Communications to the Editor

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STRUCTURES OF MOMORDICINES I, II AND III, THE BITTER PRINCIPLES IN THE LEAVES AND VINES OF MOMORDICA CHARANTIA L.[1)]

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The bitter principles in the leaves and vines of Momordica charantia L. (Cucurbitaceae), momordicines I, $C_{30}H_{48}O_4 \cdot H_2O$, and II, $C_{36}H_{58}O_9$, were isolated and their structures were elucidated as 3β,7β,23ξ-trihydroxy-cucurbita-5,24-dien-19-al and its 23-O-β-glucopyranoside, respectively. The structure of momordicine III, which was isolated as its acetate, $C_{48}H_{68}O_{16} \cdot 1/2H_2O$, is indicated to be a 23-O-β-glucopyranoside of 3β,7β,23ξ-trihydroxy-24-oxo-cucurbita-5,25-dien-19-al by the spectral and chemical evidence.

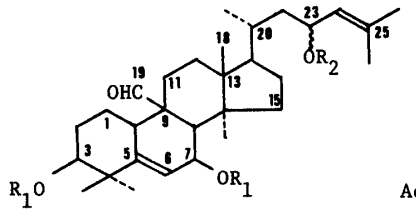
KEYWORDS ——— Momordica charantia; Cucurbitaceae; bitter principle; tetracyclic triterpene; cucurbitacin; momordicines I, II and III; 3β,7β,23ξ-trihydroxy-cucurbita-5,24-dien-19-al; 3β,7β,23ξ-trihydroxy-24-oxo-cucurbita-5,25-dien-19-al

The leaves of Momordica charantia L. (Cucurbitaceae) taste bitter and it has long been known that it contains a bitter principle named momordicine,[2)] but its structure has not yet been characterized. We have investigated the constituents of the immature fruits and reported the isolation and characterization of the bitter compounds named momordicosides K and L: 7-O-β-D-glucopyranosides of 3β,7β-dihydroxy-25-O-methyl-cucurbita-5,23-dien-19-al and 3β,7β,25-trihydroxy-cucurbita-5,23-dien-19-al, respectively.[3)]

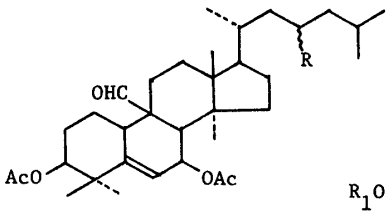
As a continuation of the studies of the constituents of this plant, leaves and vines were investigated, and two bitter compounds designated as momordicines I and II were isolated in free forms, and one related compound named momordicine III as its acetate. In this communication, we deal with the characterization of their structures.

The air-dried leaves and vines were percolated with MeOH, and the extract was partitioned between $CHCl_3$ and water, and the water layer was extracted with BuOH. From the $CHCl_3$ extract, momordicine I (yield: 0.07%) was isolated after repeated silica gel chromatography and recrystallization from $CHCl_3$. The BuOH extract afforded momordicine II (yield: 0.07%) as a colorless crystalline powder from $CHCl_3$. From the acetylation product of the mother liquor of momordicine II, momordicine III acetate (yield: 0.12%) was isolated in pure form together with momordicine II acetate (yield: 0.45%) after repeated column chromatography.

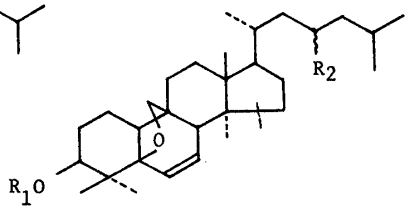
Momordicine I (I) (mp 125-128°C, $[\alpha]_D$ +81.3°, CD: $[\theta]_{209}$ +54680°) was analyzed for $C_{30}H_{48}O_4 \cdot H_2O$. The ^{1}H-NMR spectrum of I showed signals of four methyl groups on quaternary carbons (δ 0.91, 0.96, 1.20 and 1.48), two methyl groups on an olefinic



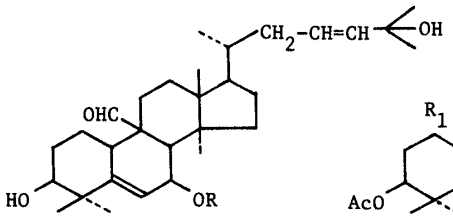
I : R_1=R_2=H
IV : R_1=R_2=Ac
XI : R_1=H, R_2= β-glu.pyr.
XII: R_1=Ac, R_2= β-glu.pyr.Ac_4



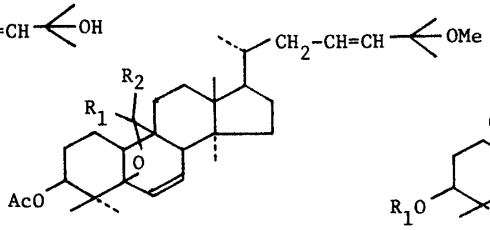
V : R=OAc
VI : R=H
XIII: R= O-β-glu.pyr.Ac_4
XIV : R= O-β-glu.pyr.



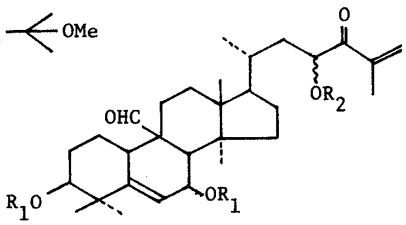
VII : R_1=Ac, R_2=H
VIII: R_1=R_2=H
XV : R_1=Ac,R_2= O-β-glu.pyr.



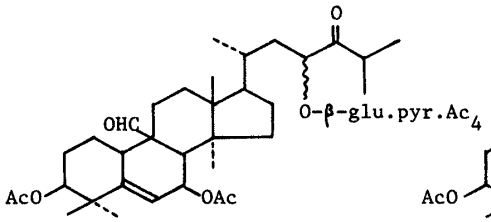
II : R=H
III: R= β-D-glu.pyr.



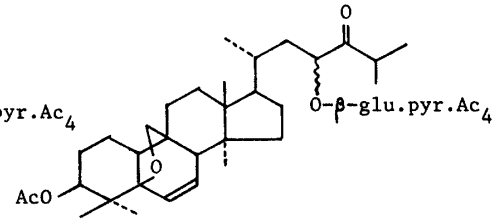
IX: R_1=OMe, R_2=H
X : R_1=H, R_2= OMe



(XVI : R_1=H, R_2= β-glu.pyr.)
XVII: R_1=Ac, R_2= β-glu.pyr.Ac_4



XVIII



XIX

carbon (δ 1.71. 6H), three protons on carbons bearing hydroxyl groups at least one of which is adjacent to an olefinic proton, and a proton of the formyl group (δ 10.62) on a quaternary carbon. The ^{13}C-NMR spectrum showed signals of at least three quaternay carbons (δ 41.7, 45.8 and 48.3), three hydroxymethine carbons (δ 65.1, 65.6 and 75.5), carbons of two trisubstituted double bonds (δ 124.1d, 130.7s, 131.7d and 145.5s) and a formyl carbon (δ 207.6d). These spectral data indicate that I has the same skeleton as the aglycone (II) of momordicoside L (III) isolated from the immature fruits,[3] and that the side chain has a double bond at $C_{24,25}$ and a hydroxyl group at C_{22} or C_{23}. On catalytic hydrogenation of the triacetate (IV) of I, a dihydrotriacetate (V), $C_{36}H_{56}O_7$ (CD: $[\theta]_{205}$ +83330°) and its desacetoxyl derivative (VI), $C_{34}H_{54}O_5$(CD: $[\theta]_{203}$ +86320°), were obtained. Reduction of VI with $NaBH_4$ and subsequent treatment with 0.1 N HCl (MeOH) gave a monoacetate (VII), $C_{32}H_{52}O_3$(CD: $[\theta]_{203}$ -81040°), with a disubstituted double bond and an ether linkage. The deacetylation product (VIII) of VII was identical with 3β-hydroxy-5β,19-epoxy-cucurbit-6-ene which we reported in the previous paper.[3] Liability of deacetylation on catalytic hydrogenation suggested that the hydroxyl group in the side chain would be

at C_{23}, viz. an allylic hydroxyl group.

When the mother liquor of crystallization of I was left to dissolve in a mixture of $CHCl_3$ and MeOH for more than 10 days in an attempt to obtain another crop of I, or was subjected to repeated column chromatography using the same solvent system, I was gradually and completely changed into less polar compounds, from which two compounds were isolated as acetates (IX and X). IX and X have an acetoxyl group, two methoxyl groups and two disubstituted double bonds, but not a formyl group nor a trisubstituted double bond. IX and X were identical with K-ag-2-Ac and K-ag-3-Ac, respectively, which were obtained by methanolysis of momordicoside K (25-O-methyl momordicoside L).[3] Treatment of IV with 0.1 N HCl (MeOH) at room temperature gave IX and X (checked by TLC). Formation of the methylhemiacetal ring and of the methyl ether of the allyl alcohol in the side chain is explained by a concerted process involving the fission of linkages between oxygens and allylic carbon atoms to give intermediate carbonium cations, migration of the double bonds followed by ring closure, and methoxylation. From this chemical and spectral evidence, the structure of I was determined to be 3β,7β,23ξ-trihydroxy-cucurbita-5,24-dien-19-al.

Momordicine II (XI), $C_{36}H_{58}O_9$ (CD: $[\theta]_{208}$ +43900°) showed ^{1}H-NMR signals of four methyl groups (δ 0.89, 0.91, 1.18 and 1.50) on quaternary carbons, two methyl groups (δ 1.70 and 1.78) on an olefinic carbon, two olefinic protons (δ 5.63, d, J=8 Hz; 6.29, d, J=5 Hz) and a formyl proton (δ 10.64s). The ^{13}C-NMR spectrum exhibited the presence of the β-glucopyranosyl group (δ 104.1(1'), 78.8(5'), 78.2 (3'), 75.5(2'), 71.8(4') and 62.9(6')). The other ^{13}C-NMR signal pattern was similar to that of I. When the hexaacetate (XII), $C_{48}H_{70}O_{15}$ (CD: $[\theta]_{206}$ +69800°), of XI was treated with 0.1 N HCl (MeOH) at room temperature, IX and X were obtained. These spectral and chemical data indicate that XI is the 7-O- or 23-O-β-glucopyranoside of I. Catalytic hydrogenation of XII gave a dihydro-derivative (XIII), $C_{48}H_{72}O_{15}$, which gave on treatment with MeONa a diacetate (XIV), $C_{40}H_{64}O_{11}\cdot 2H_2O$. XIV was reduced with $NaBH_4$ followed by treatment with 0.1 N HCl (MeOH) at room temperature to afford a compound (XV), $C_{38}H_{62}O_9$ (CD: $[\theta]_{203}$ -72000°), which has a glucopyranosyl group (^{13}C-NMR: δ 105.0, 78.7, 78.0, 75.4, 71.9 and 63.0), one acetoxyl group (^{1}H-NMR: δ 2.08. ^{13}C-NMR: δ 170.7s), a disubstituted double bond (^{1}H-NMR: δ 5.58, dd, J=10, 4 Hz; 6.16, dd, J=10, 2 Hz. ^{13}C-NMR: δ 130.2d and 133.6d), and an ether ring (^{13}C-NMR: δ 80.0t and 84.8s). The results of these chemical reactions clearly indicate that XI is a 23-O-β-glucopyranoside of I.

Momordicine III (XVI) was isolated as an acetate (XVII), $C_{48}H_{68}O_{16}\cdot 1/2H_2O$ (CD: $[\theta]_{206}$ +96800°). XVII shows in its ^{13}C-NMR spectrum the signals of an acetylated β-glucopyranosyl group (δ 101.7(1'), 73.3(3'), 72.1(5' and 2'), 69.1(4') and 62.4(6')), one terminal methylene group (δ 126.3t and 142.4s), one trisubstituted double bond (δ 119.6d and 148.9s), one carbonyl group (δ 201.0s) and a formyl group (δ 206.8d). The UV spectrum (λ_{max}: 203 nm and 221 nm (shoulder)) indicates that the carbonyl group is conjugated with a double bond. The signals of the up-field region of the ^{1}H-NMR spectrum of XVII are similar to those of XII. These spectral data strongly imply that XVII has the same skeleton as XII and that the side chain has a 24-oxo-25-ene structure. Catalytic hydrogenation of XVII gave a dihydro compound (XVIII)(FAB-MS m/z: 925$[M+Na]^+$). $NaBH_4$ reduction of XVIII and subsequent treatment with 0.1 N HCl (MeOH) at room temperature and then acetylation gave a pentaacetate (XIX), $C_{46}H_{70}O_{14}$ (CD: $[\theta]_{203}$ -88100°) with a carbonyl group (^{13}C-NMR:

δ 215.2s) and an ether ring (^{13}C-NMR: δ 80.0t and 84.9s. ^{1}H-NMR: δ 3.77, d, J=8 Hz; 3.62, d, J=8 Hz). These data indicate that the glucopyranosyl group is linked neither to the hydroxyl group at C_3 nor to that at C_7 but to the hydroxyl group in the side chain. Taking into consideration that I and XI have a C_{23}-hydroxyl group and a C_{23}-O-glucopyranosyl group, respectively, XVII is logically assumed to have an acetylated glucopyranosyl group at C_{23}. The lower ^{13}C-NMR chemical shifts of the carbons bearing acetylated glucopyranosyl groups of XVIII (δ 84.0) and XIX (δ 84.1) compared to that of XIII (δ 77.5) support this assumption. Therefore, the structure of momordicine III is tentatively proposed to be a 23-O-β-glucopyranoside of 3β, 7β,23ξ-trihydroxy-24-oxo-cucurbita-5,25-dien-19-al. Experiments on the chemical confirmation of the location of the glucopyranosyl group in the side chain is now in progress.

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REFERENCES AND NOTES

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