there had been in the spectrum of monochaetin. This was interpreted as indicating that there was in monochaetin the group



which gave the singlet at τ 8.67 and which had been transformed by hydrogenation into



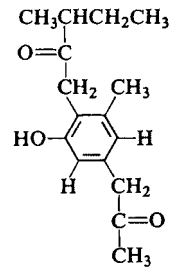
which gave rise to the doublet at τ 8.91.

Monochaetin was insoluble in water and in sodium carbonate solution but dissolved readily in dilute aqueous sodium hydroxide, from which it was recovered unchanged by the addition of acid. The amount of monochaetin recovered depended upon the temperature and the time that elapsed before acidification. After only a few minutes in alkali at room temperature the recovery was quantitative but prolonged heating caused a degradation of the molecule which is discussed in detail at a later point. Such behavior is characteristic of α- or γ-pyrones and lactones. The presence of a γ-pyrone system in monochaetin was discounted because of the complete failure of attempts to form pyrylium salts by treating ethereal solutions of monochaetin with dry hydrogen chloride gas. Confirmatory evidence for the presence of a lactone ring was obtained by allowing monochaetin to react with concentrated ammonia. This resulted in the formation of a new derivative, $C_{18}H_{23}O_5N$ (**14**), formed by the addition of the elements of ammonia. The new compound was insoluble in aqueous acids but had bands in the i.r. at 3400, 3260, and 3150 and 1672 cm^{-1}, and its p.m.r. spectrum had two broad peaks, each one proton, at τ 2.48 and 2.86, compatible with a primary amide. Only a lactone could have been converted into a primary amide with the addition of the elements of ammonia. Further evidence for the enolic nature of this lactone came from the reaction of monochaetin with Tollen's reagent. Although the p.m.r. spectrum of monochaetin had not shown any aldehydic protons a silver mirror was formed in the reaction with Tollen's reagent, implying that an aldehyde group was generated in the alkaline solution, as would be the case with an enol lactone.

The reaction between monochaetin and *N*-bromosuccinimide (1.1 mole) in carbon tetrachloride resulted in the formation of a crystalline monobromo derivative **4**. The p.m.r. spectrum of monobromomonochaetin (in deuterochloroform) was identical to that of monochaetin except for the one proton singlet at τ 4.70 which had been eliminated by bromination. Since this proton was readily replaced by bromine it must have been allylic, but in order to account for its unusually low field position in the p.m.r. spectrum, we suggest that it is allylic to two double bonds and α to a carbonyl group. With two moles of *N*-bromosuccinimide two hydrogen atoms were replaced. This dibromo derivative **5** reacted with

potassium carbonate with the elimination of HBr to give a crystalline product, $C_{18}H_{17}O_5Br$ (**6**), which showed in its p.m.r. spectrum (in $CDCl_3$) the peaks of the *sec*-butyl group at τ 9.03 (3H, triplet); 9.00 (3H, doublet); 8.40 (2H, multiplet); 6.50 (1H, sextet); the methyl ketone at 8.30 (3H, singlet), and the vinylic methyl group at 7.75 (3H, singlet). Two other protons gave rise to singlets at τ 3.32 and 1.23. The u.v. spectrum of this compound (in 50% aqueous ethanol) was different from that of monochaetin and its other derivatives, having maxima at 270 (ε 1.35×10^4), 360 (ε 1.0×10^4), and 555 nm (ε 3.03×10^3).

As mentioned earlier, heating monochaetin with aqueous sodium hydroxide caused a degradation and two smaller fragments were isolated. The first of these was acetic acid, characterized as its *p*-bromophenacyl ester, and isolated in 15% yield. Since it has already been demonstrated that there was no *O*-acetyl in monochaetin the acetic acid must have been formed from the methyl ketone via a retro-Aldol or retro-Claisen reaction. The other product was a non-volatile gum **1** (44% yield) which formed a crystalline 2,4-dinitrophenylhydrazone (**1***a*) having the formula $C_{22}H_{26}O_6N_4$. After allowance for the 2,4-dinitrophenylhydrazine residue this led to $C_{16}H_{22}O_3$ as the formula of the ketonic gum **1**. The u.v. spectrum (in 50% aqueous ethanol) of the ketone showed a single maximum at 282 nm (ε 2720) which moved to 300 nm (ε 3490) on adding 0.5 *N* potassium hydroxide, indicative of a phenolic compound. The formation of a red precipitate with diazotized aniline confirmed the phenolic nature of this product. The formation of a phenolic degradation product, under the conditions of this reaction, from a non-aromatic starting material was further strong evidence that there was in monochaetin a dienone function in a six-membered ring. The i.r. spectrum (liquid film) of the gum **1**, showed hydrogen bonded OH at 3342 cm^{-1} and a ketonic carbonyl at 1705 cm^{-1}. In its p.m.r. spectrum ($CDCl_3$) a two proton signal (broad singlet) at τ 3.5 was assigned to aromatic protons. Two singlets, each (τ 6.27 and 6.47) were assigned as benzylic protons α to the carbonyl groups, and two other singlets (τ 7.87 and 7.95, three protons each) as CH_3CO— and CH_3-aryl respectively. The protons of a *sec*-butyl group were still present as in monochaetin itself. In deuteroacetone as solvent the two aromatic protons had different chemical shifts, occurring at τ 3.4 and 3.5. The signals were broad but became clearly resolved as mutually coupled doublets (J = 1.6 Hz) upon



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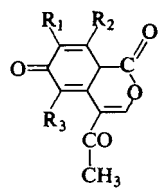
double irradiation at τ 6.47 indicating that the protons were *meta* to each other and confirming that the methylene group at τ 6.47 was α to the ring. The structure of this compound must be **1** or an isomer of this in which the positions of the nuclear substituents are interchanged.

We propose the structure **2***a* for monochaetin as the only one which incorporates all of the structural elements which have been identified and which satisfactorily explains the observed chemistry. For example, in dilute alkali the



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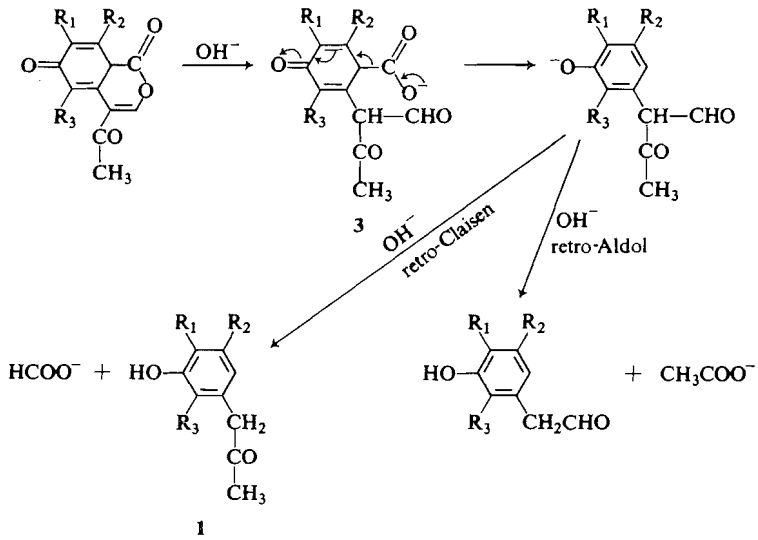
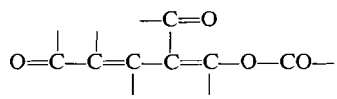
	R_1	R_2	R_3
a	$CH_2COCH(CH_3)CH_2CH_3$	CH_3	H
b	CH_3	$CH_2COCH(CH_3)CH_2CH_3$	H
c	H	$CH_2COCH(CH_3)CH_2CH_3$	CH_3
d	$CH_2COCH(CH_3)CH_2CH_3$	H	CH_3
e	CH_3	H	$CH_2COCH(CH_3)CH_2CH_3$
f	H	CH_3	$CH_2COCH(CH_3)CH_2CH_3$



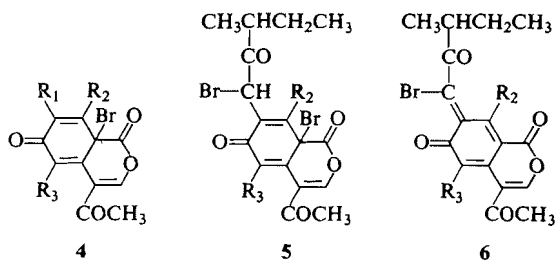
SCHEME 1

lactone ring would open as shown in Scheme 1 to give the anion **3** which is an aldehyde and would react with Tollen's reagent to give a silver mirror. Prolonged heating with alkali could cause further reaction as shown, accounting for the formation of the isolated products. The proposed structure also incorporates a chromophoric group which could reasonably be expected to give the observed u.v. spectrum *viz.*



The structure also contains a proton which is allylic to two double bonds and α to a carbonyl group, which according to Shoolery's rules (6) would resonate close to the observed value at τ 4.70 in the p.m.r. spectrum. One would expect this proton to be the one most easily replaced by reaction with *N*-bromosuccinimide leading to the monobromo derivative **4**. The next most easily replaceable hydrogen would be the one allylic to one double bond and α to a carbonyl group so that the dibromo derivative would be **5** for which the spectra are consistent. Elimination of HBr could occur to give **6** which being a quinone methide ought to be colored, as observed.

The low resolution mass spectrum of monochaetin (Table 1) also lends support to the proposed structure, **2***a*, as indicated by the following brief description of the fragmentation. One mode of α-cleavage of the methyl ketone would account for the abundant ion at *m/e* 43 (CH_3CO^+). The alternative mode of cleavage would result in the loss of CH_3 to give ion *m/e* 301 and subsequent loss of CO to give ion *m/e* 273. The latter could then lose CO_2 (from the lactone ring) to produce ion *m/e* 229.



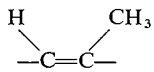
The ions *m/e* 259 (loss of C_4H_9) and 85 ($C_5H_9O^+$) are indicative of the two possible modes of α-cleavage of the *sec*-butyl ketone. Each of these ions could then lose CO, accounting for the ions *m/e* 231 and 57, respectively. A metastable peak at 38.3 confirmed the fragmentation of ion *m/e* 85 to 57. Loss of CO from ion *m/e* 231 would account for ion *m/e* 203 (this is supported by the occurrence of a metastable ion at *m/e* 178), and subsequent loss of ketone would lead to the base peak *m/e* 161.

Alternative structural proposals such as **2***b* and **2***c* were discounted because they could not

TABLE 1
The mass spectrum of monochaetin

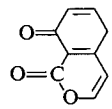
m/e	Relative abundance	m/e	Relative abundance
29	20.0	145	2.6
29.5m	0.06	146	2.5
32	2.0	148	5.3
38.3m	0.06	159	22.7
39	6.0	160	5.3
41	12.0	161	100.0
43	26.6	162	14.0
44	2.0	163	1.3
51	3.3	169m	0.2
53	2.0	175	5.3
55	2.6	178m	0.06
57	50.0	182	1.0
58	2.3	187	6.0
63	3.3	188	3.0
65	2.3	189	4.0
77	8.0	190	6.0
78	4.0	203	21.3
79	2.0	204	6.0
85	5.3	214	3.3
89	1.3	216	6.0
91	4.0	218	1.3
102	1.3	229	1.3
103	6.0	231	44.7
105	2.6	232	16.7
106	1.7	233	2.3
115	4.7	243	4.7
116	1.7	244	1.0
119	2.0	259	1.0
131	3.3	273	0.8
132	9.3	301	1.2
133	2.7	316	20.0
137	2.3	317	4.0
		318	0.5

account for the elimination of HBr. Structures such as **2***d* and **2***e* would have degraded with alkali to give a phenol having protons on adjacent nuclear positions for which the coupling constant would have been about 6 Hz and hence these two structures are untenable. The structure **2***f* was considered less likely than **2***a* because it contains the unit



in which detectable coupling between the methyl group and the vinylic proton would be expected.

Other locations of the lactone ring were also considered but deemed unsatisfactory. No structures based upon the system **7** could account for the p.m.r. spectrum of monochaetin, while the systems **8** and **9** could not provide a satisfactory explanation for either the u.v. spectrum or for the loss of the lactone carbonyl group upon treatment with sodium hydroxide.



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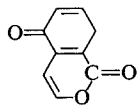

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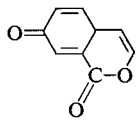

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Experimental

General Directions

The p.m.r. spectra were determined using either a Varian HA-100 or a Varian T-60 spectrometer with TMS as an internal standard. The i.r. spectra were recorded on a Perkin-Elmer 21 spectrometer and u.v. spectra were determined using a Cary 14. Mass spectra were determined on an A.E.I. MS 12 spectrometer. A Fisher hot stage m.p. apparatus was used for all m.p.'s, which are uncorrected.

Growth

A medium consisting of 1% dextrose and 1% Difco Yeast extract (50 ml) was inoculated with the organism *Monochaetia compta* (PRL 1754) and incubated at 24°, on a rotary shaker, for 4 days. The cells were collected and dispersed in water (100 ml) and the suspension spread with a small paint brush upon the growth medium, which consisted of Difco Potato Dextrose agar enriched with 20 g/l of dextrose and contained in pyrex dishes (31 cm × 46 cm, 500 ml of agar per dish) covered with aluminum lids. The cultures were incubated at 24 to 26° for 30 days.

Extraction

The whole agar culture was freeze-dried and the residue extracted exhaustively with chloroform. The white solid resulting from evaporation of the extract was washed with light petroleum (30–60°) to remove oils. The yield of monochaetin determined at this point was 1.85 g/l of agar. Treatment with charcoal and several crystallizations from ethanol gave pure monochaetin, m.p. 202.5–203.5°, $[\alpha]_D^{25} = 1040 \pm 10°$ (*c*, 0.3 $CHCl_3$), λ_{max} (50% aqueous ethanol) 248 (ε 5.83 × 10^3) and 343 nm (ε 2.53 × 10^4).

Anal. Calcd. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.26; H, 6.45.

Test for O-Acetyl

Sulfuric acid (2 *N*, 50 ml) was steam distilled until 100 ml of distillate had been collected. This was discarded and a fresh quantity of distillate (50 ml) was obtained to serve as a blank. Monochaetin (95.7 mg) was added to the sulfuric acid and the mixture heated under reflux for 1.5 h. The residual solution was again steam distilled to obtain 50 ml of distillate. Both the blank and the distillate after reaction had the same p*H* (4.8) and each required the same quantity of standard sodium hydroxide solution (0.2 ml, 0.036 *N*) to take the p*H* to 8.

Sodium Borohydride Reduction

Monochaetin (316 mg, 1.0 m*M*) and sodium borohydride (28 mg, 0.75 m*M*) were dissolved in dry methanol (15 ml) and stirred at room temperature for 2 h. The resulting solution was acidified with dilute sulfuric acid (15 ml) and extracted with chloroform. The chloroform was evaporated and the residue separated by preparative layer chromatography. The major product, **10**, crystallized from ethanol (96 mg, 30% yield), m.p. 105–107°. In

the u.v. it had λ_{max} (ethanol) 247 (ε 6.07 × 10^3) and 352 nm (ε 2.32 × 10^4).

Anal. Calcd. for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found (mol. wt. (mass spectroscopy) 318): C, 67.69; H, 7.05.

Acetylation of the Sodium Borohydride Reduction Product

The above reduction product **10** (31 mg) was dissolved in pyridine (0.5 ml) and acetic anhydride (0.5 ml) and allowed to stand at room temperature overnight. Water (1 ml) was added to the reaction mixture and the acetyl derivative **11** collected (24 mg, 69% yield) and crystallized from aqueous ethanol, m.p. 216–217°.

Anal. Calcd. for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found (mol. wt. (mass spectroscopy) 360): C, 66.83; H, 6.66.

Catalytic Hydrogenation

Monochaetin (459 mg) was dissolved in ethanol (100 ml) that had been distilled from magnesium ethoxide and the solution was shaken with hydrogen in the presence of Adams' platinum oxide (197.9 mg). Rate of uptake changed abruptly after 1.66 h when 120 ml of hydrogen had been absorbed (theoretical uptake for the catalyst and three double bonds, 122.4 ml). After filtering the catalyst, the solution was concentrated and a white precipitate (78 mg) formed. This was purified by chromatography on a silicic acid column. *Hexahydromonochaetin* (**12**) crystallized from methanol, m.p. 247–248°. No absorption in the u.v. region.

Anal. Calcd. for $C_{18}H_{26}O_5$: C, 67.06; H, 7.89. Found (mol. wt. (mass spectroscopy) 322): C, 67.05; H, 7.89.

The mother liquors were returned to hydrogenate until the uptake of hydrogen ceased. The filtrate was concentrated and *octahydromonochaetin* (**13**), m.p. 220–221°, precipitated upon standing. No absorption in the u.v. region.

Anal. Calcd. for $C_{18}H_{28}O_5$: C, 66.64; H, 8.70; Found (mol. wt. (mass spectroscopy) 324): C, 66.65; H, 8.90.

Effect of Alkali on Monochaetin

Monochaetin (24.4 mg) was dissolved in 0.02 *N* sodium hydroxide (6 ml) with a little gentle warming and immediately acidified with *N* sulfuric acid. The precipitate was collected and dried (16.8 mg) and crystallized from aqueous ethanol. The recovered material had m.p. 202.5–203.5°, and was identical with monochaetin (mixed m.p., i.r.) (starting material, m.p. 202.5–203.5°).

Hydrolysis of Monochaetin

Monochaetin (328 mg) was heated with 5% sodium hydroxide (23 ml) at reflux, in a nitrogen atmosphere, for 1.5 h. The cooled solution was acidified with dilute sulfuric acid and steam distilled until 100 ml of distillate had been collected. The residual liquor was extracted thoroughly with ether–chloroform (4:1) and the dried extract evaporated and fractionated by silicic acid column chromatography. Elution with chloroform–benzene (85:15) yielded a gum, **1**, which appeared to be homogenous (t.l.c.). In the u.v. (1:1 aqueous ethanol) it had λ_{max} 282 nm (ε 2720) which shifted in alkali to 300 nm (ε 3490).

The 2,4-dinitrophenylhydrazone derivative, **1***a*, had m.p. 180°.

Anal. Calcd. for $C_{22}H_{26}O_6N_4$: C, 59.72; H, 5.92; N, 12.66. Found: C, 59.97; H, 5.89; N, 12.55.

Mass of parent ion calcd. for $C_{22}H_{26}O_6N_4$: 442.1852. Found: 442.1847. (High resolution measurements by Dr. A. M. Hogg, University of Alberta, Edmonton, Alberta.)

The acids in the steam distillate were neutralized with 0.02 *N* sodium hydroxide and the solution evaporated to dryness. To the salts, dissolved in water (2 drops) was added *p*-bromophenacyl bromide (1.1 mole) in ethanol (100 ml) and the solution was boiled for 30 min. The solvent was evaporated and the residue chromatographed on silicic acid. Elution with $CHCl_3$–C_6H_6 (85:15 v/v) gave *p*-bromophenacyl acetate, m.p. 84° (lit. (7) m.p. 86°). The i.r. spectrum was identical with that of a standard sample.

Reaction with Ammonia

Monochaetin (200 mg) was dissolved in concentrated ammonia (8 ml) and warmed for 20 min. The solution was diluted with water and the precipitate (150 mg) collected and crystallized from aqueous ethanol to give needle-like crystals, m.p. 238–239°. In the u.v., the product **14** had λ_{max} 247 (ε 5.38 × 10^3) and 356 nm (ε 1.96 × 10^4).

Anal. Calcd. for $C_{18}H_{23}O_5N$: C, 64.85; H, 6.71; N, 4.20. Found (mol. wt. (mass spectroscopy) 333): C, 65.11; H, 6.80; N, 4.32.

Monobromomonochaetin (4)

Monochaetin (316 mg, 1 m*M*) was heated with *N*-bromosuccinimide (178 mg 1 m*M*) and a trace of benzoyl peroxide in carbon tetrachloride (30 ml). After 2 h the reaction mixture was washed with water (30 ml), dried, and evaporated to give a yellow solid (390 mg) which crystallized from ethanol as colorless needle-like crystals, m.p. 224–225°. The parent ion in the mass spectrum (mass 394) showed the appropriate isotope distribution for a compound containing one bromine atom.

Anal. Calcd. for $C_{18}H_{19}O_5Br$: C, 54.68; H, 4.81. Found: C, 54.67; H, 4.83.

Dibromomonochaetin (5)

Monochaetin (121 mg, 0.38 m*M*) was heated with *N*-bromosuccinimide (157 mg, 0.88 m*M*) and a trace of benzoyl peroxide in carbon tetrachloride (35 ml) overnight. The reaction mixture was washed with water, dried, and evaporated to give a gum (120 mg) which was separated by preparative t.l.c. on silica gel using chloroform–ether–benzene (7:2:1). The major product was a gum which decomposed to a considerable extent in 2–3 days at room temperature but was stable indefinitely at liquid nitrogen temperature. The parent ion in the mass spectrum (*m/e* 472) showed the appropriate isotope distribution for a compound containing two bromine atoms. In the u.v. it had λ_{max}(EtOH) 225 (ε 9 × 10^3), 267 (ε 1.4 × 10^4), and 357 nm (ε 1.45 × 10^4).

Anal. Calcd. for $C_{18}H_{18}O_5Br_2$: C, 45.58; H, 3.83. Found: C, 45.33, H, 3.70.

Dehydrobromination of Dibromomonochaetin

Dibromomonochaetin (80 mg) and potassium carbonate were heated together in ethanol (30 ml) for 2 h. The reaction mixture was filtered and acidified with dilute sulfuric acid, then water (15 ml), benzene (15 ml), and chloroform (15 ml) were added. The aqueous phase was separated and the non-polar layer was dried and evaporated. The residue was fractionated by preparative t.l.c.

and a crystalline product (**6**) (18 mg) m.p. 109–110° was obtained from the yellow band on the t.l.c. plates. The u.v. had λ_{max}(EtOH) 270 (ε 1.35 × 10^4), 360 (ε 1.0 × 10^4), and 555 nm (ε 3.03 × 10^3).

Anal. Calcd. for $C_{18}H_{17}O_5Br$: C, 54.98; H, 4.35. Found (mol. wt. (mass spectroscopy) 392): C, 55.22; H, 4.46.

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