Tetrahedron Letters No.32, pp. 2725-2728, 1969. Pergamon Press. Printed in Great Britain.

STRUCTURES OF IRIDOIDS FROM LONICERA MORROWII A. GRAY

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(Received in Japan 31 March 1969; received in UK for publication 5 June 1969)

In the study of the bitter components of Lonicera Morrowii A. Gray (Caprifoliaceae), we have found in the glycosidic fraction of the fruits two new glycosides, morroniside and kingiside the structures of which have now been proposed as I and II respectively.

Fractionation of the methanol extract of the fresh fruits on Celite-charcoal column afforded a glycoside mixture, which resisted further purification. Thus, the crude mixture was acetylated and separated by silica gel chromatography into two glycoside acetates, pentaacetylmorroniside (III) and tetraacetylkingiside (IV).

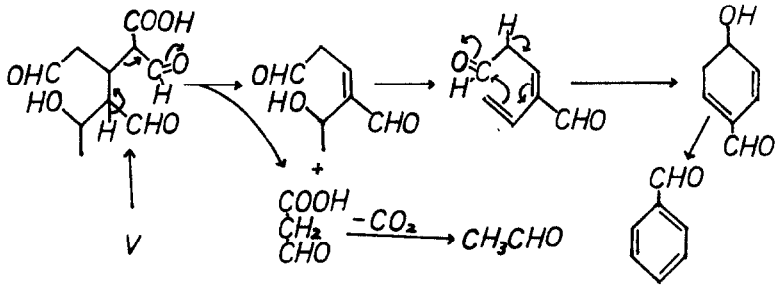
III, m.p. 148-151°, $[\alpha]_D$=-73.5° (c=0.97, $CHCl_3$) has a formula, $C_{27}H_{36}O_{16}$ (requires: C, 52.60; H, 5.89%. Found: C, 52.75; H, 5.82%). The spectroscopic data of III indicated the presence of the group -O-CO-C=CH-O- [λ_{max}^{EtOH} 236 mμ (ε, 12.200), $\nu_{max}^{CHCl_3}$ 1715, 1640 cm^{-1} τ 2.60], a methoxyl group (τ 6.27) and the absence of hydroxyl group (no absorption in 3000 cm^{-1} region). III also contains a tetraacetyl glucose residue, as shown by the characteristic and strong peak at m/e 331. Therefore, one of the acetyl groups should be attached to the non-sugar part. These data enabled us to assume the original glycoside is an iridoid derivative with one free hydroxyl group in the aglycone moiety. The free morroniside (I), $[\alpha]_D$=-72.0° (c=1.0, EtOH), ν_{max}^{neat} 1700, 1640 cm^{-1} obtained by the hydrolysis of III with ammonia in aqueous methanol, remained non-crystalline after several attempts, though it behaved as a single compound on t.l.c. and p.p.c. Reacetylation of I afforded III, showing that no change occurred during hydrolysis.

Cleavage of morroniside (I) with emulsin furnished, along with glucose, the unstable aglycone (V), ν_{max}^{neat} 1700, 1635 cm^{-1} which undergoes spontaneous internal acetalization to afford a hydroxyl free anhydro derivative, VI, m.p. 123-124°, $[\alpha]_D$=-35.6° (c=1.0, $CHCl_3$), $C_{11}H_{14}O_5$ (re-

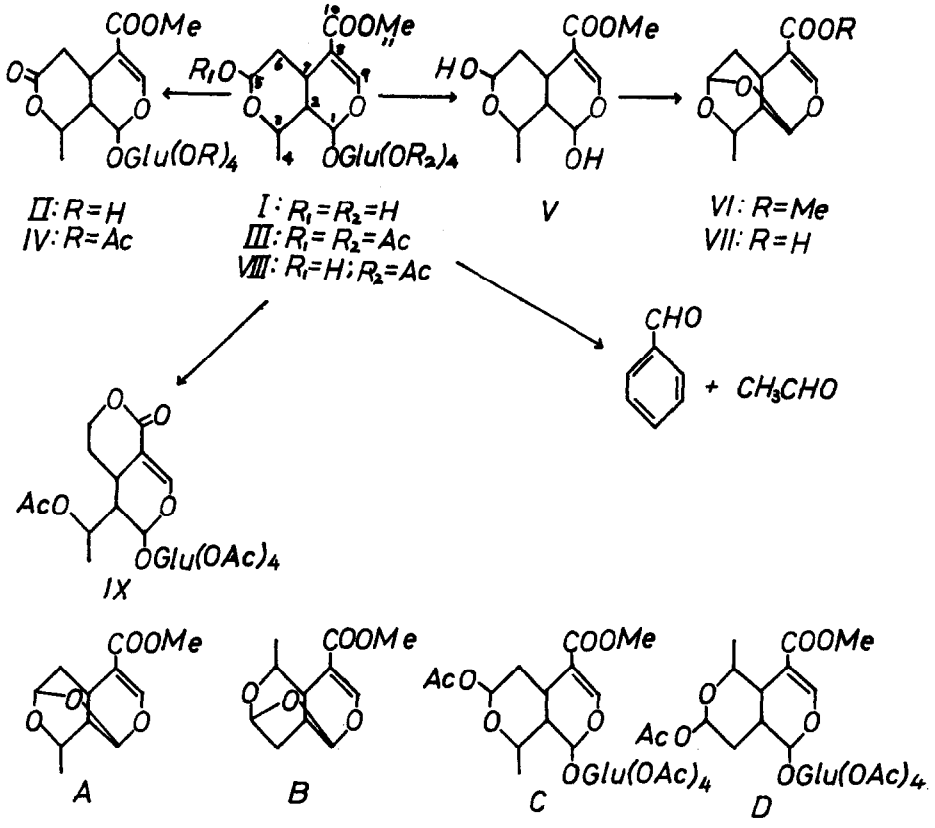
quires: C, 58.40; H, 6.42%, Found: C, 57.98; H, 6.64%), (M^+: m/e 226). This product was also obtained by acid treatment of III or the crude glycoside mixture. The spectroscopic data of VI also indicated the presence of the group -O-CO-C=CH-O- [λ_{max}^{EtOH} 233 mμ (ε, 9600), $\nu_{max}^{CHCl_3}$ 1700, 1640, 1250 cm^{-1}: τ 2.56 (s, 1H)] and Me-O- [τ 6.23 (s, 3H)]. In addition, the NMR spectrum and the decoupling experiment depicted the following partial structures, Me-CH-O- [τ 5.78 (q, J=6, 1H), τ 8.63 (d, J=6, 3H)], $\overset{-O}{-O}\rangle$CH-CH-CH- [τ 4.23 (q, J=2, 1, 1H), τ 7.00 (0, J=10, 4, 2, 1H)], (Ha, Hb), $\overset{-O}{-O}\rangle$CH-CHb- [τ 5.04 (d, J=4, 1H)], a methine proton [τ 7.60 (q, J=12,10, 1H)], and the decoupling experiment showed proton Ha and Hb assigned to a methylene envelope [τ 8.28, (m. 2H)]. Hydrolysis of VI with sodium hydroxide afforded a carboxylic acid, VII, m.p. 183-184°, $C_{10}H_{12}O_5$ (requires: C, 56.60; H, 5.70% Found: C, 56.60; H, 5.65%), $\nu_{max}^{CHCl_3}$ 3100, 2750-2550, 1685 cm^{-1}, which regenerated VI by methylation with diazomethane, confirming the presence of the partial structure MeOOC-C=CH-O-.

Based on these findings, the structure of secologanin type A or B was contemplated for the anhydro aglycone (VI). Since the location of the glycosidic linkage in the iridoids is usually limited to C-1, the structure of morroniside can be represented by the structure C or D. To distinguish both possibilities, III was hydrolyzed with sodium hydroxide and reduced with sodium borohydride. The product isolated after acetylation was a lactone, IX, amorphous, $C_{26}H_{34}O_{15}$ (requires: C, 53.25; H, 5.85%, Found: C, 53.32; H, 5.99%), λ_{max}^{EtOH} 243 mμ (ε, 8400), $\nu_{max}^{CHCl_3}$ 1710 cm^{-1} (α,ß-unsaturated δ-lactone), τ 2.50 (d,J=3, 1H), τ 8.69 (d, J=7, 3H) (1). This lactone formation excludes the structure D.

In the earlier stage of this study, the treatment of V with 20% sulfuric acid was found to yield approximately equal amounts of benzaldehyde and acetaldehyde. The apparent anomaly of this transformation can be rationalized in terms of structure (A, VI) by the following mechanism which involves retro-Michael reaction and Prins type cyclization.



Kingiside tetraacetate (IV), m.p. 165-166°, $[\alpha]_D^{25}$ -80.0° (c=1.0, $CHCl_3$), has a formula $C_{25}H_{32}O_{15}$


COOMe
COOMe
COOMe
COOR
R1O
HO
OGlu(OR)4
OGlu(OR2)4
OH
II: R=H
IV: R=Ac
I: R1=R2=H
III: R1=R2=Ac
VIII: R1=H; R2=Ac
V
VI: R=Me
VII: R=H
CHO
+ CH3CHO
AcO
OGlu(OAc)4
IX
A
B
C
D

(requires: C, 52.43, H, 5.59% Found: C, 52.44; H, 5.72%).

Hydrolysis with ammonia in aqueous dioxane followed by ion-exchange resin treatment gave the free kingiside (II), $[\alpha]_D$=-91.0° (c=0.7, EtOH), ν_{max}^{neat} 3350, 1740, 1705, 1640 cm^{-1} reacetylation of II afforded IV.

The spectral data of IV, λ_{max}^{EtOH} 233 mμ (ε, 11.500), $\nu_{max}^{CHCl_3}$ 1750, 1705, 1640 cm^{-1} τ 2.56, (s, 1H), τ 6.27 (s, 3H), τ 7.90-8.04 (five acetate signals) implied its close association with morroniside, and the structure was established by the following experiment.

Hydrolysis of III with one equivalent potassuim bicarbonate afforded tetraacetyl morroniside (VIII), which was oxidized with Jones' reagent to a δ-lactone. This is identical with IV, therefore, kingiside (II) is designated as 5-dehydromorroniside. This correlation also supports the existence of a six-membered hemiacetal in I (1).

The stereochemistry of I and II is considered to follow that of other iridoids, but correlational work is now under way to obtain unequivocal determination.

Recently the isolation of a group of compounds of secologanin type with a masked aldehyde at C-5 has been reported (2) and their important roles in indole alkaloids biogenesis have been discussed. Comparing the structures of secologanin and morroniside, it seems very probable that the latter is the more direct precursor of ajmalicine type alkaloids with methylcarbinol moiety at C-20 (3).

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3) A.R. Battersby, A.R. Burnett and P.G. Parsons, ibid., 1968, 1280, 1282.