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PICRASINS, SIMAROUBOLIDES OF JAPANESE QUASSIA TREE *PICRASMA QUASSIOIDES**

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Key Word Index—*Picrasma quassioides*; Simaroubaceae; Japanese quassia tree; simaroubolides; picrasins.

Abstract—From the Japanese quassia tree, *Picrasma quassioides* (Simaroubaceae), new bitter principles (simaroubolides), picrasin *A*, *B*, *C*, *D*, *E*, *F* and *G* have been isolated whose stereostructures have been elucidated on the basis of chemical and physical evidence. The relative bitterness of the picrasins and the related simaroubolides has been measured.

INTRODUCTION

The crude drug Lignum Picrasmae, the wood of *Picrasma quassioides* Bennett (*P. ailanthoides* Planchon) (Simaroubaceae), is widely used as a stomachic in Japan because of its remarkably bitter taste and its innocuous nature.

Efforts directed towards isolation of its bitter principles were initiated as early as the last century. Thus, Simoyama and Hirano [1] reported the isolation of a bitter principle quassiin having the composition $C_{31}H_{42}O_9$ which, however, was not well characterized. Since then a number of substances such as the alcohol, nigakinol, the quinone, 2,6-dimethoxy-*p*-benzoquinone, and the canthine alkaloids, nigakinone and methylnigakinone, have been isolated [2–4] none of which, however, are the bitter components of the plant. In order to clarify the chemistry of the bitter principles of this important crude drug, therefore, an investigation seemed called for. However, our attempts to isolate quassiin were unsuccessful. Instead, we isolated and characterized seven new bitter substances (simaroubolides) designated as picrasin *A* to *G* whose stereostructures have been determined. While these investigations were under way, the isolation of a number of substances from the same plant was announced by Takahashi and his co-workers [5–14]; i.e. nigakilactones *A–C*, *E*, *F*, *H* and *J–N*, and nigakihemiacetal *A* and *C* as well as quassin (nigakilactone *D*), picrasin *A* (nigakilactone *G*), picrasin *B* (nigakilactone *I*) and neoquassin (nigakihemiacetal *B*). We have also isolated nigakilactone *B*, *F* and *H*, besides the new simaroubolides from our plant material. In the present report, we wish to present our results in detail which indicate the stereostructures **1**–**7** for picrasin *A–G*, respectively.

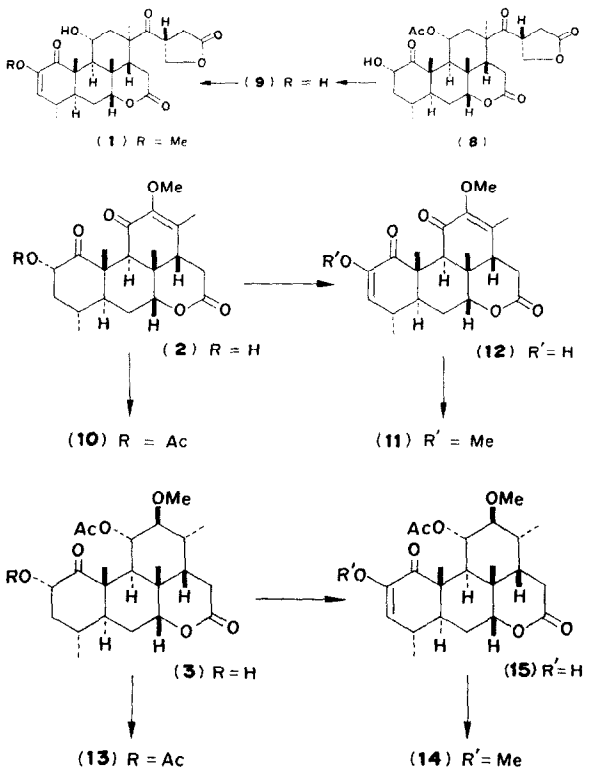
RESULTS

Isolation of the simaroubolides was performed first by extraction with ethyl acetate of the methanol extract of the crude drug and then by repeated liquid chromatography over silica gel.

Picrasin *A* (**1**), $C_{26}H_{34}O_8$ (M^+ *m/e* 474), was shown by its spectral properties to possess a secondary methyl (δ 0·89), three tertiary methyls (δ 0·94, 0·97, 1·39), an α,β-disubstituted, α,β-unsaturated carbonyl in a six- or larger-membered ring (λ_{max} 271 nm, ν_{max} 1680, 1645 cm^{-1}, δ 5·34), a saturated carbonyl (ν_{max} 1720 cm^{-1}), a δ-lactone (ν_{max} 1733 cm^{-1}), a γ-lactone (ν_{max} 1775 cm^{-1}), a methoxyl (δ 3·45), and a hydroxyl (δ_{max} 3470 cm^{-1}). The hydroxyl is resistant to acetylation, indicating it to be tertiary or sterically hindered secondary. Picrasin *A* therefore possesses a

* Part of the research described here has been presented in preliminary form: Hikino, H., Ohta, T. and Takemoto, T. (1970) *Chem. Pharm. Bull.* **18**, 219; (1970) *ibid*, **18**, 1082; (1971) *ibid*, **19**, 212; (1971) *ibid*, **19**, 2203; (1971) *ibid*, **19**, 2211; (1971) *ibid*, **19**, 2651.

C_{25} skeleton which consists of three carbocycles and two lactone rings, and is obviously closely related to simarolide (**8**), the bitter substance in *Simaruba amara* L. of the same family [15, 16]. This relationship was confirmed by methylation of deacetyl-dehydrosimarolide (**9**) [15] to furnish a methyl ether which was shown to be identical with picrasin *A*. The stereostructure of picrasin *A* is consequently represented by formula **1**.



Picrasin *A* is thus the second example of the simaroubolides having the C_{25} simarolidane skeleton. Since an oxygen function (carbonyl) is once introduced to the C-12 position of a simarolidane derivative possessing a carbonyl group at C-17, the C_5 side-chain at C-13 can be readily split off to give a quassolidane derivative, and therefore picrasin *A* may be an intermediate for certain other bitter principles having the quassolidane skeleton in this plant.

Picrasin *B*, $C_{21}H_{28}O_6$ (M^+ *m/e* 376), was indicated by its spectral properties to have a secondary methyl (δ 0·90), two tertiary methyls (δ 1·16, 1·42), a vinyl methyl (δ 1·87), an α,β,β-trisubstituted, α,β-unsaturated carbonyl in a six- or larger-membered ring (λ_{max} 254 nm, ν_{max} 1677, 1640 cm^{-1}, no vinyl hydrogen signal), a saturated carbonyl in a six- or larger-membered ring (ν_{max} 1722 cm^{-1}), δ-lactone (ν_{max} 1737 cm^{-1}, δ 4·22, solution in aqueous alkali, no reaction with diazomethane), a methoxyl (δ 3·62), and a secondary hydroxyl (ν_{max} 3520 cm^{-1}, δ 4·80). Picrasin *B* formed the monoacetate (**10**), in which the NMR carbinyl hydrogen signal is shifted at a notably lower field (δ 5·83). Since the carbinyl hydrogen signal is fairly deshielded and since picrasin *B* consumed periodate, the carbonyl and the hydroxyl must be vicinal. Further, all the NMR signals were analyzed thoroughly with the aid of extensive double resonance experiments to establish the presence of the partial structures involving C-1–C-7, C-8–C-10, C-11–C-13, and C-14–C-15 in formula **2**. The somewhat deshielded line positions (δ 2·55, 2·97) and the large coupling constant (*J* 16 Hz) of the C-15 methylene hydrogens suggest the methylene to be adjacent to a carbonyl. These data have many features in common with those of the other quassinoids, e.g. quassin (**11**) [16–18] from *Quassia amara* L., and furthermore, the chemical shifts and splitting patterns of certain NMR signals in picrasin *B* coincide with those in quassin except for those due to the hydrogens in the environment of C-2 and C-3. The combined evidence demonstrates that picrasin *B* is similar in structure to quassin. Consequently, picrasin *B* on bismuth trioxide oxidation afforded the diosphenol (**12**) which was methylated with diazomethane to give quassin. The accumulated results have thus established the stereostructure of picrasin *B* except for the configuration at C-2. The disposition of the C-2 hydrogen was deduced by its NMR signal [δ 4·80 in picrasin *B* or δ 5·83 in the acetate (**10**)], whose splitting pattern (*J* 7, 11 Hz or 7, 12 Hz, respectively) indicates it to be an axial hydrogen, leading to the conclusion that the C-2 hydrogen is β. The stereostructure **2** has thus been deduced for picrasin *B*.

Picrasin *C*, $C_{23}H_{34}O_7$ (M^+ *m/e* 422), was shown by its spectral properties to have two secondary methyls (δ 0·88, 1·03), two tertiary methyls (δ 1·24, 1·27), a δ-lactone (ν_{max} 1724 cm^{-1}, δ 4·15, solution in aqueous alkali, no reaction with diazomethane), a saturated carbonyl in a six- or larger-membered ring (ν_{max} 1705 cm^{-1}), a

methoxyl (δ 3·40), a secondary hydroxyl (ν_{max} 3470 cm^{-1}, δ 4·68), and a secondary acetoxyl (ν_{max} 1720, 1247 cm^{-1}, δ 1·90, 5·22). The presence of the secondary hydroxyl was corroborated by the formation of the monoacetate (**13**) whose NMR carbinyl hydrogen signal showed an acetylation shift (δ 5·56). Consumption of the reagent on periodate oxidation of picrasin *C* indicated the hydroxyl and the ketonic carbonyl to constitute an α-ketol system. These results have led us to conclude that the structure of picrasin *C* is similar to that of nigakilactone *C* (**14**) [5,9]. In confirmation, picrasin *C* was oxidized with bismuth trioxide to give the diosphenol (**15**) which on methylation with diazomethane yielded nigakilactone *C*. The C-2 hydrogen signal (δ 4·68) in the NMR spectrum of picrasin *C* has the band width at half-height of 24 Hz, demonstrating that it is axially- and consequently α-oriented. The stereostructure **3** has thus been established for picrasin *C*.

Picrasin *D*, $C_{22}H_{30}O_6$ (M^+ *m/e* 390), was exhibited by its spectral properties to contain two secondary methyls (δ 1·08, 1·10), two tertiary methyls (δ 1·27, 1·42), an α,β-disubstituted, α,β-unsaturated carbonyl in a six- or larger-membered ring (λ_{max} 262 nm, ν_{max} 1705, 1635 cm^{-1}, δ 5·23), a δ-lactone (ν_{max} 1722, 1235 cm^{-1}, δ 4·18), and a methoxyl (δ 3·56). Assignment of the two remaining oxygen atoms was a problem awaiting solution. The occurrence in the NMR spectrum of two carbinyl hydrogen signals at 3·40 and 3·56 ppm which are coupled to each other indicated that the two oxygens are situated at two vicinal carbons. Further, two significant signals were visible at a considerably low field region (δ 4·98, 5·15) and were coupled to each other by a rather small coupling constant (*J* 1 Hz). This finding together with the appearance of a characteristic IR band at 2770 cm^{-1} were interpreted as originating from the presence of an unexpected methylenedioxy ring whose occurrence in the aliphatic substances in Nature is extremely rare. Analysis of the NMR spectrum with the aid of double resonance experiments showed the presence of the partial structures participating C-1–C-7 and C-8–C-15 in formula **4**. The somewhat deshielded line position of the signal (δ 2·40 in $CDCl_3$–C_6D_6 = 1:1) for the C-15 methylene may be rationalized by its location α to a carbonyl. Since there is no other center of unsaturation, picrasin *D* contains three carbocyclic rings. The partial structures thus deduced have many common features with those of nigakilactone *B* (**16**) [5,9]. In fact, the NMR parameters for certain hydrogens and the ORD and CD data (Fig. 1) of picrasin *D* agree with those of nigakilactone *B* (**16**). Whereupon it was concluded that picrasin *D* is a congener of nigakilactone *B* (**16**) where the glycol monomethyl ether system in the latter is replaced by a methylenedioxy ring in the former. The similarity of the ORD and CD curves of picrasin *D* and quassin [19] defined the stereochemistry on the A/B ring junction. The *trans*-diaxial relationship between the C-4 and C-5 hydrogens was evidenced by the large coupling constant (*J* 9·5 Hz), showing the α-equatorial orientation of the C-4 methyl. The pattern for the C-7 hydrogen signal (*J* 2, 2·5 Hz) indicates it to be in the β-equatorial configuration. The long range couplings between the C-8 methyl hydrogens and C-9 hydrogen and between the C-10 methyl hydrogens and C-9 hydrogen are taken as two pairs of functions being both in the antiparallel situation. The coupling constants between the C-9 and C-11 hydrogens, the C-11 and C-12

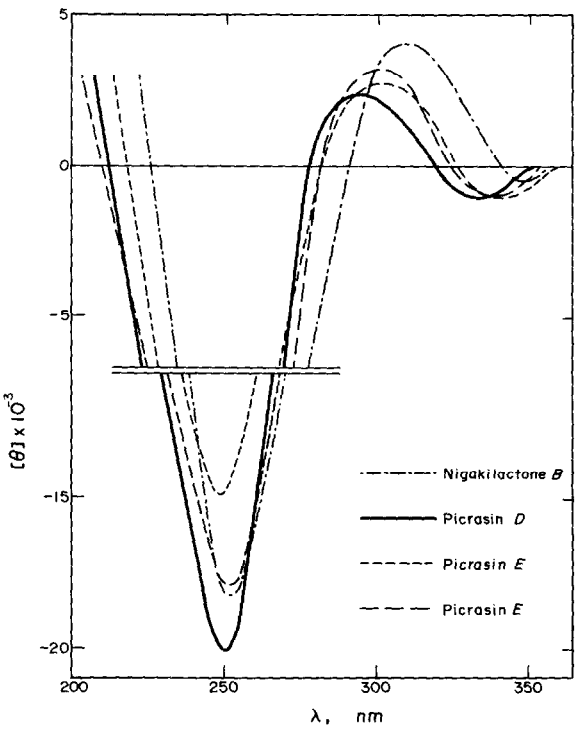
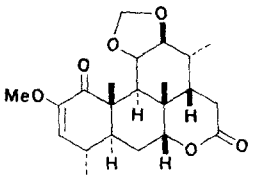


Fig. 1.

hydrogens, the C-12 and C-13 hydrogens, and the C-13 and C-14 hydrogens are 11, 8·5, 11, and 5 Hz, respectively, indicating the *trans*-diaxial, *trans*-diaxial, *trans*-diaxial, and gauche relationship of each pair of the hydrogens. These observations have led to the conclusion that picrasin *D* has the structure **4**.



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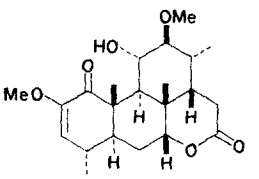

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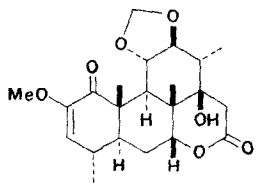

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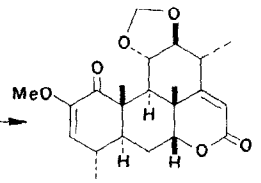
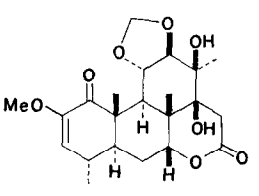


(17)

Picrasin *E*, $C_{22}H_{30}O_7$ (M^+ *m/e* 406), was demonstrated to have the functional groups similar to those of picrasin *D*. Thus, from the spectral properties, the presence of two secondary methyls (*δ* 0·90, 1·28), two tertiary methyls (*δ* 1·33, 1·47), an *α,β*-disubstituted, *α,β*-unsaturated carbonyl in a six- or larger-membered ring (λ_{max} 262 nm, ν_{max} 1700, 1635 cm^{-1}, *δ* 5·21), a *δ*-lactone (ν_{max} 1715, 1260 cm^{-1}, *δ* 4·75), and a methoxyl (*δ* 3·47) was revealed. Occurrence of the unusual methylenedioxy ring as in picrasin *D* was again substantiated by the NMR signals at 3·54 and 3·80 ppm (mutual *J* 9 Hz), and 5·15 and 5·31 ppm (mutual *J* 1 Hz) and also by the characteristic IR band at 2770 cm^{-1}. Analysis of the NMR spectrum demonstrated that picrasin *E* also possesses the part structures involving C-2–C-7, C-8–C-13, and C-15 in formula **5** as picrasin *D*. The chemical shifts and splitting patterns of certain NMR signals and ORD and CD data (Fig. 1) of picrasin *E* are in accord with those of picrasin *D*. The accumulated data suggested that picrasin *E* is a derivative of picrasin *D*. Picrasin *E* differs in having one extra tertiary hydroxyl (ν_{max} 3530 cm^{-1}, no NMR carbinyl hydrogen signal), which, taking into account the above deduced partial structures, can only be accommodated at C-14. This assignment was supported by the appearance of signals in an AB spectrum at a rather deshielded region (*δ* 2·95, 3·27) which, along with the considerably large coupling constant (*J* 19 Hz) found between these two signals, are considered to be due to an HO⩾C–CH_2–CO-moiety. Picrasin *E* was thus treated with thionyl chloride in pyridine to afford anhydropicrasin *E* (**17**) whose spectral properties indicated the disappearance of the *δ*-lactone having the isolated *α*-methylene present in picrasin *E* and instead the formation of a *β,β*-disubstituted *α,β*-unsaturated *δ*-lactone [λ_{max} 214 nm, ν_{max} 1727 cm^{-1}, *δ* 5·85 (no coupling to other hydrogen signals)]. The *β*-orientation of the C-14 hydroxyl in picrasin *E* is revealed by the downfield shift [20] ($\Delta\delta$ −0·52 ppm) of the C-7 hydrogen signal in comparison with that of picrasin *D*. The observation of the nuclear Overhauser effect (NOE, 10%) between one of the C-15 hydrogens (*δ* 2·95) and the C-13 methyl hydrogens (*δ* 1·28) demonstrates their spatially close relationship, corroborating the *α*-configuration of the C-13 methyl. The NOE's (14 and 13%) were also found between the C-7 carbinyl hydrogen (*δ* 4·75) and the C-8 methyl hydrogens (*δ* 1·33) and between the C-11 carbinyl hydrogen (*δ* 3·80) and the C-8 methyl hydrogens (*δ* 1·33), a fact which showed the *cis*-relation of the two pairs of hydrogens. Based on the above evidence, it has been concluded that picrasin *E* is represented by formula **5**.

Picrasin *F*, $C_{22}H_{30}O_8$ (M^+ *m/e* 422), was also revealed to possess a secondary methyl (*δ* 0·87), three tertiary methyls (*δ* 1·50, 1·54, 1·62), an *α,β*-disubstituted, *α,β*-unsaturated carbonyl in a six- or larger-membered ring (λ_{max} 262 nm, ν_{max} 1709, 1630 cm^{-1}, *δ* 5·21), a *δ*-lactone (ν_{max} 1720, 1240 cm^{-1}, *δ* 4·67), a methoxyl (*δ* 3·48), a methylenedioxy ring [ν_{max} 2750 cm^{-1}, *δ* 3·44, 4·29 (*J* 9·5 Hz), *δ* 5·18, 5·37 (*J* 1 Hz)], and a tertiary hydroxyl (ν_{max} 3475 cm^{-1}, no NMR carbinyl hydrogen signal). Further analysis of the NMR spectrum with the aid of double resonance experiments has demonstrated the presence of the partial structures involving C-2–C-5–C-8–C-12, C-6–C-7, C-13, and C-15 in formula **6**. *Inter alia*, NOE's (11 and 12%) were found between the C-11 hydrogen (*δ* 4·29) and the C-8 methyl hydrogens (*δ* 1·62) and between one of the C-15 hydrogens

(δ 2·91) and the C-13 methyl hydrogens (δ 1·54). These data together with the NMR parameters for certain hydrogens and ORD and CD data (Fig. 1) of picrasin *F*, also in agreement with those of picrasin *D* and *E*, indicate the close relationship of picrasin *F* to picrasin *D* and *E*. Picrasin *F* differs from picrasin *E* in having one extra tertiary hydroxyl which can only be accommodated at C-13 by the facts that the C-12 hydrogen signal in the NMR spectrum appears as a doublet showing coupling only with the C-11 hydrogen, and the C-13 methyl hydrogen signal occurs as a singlet at a deshielded position (δ 1·54). The large coupling constants between the C-9 and the C-11 hydrogens, and the C-11 and the C-12 hydrogens (*J* 11 and 9·5 Hz, respectively) show the *trans*-diaxial relation of each pair of the hydrogens. The considerable lower-field displacement of the NMR signal for the C-11 hydrogen relative to the corresponding signals in picrasin *D* and *E* which is caused by the effect from the C-13 hydroxyl situated in the 1,3-diaxial relationship. This finding, together with the NOE observed between one of the C-15 hydrogens and the C-13 methyl hydrogens, indicate the α-configuration of the C-13 methyl group. Accumulated data has led to the conclusion that picrasin *F* has the stereostructure **6.**

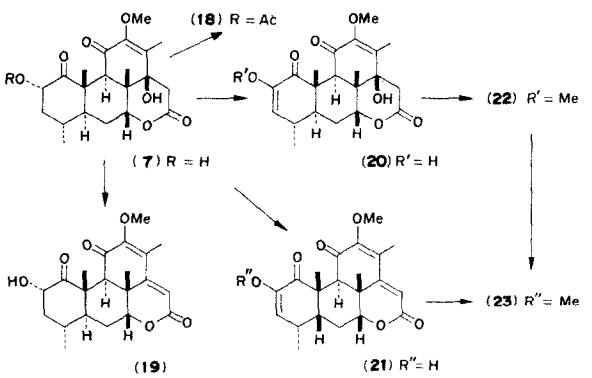


(6)

From the biogenetic viewpoint, it is assumed that the C-12 methoxyl and the neighboring C-11 hydroxyl of nigakilactone *B* (**16**) are subjected to an oxidative cyclization to give picrasin *D* (**4**) which on successive hydroxylation at C-14 and C-13 furnishes picrasin *E* (**5**) and picrasin *F* (**6**). Picrasin *D*, *E* and *F* provide three of the rare examples of methylenedioxy groups attached to saturated carbons.

Picrasin *G*, $C_{21}H_{28}O_7$ (M^+ *m/e* 392), was shown by its UV, IR, and NMR spectra to have a secondary methyl (δ 0·92), two tertiary methyls (δ 1·12, 1·45), a vinyl methyl (δ 1·90), a secondary hydroxyl [ν_{max} 3440 cm^{-1}, δ 4·84, formation of the monoacetate (**18**) (ν_{max} 1720, 1230 cm^{-1}, δ 2·11, 5·87)], a saturated carbonyl in a six- or larger-membered ring (ν_{max} 1710 cm^{-1}), a fully substituted, α,β-unsaturated carbonyl in a six- or larger-membered ring (λ_{max} 252 nm, ν_{max} 1685, 1630 cm^{-1}), a δ-lactone (ν_{max} 1722, 1230 cm^{-1}, δ 4·62), and a methoxyl (δ 3·62). Since the monoacetate (**18**) still exhibits in the IR spectrum a hydroxyl band at 3430 cm^{-1} and since no more carbinyl hydrogen signal is present in the NMR spectrum, the remaining yet unassigned oxygen in picrasin *G* must be present as a tertiary hydroxyl. The location of the secondary hydroxyl next to a carbonyl is concluded by the facts that, in the NMR spectrum, the carbinyl hydrogen is somewhat deshielded and that picrasin *G* consumed sodium periodate. Further analysis of the NMR spectrum with the aid of double resonance experiments has demonstrated the presence of the partial structures involving C-2–C-7, C-8–C-10, C-12–C-13, and C-15 in formula **7**. These results and the NMR parameters for certain hydrogens of picrasin *G* in accord with those of picrasin *B* (**2**) indicate that picrasin *G* is similar in structure differing in having one extra tertiary hydroxyl. The C-15 methylene hydrogens in picrasin *G* appear as a singlet at 3·00 ppm, showing no coupling with other hydrogens, demonstrating the hydroxyl to be located at C-14. The paramagnetic shift of 0·40 ppm for the C-7 hydrogen signal of picrasin *G* as compared with that of picrasin *B* shows the β-orientation of the C-14 hydroxyl [20]. The accumulated data point to formula **7** for picrasin *G*. Treatment of picrasin *G* with thionyl chloride in pyridine gave anhydropicrasin *G* (**19**), whose UV absorption (λ_{max} 225, 302 nm) indicates that the conjugated chromophore in the original substance (**7**) has been extended. In the NMR spectrum of the anhydro-derivative (**19**), the C-15 methylene hydrogen signals found in the spectrum of picrasin *G* are absent and, instead, a singlet for an α-hydrogen in an α,β-unsaturated carbonyl is observed (δ 6·04). Picrasin *G* on bismuth trioxide oxidation afforded dehydropicrasin *G* (**20**) and anhydrodehydropicrasin *G* (**21**). The former (**20**) was methylated with diazomethane to give methyl dehydropicrasin *G* (**22**), whose spectral properties (λ_{max} 256 nm, ν_{max} 3420, 1723, 1703, 1690, 1633 cm^{-1}) are consistent with the

expectation that the methyl ether (**22**) is the 14β-hydroxy-derivative of quassin (**11**). The latter (**21**) was treated with diazomethane to yield methyl anhydrodehydropicrasin *G* (**23**) which was also obtained by dehydration of methyl dehydropicrasin *G* (**22**) with thionyl chloride. The spectral properties of the methyl ether (**23**) thus obtained are found to be identical with those reported for dehydroquassin [17]. Picrasin *G* has thus been deduced to possess the stereostructure **7**.



Since a number of the picrasins and the nigakilactones are now available, determination of the relative bitterness of these simaroubolides and their derivatives was the second objective of our interests. Although paucity of the materials did not permit precise measurements of the intensity of taste stimuli, the results demonstrate that picrasin *A*, *C*, *D*, *E*, *F* and *G*, anhydropicrasin *E*, nigakilactone *A*, *B*, *C*, *E*, *F* and *H*, dehydronigakilactone *H*, and quassin are 300–1000 times bitterer than caffeine, a reference substance, and the only exception being picrasin *B* which is only 30 times bitterer than caffeine. Among them, those which have the strongest bitterness are picrasin *A*, picrasin *F*, and nigakilactone *E*. It was thus clarified that these simaroubolides are the very principles responsible for the bitter taste of the crude drug, but any definite conclusion about the structure-bitterness relationship cannot be drawn at this point.

EXPERIMENTAL

Mps are uncorrected. CD curves were recorded in MeOH soln. NMR spectra were determined on a Varian HA-100 and a Hitachi R-20 spectrometer. Chemical shifts are expressed in ppm downfield from internal TMS and coupling constants (*J*) in Hz.

Isolation of picrasin A, B, C, D, E, F *and* G, *and nigakilactone* B, F *and* H. The crude drug Lignum Picrasmae (100 kg), the dried woods of *Picrasma quassioides* Bennett (Simaroubaceae), was extracted 3× with refluxing MeOH (500 l. each) for 5 hr (each extraction). The combined MeOH soln was concentrated to yield an extract (2·2 kg), which on extraction with EtOAc and evaporation gave a residue (120 g). Chromatography of residue (120 g) over Si gel (1 kg) and elution with EtOAc afforded Fraction A (35 g), Fraction B (30 g) and Fraction C (4·7 g). Fraction A (35 g) was chromatographed over Si gel (350 g) and elution with C_6H_6–EtOAc (1:1) yielded a fraction (7·6 g) which was further chromatographed over Si gel and elution with EtOAc furnished Fraction A_1 (0·56 g) and Fraction A_2 (1·97 g). Fraction A_1 (0·56 g) was subjected to chromatography on Si gel. Elution with $CHCl_3$ gave a crystalline mass (0·10 g) which on crystallization from MeOH yielded *picrasin* D(4) as colourless needles (0·09 g), mp 283·5–285°. CD (*c* 0·117): $[\theta]_{250}$ −20300, $[\theta]_{295}$ +2430, $[\theta]_{335}$ −1030. MS *m/e*: 390 (M^+). UV λ_{max}^{MeOH} nm (log ε): 262 (3·73); IR ν_{max}^{KBr} cm^{-1}: 2770 (methylene dioxy), 1722, 1235 (δ-lactone), 1705, 1635 (cyclohexenone): NMR ($CDCl_3$, 100 sQ MHz): 3H *d* at 1·08 (*J* 6·5 Hz, $C_{(4)}C\underline{H}_3$), 3H *d* at 1·10 (*J* 6·5 Hz, $C_{(13)}C\underline{H}_3$), 3H *s* at 1·27 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·42 ($C_{(10)}C\underline{H}_3$), 1H *d* at 2·42 (*J* 11 Hz, $C_{(9)}\underline{H}$), 1 H *dd* at 3·40 (*J* 8·5, 11 Hz, $C_{(12)}\underline{H}$), 1H *dd* at 3·56 (*J* 8·5, 11 Hz, $C_{(11)}\underline{H}$), 3H *s* at 3·56 ($C_{(2)}OC\underline{H}_3$), 1H *dd* at 4·18 (*J* 2, 2·5 Hz, $C_{(7)}\underline{H}$), two 1H *d*'s at 4·98, 5·15 (*J* 1 Hz, $C_{(11)}OC\underline{H}_2OC_{(12)}$), 1 H *d* at 5·23 (*J* 2·5 Hz, $C_{(3)}\underline{H}$); NMR (C_5D_5N, 100 MHz): 3H *d* at 0·87 (*J* 6·5 Hz, $C_{(4)}CH_3$), 3H *d* at 1·02 (*J* 6·5 Hz, $C_{(13)}C\underline{H}_3$), 3H *s* at 1·17 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·40 ($C_{(10)}C\underline{H}_3$), 1H *m* at 1·85 ($C_{(5)}\underline{H}$), 2H *m* at 2·31 ($C_{(4)}\underline{H}$, $C_{(13)}\underline{H}$), 1H *d* at 2·73 (*J* 11 Hz, $C_{(9)}\underline{H}$), 3H *s* at 3·48 ($C_{(2)}OC\underline{H}_3$), 1H *dd* at 3·64 (*J* 8·5, 11 Hz, $C_{(12)}\underline{H}$), 1H *dd* at 3·69 (*J* 8·5, 11 Hz, $C_{(11)}\underline{H}$), 1H *dd* at 4·23 (*J* 2, 2·5 Hz, $C_{(7)}\underline{H}$), two 1H *d*'s at 5·12, 5·27 (*J* 1 Hz, $C_{(11)}OC\underline{H}_2OC_{(12)}$), 1H *d* at 5·20 (*J* 2·5 Hz, $C_{(3)}\underline{H}$). (Found: C, 67·43; H, 7·73. $C_{22}H_{30}O_6$ requires: C, 67·67; H, 7·74%). Chromatography of Fraction A_2 and elution with $CHCl_3$–EtOAc (5:1) afforded a crystalline mass (0·15 g) which was crystallized from MeOH to yield *picrasin* B (**2**) as colourless needles (0·13 g), mp 255–257°. CD (*c* 0·122): $[\theta]_{246}$ −16400, $[\theta]_{300}$ +2690, $[\theta]_{341}$ −100. MS *m/e*: 376 (M^+). UV λ_{max}^{MeOH} nm (log ϵ): 254 (3·88); IR ν_{max}^{KBr} cm^{-1}: 3520 (hydroxyl), 1737, 1230 (δ-lactone), 1722 (cyclohexanone), 1677, 1640 (cyclohexenone); NMR ($CDCl_3$, 100 MHz): 3H *d* at 0·90 (*J* 6 Hz, $C_{(4)}C\underline{H}_3$), 1H *ddd* at 1·11 (*J* 11, 12, 13 Hz, $C_{(3\alpha)}\underline{H}$), 3H *s* at 1·16 ($C_{(8)}C\underline{H}_3$), 1H *m* at 1·36 ($C_{(5)}\underline{H}$), 3H *s* at 1·42 ($C_{(10)}C\underline{H}_3$), 1H *ddd* at 1·78 (*J* 3, 14·5, 14·5 Hz, $C_{(6\beta)}\underline{H}$), 3H *s* at 1·89 ($C_{(13)}C\underline{H}_3$), 1H *m* at 2·00 ($C_{(15)}\underline{H}$), 1H *ddd* at 2·01 (*J* 3, 4·5, 14·5 Hz, $C_{(6\alpha)}\underline{H}$), 1H *m* at 2·35 ($C_{(14)}\underline{H}$), 1H *ddd* at 2·45 (*J* 4, 7, 13 Hz, $C_{(3\beta)}\underline{H}$), 1H *m* at 2·55 ($C_{(15\alpha)}\underline{H}$), 1H *dd* at 2·97 (*J* 5·5, 16·5 Hz, $C_{(15\beta)}\underline{H}$), 1H *s* at 3·27 ($C_{(9)}\underline{H}$), 3H *s* at 3·62 ($C_{(12)}OC\underline{H}_3$), 1H *dd* at 4·22 (*J* 3, 3 Hz, $C_{(7)}\underline{H}$), 1H *dd* at 4·80 (*J* 7, 11 Hz, $C_{(2)}\underline{H}$). (Found: C, 66·67; H, 7·43. $C_{21}H_{28}O_6$ requires: C, 67·00; H, 7·50%). The mother liquor of picrasin *B* was chromatographed on Si gel and elution with $CHCl_3$–MeOH (50:1) gave a crystalline mass (0·12 g) which was crystallized from MeOH to yield *picrasin* C (**3**) as colourless needles (0·10 g), mp 250–252°. CD (*c* 0·106): $[\theta]_{237}$ −312, $[\theta]_{254}$ +175, $[\theta]_{293}$ −2310. MS *m/e*: 422 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3570, 3470 (hydroxyl), 1724, 1720, 1247 (δ-lactone, acetoxyl), 1705 (cyclohexanone); NMR ($CDCl_3$, 100 MHz): 3H *d* at 0·88 (*J* 6·5 Hz, $C_{(4)}C\underline{H}_3$), 3H *d* at 1·03 (*J* 6·5 Hz, $C_{(13)}C\underline{H}_3$), 3H *s* at 1·24 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·27 ($C_{(10)}CH_3$), 3H *s* at 1·90 ($C_{(11)}OCOC\underline{H}_3$), 1H *d* at 2·79 (*J* 11·5 Hz, $C_{(9)}\underline{H}$), 1H *dd* at 3·13 (*J* 9, 11 Hz, $C_{(12)}\underline{H}$), 3H *s* at 3·40 ($C_{(12)}OC\underline{H}_3$), 1H *dd* at 4·15 (*J* 2·5, 3 Hz, $C_{(7)}\underline{H}$), 1H *m* at 4·68 ($C_{(2)}\underline{H}$), 1H *dd* at 5·22 (*J* 9, 11·5 Hz, $C_{(11)}\underline{H}$). (Found: C, 64·92; H, 8·26.

$C_{23}H_{34}O_7$ requires: C, 65·38; H, 8·11%). On chromatography of Fraction A_2, successive elution with the same solvent yielded a crystalline mass. Crystallization from MeOH gave *picrasin* E (**5**) as colourless needles, mp 293–295° (0·06 g). CD (*c* 0·111): $[\theta]_{249}$ −15000, $[\theta]_{304}$ +2800, $[\theta]_{342}$ −1070. MS *m/e*: 406 (M^+). UV λ_{max}^{MeOH} nm (log ε): 262 (3·68); IR ν_{max}^{KBr} cm^{-1}: 3530 (hydroxyl), 2770 (methylenedioxy), 1715, 1260 (δ-lactone), 1700, 1635 (cyclohexenone); NMR (C_5D_5N, 100 MHz): 3H *d* at 0·90 (*J* 6·5 Hz, $C_{(4)}C\underline{H}_3$), 3H *d* at 1·28 (*J* 6·5 Hz, $C_{(13)}\underline{H}_3$), 3H *s* at 1·33 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·47 ($C_{(10)}C\underline{H}_3$), 1H *m* at 2·33 ($C_{(4)}\underline{H}$), 1H *d* at 2·75 (*J* 11 Hz, $C_{(9)}\underline{H}$), 1H *d* at 2·95 (*J* 19 Hz, $C_{(15\beta)}\underline{H}$), 1H *d* at 3·27 (*J* 19 Hz, $C_{(15\alpha)}\underline{H}$), 3H *s* at 3·47 ($C_{(2)}OC\underline{H}_3$), 1H *dd* at 3·54 (*J* 9, 11 Hz, $C_{(12)}\underline{H}$), 1H *dd* at 3·80 (*J* 9, 11 Hz, $C_{(11)}\underline{H}$), 1H *dd* at 4·75 (*J* 2, 3 Hz, $C_{(7)}\underline{H}$), two 1H *d*'s at 5·15, 5·31 (*J* 1 Hz, $C_{(11)}OC\underline{H}_2OC_{(12)}$), 1H *d* at 5·21 (*J* 2·5 Hz, $C_{(3)}\underline{H}$). (Found: C, 64·45; H, 7·47. $C_{22}H_{30}O_7$ requires: C, 65·01; H, 7·44%). Fraction B was chromatographed on Si gel. Elution with C_6H_6–EtOAc (1:2) gave Fraction B_1 (10·7 g) and Fraction B_2 (1·9 g). Fraction B_1 was subjected to chromatography on Si gel. Elution with $CHCl_3$–EtOAc (5:1) and crystallization from MeOH gave nigakilactone *B* (**16**) as colourless needles (0·03 g), mp 284·5–286°. CD (*c* 0·100): $[\theta]_{253}$ − 18400, $[\theta]_{312}$ + 4100, $[\theta]_{348}$ − 530. MS *m/e*: 392 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3520 (hydroxyl), 1730, 1230 (δ-lactone), 1680, 1640 (cyclohexenone); NMR ($CDCl_3$, 100 MHz): 3H *d* at 1·00 (*J* 6·5 Hz, $C_{(4)}C\underline{H}_3$), 3H *d* at 1·13 (*J* 6·5 Hz, $C_{(13)}C\underline{H}_3$), 3H *s* at 1·21 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·45 ($C_{(10)}C\underline{H}_3$), 1H *d* at 2·15 (*J* 11 Hz, $C_{(9)}\underline{H}$), 1H *dd* at 2·85 (*J* 9, 11 Hz, $C_{(12)}\underline{H}$), 3H *s* at 3·60 ($C_{(2)}OC\underline{H}_3$), 3H *s* at 3·65 ($C_{(12)}OC\underline{H}_3$), 1H *dd* at 3·72 (*J* 9, 11 Hz, $C_{(11)}\underline{H}$), 1H *m* at 4·15 ($C_{(7)}\underline{H}$), 1H *d* at 5·45 (*J* 2·5 Hz, $C_{(3)}\underline{H}$). Identification was carried out in the usual criteria. Elution with $CHCl_3$–EtOAc (1:1) and crystallization from $CHCl_3$–MeOH furnished nigakilactone *H* as colourless needles (0·14 g), mp 292–294°. CD (*c* 0·100): $[\theta]_{254}$ −14700, $[\theta]_{310}$ +3640, $[\theta]_{348}$ −560. MS *m/e*: 424 (M^+). UV λ_{max}^{MeOH} nm (log ε): 271 (3·72); IR ν_{max}^{KBr} cm^{-1}: 3500 (hydroxyl), 1723, 1230 (δ-lactone), 1675, 1640 (cyclohexenone); NMR (C_5D_5N, 100 MHz): 3H *d* at 0·88 (*J* 7 Hz, $C_{(4)}C\underline{H}_3$), 3H *s* at 1·46 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·53 ($C_{(10)}C\underline{H}_3$), 3H *s* at 1·56 ($C_{(13)}C\underline{H}_3$), 1H *d* at 2·58 (*J* 11 Hz, $C_{(9)}\underline{H}$), 1H *d* at 3·02 (*J* 19 Hz, $C_{(15)}\underline{H}$), 1H *d* at 3·40 (*J* 19 Hz, $C_{(15)}\underline{H}$), 1H *d* at 3·43 (*J* 9·5 Hz, $C_{(12)}\underline{H}$), 3H *s* at 3·48 ($C_{(12)}OC\underline{H}_3$), 3H *s* at 3·75 ($C_{(2)}OC\underline{H}_3$), 1H *dd* at 4·40 (*J* 9·5, 11 Hz, $C_{(11)}\underline{H}$), 1H *m* at 4·75 ($C_{(7)}H$), 1H *d* at 5·35 (*J* 2·5 Hz, $C_{(3)}H$). (Found: C, 62·30; H, 7·63. Calc. for $C_{22}H_{32}O_8$: C, 62·25; H, 7·60%). Identification was performed by comparison of the physical and chemical properties with those reported [10]. Chromatography of Fraction B_2, elution with $CHCl_3$–EtOAc (5:1) and crystallization from $CHCl_3$–MeOH gave *picrasin* F (**6**) as colourless needles (0·015 g), mp 282–283°. CD (*c* 0·120): $[\theta]_{252}$ −18100, $[\theta]_{301}$ +3210, $[\theta]_{340}$ −950. Ms *m/e*: 422 (M^+). UV λ_{max}^{MeOH} nm (log ε): 262 (3·69); IR ν_{max}^{KBr} cm^{-1}: 3475 (hydroxyl), 2750 (methylenedioxy), 1720, 1240 (δ-lactone), 1709, 1630 (cyclohexenone); NMR (C_5D_5N, 100 MHz): 3H *d* at 0·87 (*J* 7 Hz, $C_{(4)}C\underline{H}_3$), 3H *s* at 1·50 ($C_{(10)}C\underline{H}_3$), 3H *s* at 1·54 ($C_{(13)}C\underline{H}_3$), 3H *s* at 1·62 ($C_{(8)}C\underline{H}_3$), 1H *m* at 1·85 ($C_{(5)}\underline{H}$), 1H *m* at 2·30 ($C_{(4)}\underline{H}$), 1H *d* at 2·80 (*J* 11 Hz, $C_{(9)}\underline{H}$), 1H *d* at 2·91 (*J* 18·5 Hz, $C_{(15\beta)}\underline{H}$), 1 H *d* at 3·39 (*J* 18·5 Hz, $C_{(15\alpha)}\underline{H}$), 1H *d* at 3·44 (*J* 9·5 Hz, $C_{(12)}\underline{H}$), 3H *s* at 3·48 ($C_{(2)}OC\underline{H}_3$), 1H *dd* at 4·29 (*J* 9·5, 11 Hz, $C_{(11)}\underline{H}$), 1H *dd* at 4·67 (*J* 2, 2 Hz, $C_{(7)}\underline{H}$), two 1H *d*'s at 5·18, 5·37 (*J* 1 Hz, $C_{(11)}OC\underline{H}_2OC_{(12)}$), 1H *d* at 5·21 (*J* 2·5 Hz, $C_{(3)}\underline{H}$). Fraction C was chromatographed on Si gel. Elution with C_6H_6–EtOAc (1:2) afforded a fraction (0·76 g) which on chromatography on Si gel. Elution with $CHCl_3$–EtOAc (5:1) and crystallization with MeOH yielded nigakilactone *F* as colourless needles (0·11 g), mp 266–268°. MS *m/e*: 408 (M^+). UV λ_{max}^{MeOH} nm (log ε): 271 (3·71); IR ν_{max}^{KBr} cm^{-1}: 3460, 3430 (hydroxyl), 1712, 1230 (δ-lactone), 1675, 1640 (cyclohexenone); NMR (C_5D_5N, 100 MHz): 3H *d* at 0·88 (*J* 7 Hz, $C_{(4)}C\underline{H}_3$), 3H *s* at 1·28 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·45 ($C_{(10)}C\underline{H}_3$), 3H *s* at 1·54 ($C_{(13)}C\underline{H}_3$), 1H *d* at 2·48 (*J* 11 Hz, $C_{(9)}\underline{H}$), 1H *d* at 3·25 (*J* 9 Hz, $C_{(12)}\underline{H}$), 3H *s* at 3·44 ($C_{(12)}OC\underline{H}_3$), 3H *s* at 3·67 ($C_{(2)}OC\underline{H}_3$), 1H *m* at 4·11 ($C_{(7)}\underline{H}$), 1H *dd* at 4·29 (*J* 9, 11 Hz, $C_{(11)}\underline{H}$), 1H *d* at 5·30 (*J* 2·5 Hz, $C_{(3)}\underline{H}$). The identity was confirmed by direct comparison. Successive elution with the same solvent and crystallization from MeOH furnished *picrasin* A (**1**) as colourless needles (0·075 g), mp 297–299°. CD (*c* 0·066): $[\theta]_{220}$ −5860, $[\theta]_{261}$ −19700, $[\theta]_{306}$ +3790, $[\theta]_{344}$ −390. MS *m/e*; 474 (M^+). UV λ_{max}^{MeOH} nm (log ε): 271 (3·708); IR ν_{max}^{KBr} cm^{-1}: 3470 (hydroxyl), 1775, 1733, 1240 (γ-lactone, δ-lactone), 1720 (ketone), 1680, 1645 (cyclohexenone); NMR (C_5D_5N, 100 MHz): 3H *d* at 0·89 (*J* 7 Hz, $C_{(4)}C\underline{H}_3$), two 3H *s*'s at 0·94 and 0·97 ($C_{(8)}C\underline{H}_3$ and $C_{(13)}C\underline{H}_3$), 3H *s* at 1·39 ($C_{(10)}$ $C\underline{H}_3$), 1H *d* at 2·45 (*J* 11 Hz, $C_{(9)}\underline{H}$), 3H *s* at 3·45 ($C_{(2)}OC\underline{H}_3$), 1H *d* at 5·34 (*J* 2·5 Hz, $C_{(3)}\underline{H}$). (Found: C, 65·66; H, 7·24. $C_{26}H_{34}O_8$ requires: C, 65·80; H, 7·22%). Further elution with the same solvent afforded a fraction which was submitted to Si gel chromatography. A fraction eluted with $CHCl_3$–MeOH (50:1) was chromatographed on alumina. Elution with EtOAc furnished *picrasin* G (**7**) as colourless powder (0·70 g). CD (*c* 0·106): $[\theta]_{280}$ + 4310, $[\theta]_{329}$ −5420. MS *m/e*: 392 (M^+). UV λ_{max}^{MeOH} nm (log ε): 252 (3·85); IR ν_{max}^{KBr} cm^{-1}: 3440 (hydroxyl), 1722 (δ-lactone), 1710 (cyclohexanone), 1685, 1630 (cyclohexenone); NMR ($CDCl_3$, 100 MHz): 3H *d* at 0·92 (*J* 6 Hz, $C_{(4)}C\underline{H}_3$), 1H *m* at 1·05 ($C_{(3\alpha)}\underline{H}$), 3H *s* at 1·12 ($C_{(8)}C\underline{H}_3$), 1H *m* at 1·35 ($C_{(5)}\underline{H}$), 3H *s* at 1·45 ($C_{(10)}C\underline{H}_3$), 1H *m* at 1·78 ($C_{(6\beta)}\underline{H}$), 3H *s* at 1·90 ($C_{(13)}C\underline{H}_3$), 1H *m* at 2·00 ($C_{(4)}\underline{H}$), 1H *m* at 2·04 ($C_{(6\alpha)}\underline{H}$), 1H *m* at 2·44 ($C_{(3\beta)}\underline{H}$), 2H *s* at 3·00 ($C_{(15)}\underline{H}_2$), 1H *s* at 3·15 ($C_{(9)}\underline{H}$), 3H *s* at 3·62 ($C_{(13)}OC\underline{H}_3$), 1H *m* at 4·62 ($C_{(7)}\underline{H}$), 1H *dd* at 4·84 (*J* 7·5, 11 Hz, $C_{(2)}\underline{H}$).

Methylation of deacetyl-dehydrosimarolide. Deacetyl-dehydrosimarolide (**9**) (5 mg) in MeOH (1 ml) was treated with an excess of CH_2N_2 in Et_2O at room temp overnight. Evaporation of the solvent and crystallization of the residue from MeOH gave *methyl deacetyl-dehydrosimarolide* (**1**) as colourless needles (1 mg), mp 292–294°. The identity with picrasin *A* was confirmed by mixed melting point and IR comparison.

Acetylation of picrasin B. Picrasin *B* (**2**) (30 mg) in Ac_2O (0·5 ml) and C_5H_5N (1 ml) was set aside at room temp for 1 day. Isolation in the usual manner gave *picrasin B acetate* (**5**) as a colourless amorphous mass (24 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1738, 1726, 1230 (δ-lactone, acetoxyl), 1700, 1630 (cyclohexenone); NMR ($CHCl_3$, 60 MHz): 3H *d* at 0·95 (*J* 6 Hz, $C_{(4)}C\underline{H}_3$), 3H *s* at 1·19 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·50 ($C_{(10)}C\underline{H}_3$), 3H *s* at 1·88 ($C_{(13)}C\underline{H}_3$), 3H *s* at 2·11 ($C_{(2)}OCOC\underline{H}_3$), 1H *s* at 3·18 ($C_{(9)}\underline{H}$), 3H *s* at 3·61 ($C_{(12)}OC\underline{H}_3$), 1H *dd* at 4·26 (*J* 3, 3 Hz, $C_{(7)}\underline{H}$), 1 H *dd* at 5·83 (*J* 7, 12 Hz, $C_{(2)}\underline{H}$).

Bismuth trioxide oxidation of picrasin B. To picrasin *B* (**4**) (47 mg) in EtOAc (2 ml) was added Bi_2O_3 (70 mg), and the mixture was heated under reflux for 10 hr. After isolation in the customary way, the product (54 mg) was chromatographed over Si gel (2·5 g). $CHCl_3$ eluate (21 mg) was further submitted to rechromatography over Si gel (2·5 g). Elution with C_6H_6–EtOAc (1:1) gave a crystalline mass (17 mg) which on crystallization from MeOH yielded *dehydropicrasin B* (**12**) as colourless needles (15 mg), mp 252–253·5°. UV λ_{max}^{MeOH} nm (log ε): 255 (4·00), $\lambda_{max}^{MeOH(KOH)}$ nm: 255, 307; IR ν_{max}^{KBr} cm^{-1}: 3450 (hydroxyl), 1733, 1230 (δ-lactone), 1683, 1675, 1635 (cyclohexenones).

Methylation of dehydropicrasin B. Dehydropicrasin *B* (**12**) (12 mg) in MeOH (3 ml) was treated with an excess of CH_2N_2 in ether at room temp overnight. After evaporation of solvent,

residue was chromatographed over Si gel (2 g). Elution with C_6H_6–EtOAc (1:1) gave a crystalline mass (3 mg) which was crystallized from MeOH to furnish *methyl dehydropicrasin* B (**11**) as colourless needles (2·7 mg), mp 212·5–214·5°. IR ν_{max}^{KBr} cm^{-1}: 1743, 1225 (δ-lactone), 1700, 1690, 1635 (cyclohexenone). Identification with quassin (**11**) was performed by mixed fusion test and IR comparison.

Acetylation of picrasin C. Picrasin *C* (**3**) (15 mg) in Ac_2O (0·25 ml) and C_5H_5N (0·5 ml) was set aside at room temp overnight. Working up in the usual manner and extraction with EtOAc gave a product which was subjected to preparative Si gel TLC (developed with EtOAc) and crystallized from MeOH to furnish *picrasin* C *acetate* (**13**) as colourless prisms (10 mg), mp 296–299°. IR ν_{max}^{KBr} cm^{-1}: 1730, 1720, 1240 (δ-lactone, acetoxyl); NMR ($CDCl_3$, 100 MHz): 3H *d* at 0·95 (*J* 6·5 Hz, $C_{(4)}C\underline{H}_3$), 3H *d* at 1·02 (*J* 6·5 Hz, $C_{(13)}C\underline{H}_3$), 3H *s* at 1·29 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·32 ($C_{(10)}C\underline{H}_3$), 3H *s* at 2·00 ($C_{(11)}OCOC\underline{H}_3$), 3H *s* at 2·12 ($C_{(2)}OCOC\underline{H}_3$), 1H *d* at 2·74 (*J* 11·5 Hz, $C_{(9)}\underline{H}$), 1H *dd* at 3·10 (*J* 9, 11 Hz, $C_{(12)}\underline{H}$), 3H *s* at 3·41 ($C_{(12)}OC\underline{H}_3$), 1H *m* at 4·17 ($C_{(7)}\underline{H}$), 1H *dd* at 5·28 (*J* 9, 11·5 Hz, $C_{(11)}\underline{H}$), 1H *dd* at 5·57 (*J* 7, 12 Hz, $C_{(2)}\underline{H}$).

Bismuth trioxide oxidation of picrasin C. Picrasin *C* (**3**) (20 mg) and Bi_2O_3 (15 mg) in AcOH (1 ml) were heated under reflux for 10 hr, and the solvent was removed under red pres. The EtOAc extract (12 mg) of the residue was submitted to preparative Si gel TLC (developed with EtOAc) and crystallization from MeOH yielded *dehydropicrasin* C (**15**) (8 mg), mp 184–188°. UV λ_{max}^{MeOH} nm: 268 (3·28), $\lambda_{max}^{MeOH(KOH)}$ nm: 303; IR ν_{max}^{KBr} cm^{-1}: 3370 (hydroxyl), 1730, 1720, 1225 (δ-lactone, acetoxyl), 1690, 1640 (α-hydroxy-cyclohexenone).

Methylation of dehydropicrasin C. Dehydropicrasin *C* (**15**) (6 mg) in MeOH (5 ml) was treated with an excess of CH_2N_2 in ether at room temp for one day. Evaporation of the solvent and purification by means of Si gel TLC (developed with $CHCl_3$–MeOH (20:1)) gave *methyl dehydropicrasin* C (**14**) as colourless prisms (2 mg), mp 251–254°. IR ν_{max}^{KBr} cm^{-1}: 1730, 1720, 1225 (δ-lactone, acetoxyl), 1705 (cyclohexenone). Identification with nigakilactone *C* (**14**) was performed by m.m.p. and IR comparison.

Dehydration of picrasin E. To picrasin *E* (**5**) (50 mg) in C_5H_5N (1 ml) was added $SOCl_2$ (0·1 g) and the mixture was left standing at room temp overnight. Isolation in the customary way and crystallization from MeOH gave *anhydropicrasin* E (**17**) as colourless prisms (29 mg), mp 268–270°. MS *m/e*: 388 (M^+). UV λ_{max}^{MeOH} nm (log ε): 214 (3·92), 261 (3·54); IR ν_{max}^{KBr} cm^{-1}: 2770 (methylenedioxy), 1727, 1263 (δ-lactone), 1703, 1640 (α-methoxycyclohexenone); NMR ($CHCl_3$, 60 MHz): 3H *d* at 1·13 (*J* 6·5 Hz, $C_{(4)}C\underline{H}_3$), 3H *d* at 1·29 (*J* 6·5 Hz, $C_{(13)}C\underline{H}_3$), 3H *s* at 1·32 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·39 ($C_{(10)}C\underline{H}_3$), 3H *s* at 3·55 ($C_{(12)}OC\underline{H}_3$), 1H *m* at 4·24 ($C_{(7)}\underline{H}$), two 1H *s*'s at 5·05 and 5·21 ($C_{(11)}OC\underline{H}_2OC_{(12)}$), 1H *d* at 5·25 (*J* 2·5 Hz, $C_{(3)}\underline{H}$), 1H *s* at 5·85 ($C_{(15)}\underline{H}$).

Acetylation of picrasin G. Picrasin *G* (**7**) (210 mg) in Ac_2O (1 ml) and C_5H_5N (2 ml) was set aside at room temp for 1 day. The mixture was poured into H_2O and extracted with EtOAc. Chromatography over alumina and elution with EtOAc gave *picrasin* G *acetate* (**18**) as colourless amorphous mass (190 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430 (hydroxyl), 1722, 1720, 1230 (δ-lactone, acetoxyl), 1710 (cyclohexanone), 1690, 1630 (cyclohexenone); NMR ($CHCl_3$, 60 MHz): 3H *d* at 0·98 (*J* 6 Hz, $C_{(4)}C\underline{H}_3$), 3H *s* at 1·13 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·54 ($C_{(10)}C\underline{H}_3$), 3H *s* at 1·90 ($C_{(13)}C\underline{H}_3$), 3H *s* at 2·11 ($C_{(2)}OCOC\underline{H}_3$), 2H *s* at 3·01 ($C_{(15)}\underline{H}_2$), 1H *s* at 3·12 ($C_{(9)}\underline{H}$), 3H *s* at 3·62 ($C_{(12)}OC\underline{H}_3$), 1H *m* at 4·64 ($C_{(7)}\underline{H}$), 1H *dd* at 5·87 (*J* 8, 12 Hz, $C_{(2)}\underline{H}$).

Dehydration of picrasin G. Picrasin *G* (**7**) (90 mg) in C_5H_5N (1·5 ml) was added $SOCl_2$ (0·1 g) at 0° and the mixture was left standing at room temp for 1 day. After working up in the customary manner, extraction with EtOAc afforded a product which was chromatographed over alumina. Elution with EtOAc and crystallization from MeOH yielded *anhydropicrasin* G (**19**) as colourless prisms (43 mg), mp 196–199°. CD (*c* 0·034): $[\theta]_{225}$ −5410, $[\theta]_{255}$ +1350, $[\theta]_{269}$ +530, $[\theta]_{309}$ +4980, $[\theta]_{354}$ −500. UV λ_{max}^{MeOH} nm (log ε): 225 (3·88), 302 (3·95); IR ν_{max}^{KBr} cm^{-1}: 3450 (hydroxyl), 1723, 1230 (δ-lactone), 1710 (cyclohexanone), 1690, 1613 (α,β,γ,δ-unsat. ketone); NMR ($CHCl_3$, 60 MHz): 3H *d* at 1·00 (*J* 6 Hz, $C_{(4)}C\underline{H}_3$), 3H *s* at 1·28 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·47 ($C_{(10)}C\underline{H}_3$), 3H *s* at 2·07 ($C_{(13)}C\underline{H}_3$), 1H *s* at 3·33 ($C_{(9)}C\underline{H}_3$), 3H *s* at 3·72 ($C_{(12)}OC\underline{H}_3$), 1H *m* at 4·32 ($C_{(7)}\underline{H}$), 1H *dd* at 4·81 (*J* 7·5, 11·5 Hz, $C_{(2)}\underline{H}$), 1H *s* at 6·04 ($C_{(15)}\underline{H}$).

Bismuth trioxide oxidation of picrasin G. Picrasin *G* (**7**) (200 mg) and Bi_2O_3 (250 mg) in AcOH (2 ml) was refluxed for 5 hr. After isolation in the usual way, the product (155 mg) was submitted to chromatography over Si gel. Elution with C_6H_6–EtOAc (5:1) gave *anhydrodehydropicrasin* G (**17**) as colourless powder (40 mg). UV λ_{max}^{MeOH} nm (log ε): 221 (3·77), 265 (3·72), 300 (3·74), $\lambda_{max}^{MeOH(KOH)}$ nm: 214, 301; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3420 (hydroxyl), 1720, 1230 (unsat. δ-lactone), 1700, 1630 (cyclohexenone), 1680, 1630 (α,β,γ,δ-unsat. ketone); NMR ($CHCl_3$, 60 MHz): 3H *d* at 1·06 (*J* 7 Hz, $C_{(4)}C\underline{H}_3$), 3H *s* at 1·28 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·55 ($C_{(10)}C\underline{H}_3$), 3H *s* at 2·03 ($C_{(13)}C\underline{H}_3$), 1H *s* at 3·07 ($C_{(9)}\underline{H}$), 3H *s* at 3·85 ($C_{(12)}OC\underline{H}_3$), 1H *m* at 4·32 ($C_{(7)}\underline{H}$), 1H *d* at 5·77 (*J* 2·5 Hz, $C_{(3)}\underline{H}$), 1H *s* at 6·02 ($C_{(15)}\underline{H}$). Elution with C_6H_6–EtOAc (5:1) gave *dehydropicrasin* G (**20**) as colourless powder (89 mg). UV λ_{max}^{MeOH} nm (log ε): 255 (3·94), $\lambda_{max}^{MeOH(KOH)}$ nm: 258, 303; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3480 (hydroxyl), 1720, 1250 (δ-lactone), 1702, 1690, 1638 (two cyclohexenones); NMR ($CDCl_3$, 60 MHz): 3H *d* at 1·12 (*J* 6·5 Hz, $C_{(4)}C\underline{H}_3$), 3H *s* at 1·17 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·60 ($C_{(10)}C\underline{H}_3$), 3H *s* at 1·91 ($C_{(13)}C\underline{H}_3$), 1H *s* at 2·88 ($C_{(9)}\underline{H}$), 2H *s* at 3·01 ($C_{(15)}\underline{H}_2$), 3H *s* at 3·68 ($C_{(12)}OC\underline{H}_3$), 1H *m* at 4·71 ($C_{(7)}\underline{H}$), 1H *d* at 5·72 (*J* 2·5 Hz, $C_{(3)}\underline{H}$).

Methylation of dehydropicrasin G. An excess of CH_2N_2 in Et_2O was added to dehydropicrasin *G* (**20**) (45 mg) in MeOH (10 ml) and the mixture was set aside at room temp for 1 day and the solvents were evaporated to give a product. The product was chromatographed over Si gel and elution with C_6H_6–EtOAc (5:1) gave *methyl dehydropicrasin* G (**22**) as colourless amorphous mass (20 mg). CD (*c* 0·106): $[\theta]_{331}$ −3640. UV λ_{max}^{MeOH} nm (log ε): 256 (3·94); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3420 (hydroxyl), 1723, 1250 (δ-lactone), 1703, 1690, 1633 (two cyclohexenones); NMR ($CHCl_3$, 60 MHz): 3H *d* at 1·14 (*J* 7 Hz, $C_{(4)}C\underline{H}_3$), 3H *s* at 1·15 ($C_{(8)}C\underline{H}_3$), 3H *s* at 1·60 ($C_{(10)}C\underline{H}_3$), 3H *s* at 1·92 ($C_{(13)}C\underline{H}_3$), 1H *s* at 2·93 ($C_{(9)}\underline{H}$), 2H *s* at 3·03 ($C_{(15)}\underline{H}_2$), 3H *s* at 3·60 ($C_{(2)}OC\underline{H}_3$), 3H *s* at 3·69 ($C_{(12)}OC\underline{H}_3$), 1H *m* at 4·70 ($C_{(7)}\underline{H}$), 1H *d* at 5·36 (*J* 2 Hz, $C_{(3)}\underline{H}$).

Dehydration of methyl dehydropicrasin G. To methyl dehydropicrasin G (**22**) (51 mg) in C_5H_5N (1·5 ml) was added $SOCl_2$ (0·15 g) at 0°. The mixture was set aside at room temp overnight and poured into H_2O. Extraction with EtOAc, chromatography over Si gel, and crystallization from MeOH gave *methyl anhydrodehydropicrasin* G (**23**) as colourless prisms (31 mg), mp 214–216·5°. UV λ_{max}^{MeOH} nm (log ε): 229 (3·92), 271 (3·96), 304 (4·07); IR ν_{max}^{KBr} cm^{-1}: 1723, 1250 (unsat. δ-lactone), 1699, 1632 (cyclohexenone), 1688, 1620 (α,β,γ,δ-unsat. ketone). Identification with dehydroquassin (**23**) was performed by comparison of the physical properties with those reported.

Methylation of anhydrodehydropicrasin G. To anhydrodehydropicrasin *G* (**21**) (10 mg) in MeOH (10 ml), an excess CH_2H_2 in Et_2O was added and the mixture was left standing at room temp for 1 day. Removal of the solvent gave a product which was chromatographed on Si gel (3 g). Elution with

C_6H_6–EtOAc (5:1) and crystallization from MeOH gave methyl anhydrodehydropicrasin *G* (**23**) as colourless prisms (2·5 mg), mp 214–217°. IR ν_{max}^{KBr} cm^{-1}: 1723, 1250 (unsat. δ-lactone), 1699, 1632 (cyclohexenone), 1688, 1620 ($\alpha,\beta,\gamma,\delta$-unsat. ketone). Identification with methyl anhydrodehydropicrasin *G* (**23**) prepared above was carried out by mixed fusion test and IR comparison.

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