The stoichiometry of the reaction was then investigated in the EtOH solution. The degree of methyl displacement after 110 hours reaction (conversion) was plotted against the initial molar ratio of $CuCl_2$ to Me-Co ([Cu]/[Co]) in Fig. 2. The open circles indicate the average values of runs performed with three different initial concentrations of Me-Co (60, 85 and 150 μM) and adjusted amounts of $CuCl_2$ at room temperature. The observed results preferred a 1: 1 ratio of $CuCl_2$ to Me-Co (solid line a), to a 2: 1 ratio (solid line b), in support of eq. 1.

The equimolar mixture of Me-Co and $CuCl_2$ in EtOH was then subjected to electron spin resonance measurements at suitable time intervals at liquid nitrogen temperature, and it was found that the concentration of Cu(II) decreases with time while no Co(II) (cobalamin r) signal can be detected at any stage of the reaction. The gas-liquid chromatography analysis of the product indicated that methyl chloride and methyl ethyl ether are equally formed. Neither hydrogen nor methane was perceptible. On the basis of these observations, it is assumed that the Cu(II)-promoted cleavage of Me-Co proceeds principally through the methyl transfer reaction between Me-Co and $CuCl_2$ as expressed by

$$\text{Me-Co} + CuCl_2 \longrightarrow \text{Me-CuCl} + \text{Cl-Co} \qquad (1)$$

The methylcopper intermediates (Me-CuCl) produced are so unstable that they would have decomposed to methyl chloride and copper or methyl ethyl ether when reacted with EtOH, although metallic copper was seemingly absent probably due to its low concentrations.

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The Structures of Nigakihemiacetals E and F

The structures of two new bitter principles, nigakihemiacetals E and F, isolated from *Picrasma ailanthoides* PLANCHON were shown to be **1** and **2**, respectively.

The isolation of a number of bitter principles from *Picrasma ailanthoides* PLANCHON (=*P. quassioides* BENNETT; Simaroubaceae) and the determination of their structures have been described.[1,2] Two additional new bitter principles, nigakihemiacetals E and F, have now been isolated from the same plant. In this communication, we wish to report evidence leading to structures **1** and **2** for nigakihemiacetals E and F, respectively.

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1) *a*) T. Murae, T. Tsuyuki, T. Ikeda, T. Nishihama, S. Masuda, and T. Takahashi, *Tetrahedron*, **27**, 1545 (1971); *b*) T. Murae, T. Tsuyuki, T. Ikeda, T. Nishihama, S. Masuda, and T. Takahashi, *Tetrahedron*, **27**, 5147 (1971); *c*) T. Murae, A. Sugie, T. Tsuyuki, S. Masuda, and T. Takahashi, *Tetrahedron*, **29**, 1515 (1973). And the references cited therein.

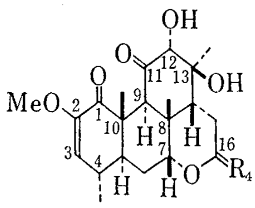
2) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 2651 (1971). And the references cited therein.

The molecular formula of nigakihemiacetal E[3] (**1**), $C_{21}H_{30}O_7$, mp 255°, $[\alpha]_D$ −11° (MeOH), was determined by mass spectrometry (M^+ at *m/e* 394.1995; Calcd. 394.1991). The infrared (IR) (ν_{max}^{Nujol} 3550, 3490, 1717, 1680, and 1625 cm^{-1}) and the ultraviolet (UV) (λ_{max}^{MeOH} 263 nm, ε 5400) spectra show characteristic absorption bands for an α,β-unsaturated ketone, a ketone, and hydroxyl groups. The proton magnetic resonance (PMR) spectral data are given in Table I.

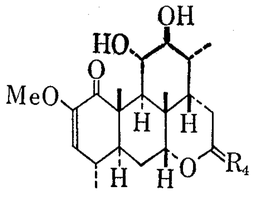
Table I. PMR Spectral Data (δ values)[a]

Compounds	$C_{(4)}$-Me	$C_{(8)}$-Me	$C_{(10)}$-Me	$C_{(13)}$-Me	$C_{(2)}$-OMe	$C_{(7)}$-H	$C_{(3)}$-H
1	1.10 d J=6.5	1.22 s[b] 1.25 s[c]	1.61 s	1.33 s[c] 1.36 s[b]	3.54 s	—	5.51 d J=2.5
2[d]	1.10 d J=7	1.12 s	1.38 s	0.98 d J=7	3.52 s	—	5.33 d J=2.5
3[e]	1.10 d J=7	1.31 s	1.58 s	1.39 s	3.54 s	4.26m	5.36 d J=2.5
4	1.10 d J=6	1.05 s	1.64 s	1.17 d J=6.5	3.55 s	4.30m	5.37 d J=2.5
6	1.16 d J=7	1.22 s	1.51 s	1.89 s	3.60 s	4.28m	5.32 d J=2.5
10	1.13 d J=6	1.16 s	1.45 s	1.05 d J=7	3.53 s	—	5.48 d J=2

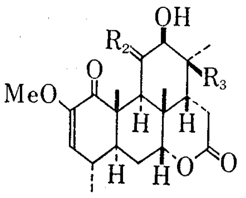
[a] Determined in $CDCl_3$ at 60 MHz. Coupling constants are expressed in Hz (s: singlet, d: doublet, and m: multiplet).
[b] Integrated signal intensity: *ca.* 2H.
[c] Integrated signal intensity: *ca.* 1H.
[d] A singlet due to $C_{(16)}$-OMe appears at δ 3.25.
[e] Signals due to $C_{(9)}$-H and $C_{(12)}$-H appear at δ 3.42 (singlet) and δ 3.76 (singlet), respectively.



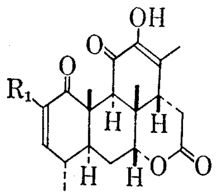
1: R_4=OH, H
3: R_4=O



2: R_4=β-OMe, α-H
10: R_4=OH, H



4: R_2=O, R_3=H
5: R_2=α-OH, β-H; R_3=H
8: R_2=α-OH, β-H; R_3=OH
9: R_2=O, R_3=OH



6: R_1=OMe
7: R_1=OH

Oxidation of **1** with silver oxide gave a lactone (**3**), $C_{21}H_{28}O_7$ (M^+ at *m/e* 392), amorphous solid, ν_{max}^{Nujol} 3580, 3450, 1730, 1700, and 1640 cm^{-1}; λ_{max}^{MeOH} 263 nm, ε 3900. An IR absorption at 1730 cm^{-1} is indicative of the presence of a lactone grouping in a six-membered or larger ring. This received support from the appearance of signals at δ 4.26 (1H, m) due to a proton at the lactone terminus ($-\overset{|}{C}\underline{H}-O-CO-$) in the PMR spectrum of **3**. The compound (**1**) must therefore be a hemiacetal corresponding to this lactone.

The PMR spectrum of **3** is related to the spectrum of the known 11-keto compound (**4**; $C_{21}H_{28}O_6$)[1a] derived from nigakilactone A (**5**).[1a] The marked differences between the two spectra are that the signals due to one secondary and three tertiary methyls appear in the spectrum of **3**, while the signals due to two secondary and two tertiary methyls are observed in that of **4** (Table I). These spectral data of the lactone (**3**) can be best interpreted on the basis of the structure (**3**),[4] which contains one hydroxyl group (at C-13) more than the structure (**4**). This was confirmed by the following observations.

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[3] The hemiacetal of this type exists as a mixture of isomers at C-16. Separation on preparative thin-layer chromatography (TLC) followed by elution of each component with solvent such as acetone and methanol resulted in formation of the same mixture.

[4] The configurations at C-12 and C-13 of **3** were determined as described below.

On treatment with bismuth trioxide in acetic acid at 100°, **3** afforded a dehydrated product (**6**),[1a,5] $C_{21}H_{26}O_6$ (M^+ at *m/e* 374), amorphous solid, ν_{max}^{Nujol} 3400, 1730, 1700, 1658, and 1630 cm^{-1}; λ_{max}^{MeOH} 270 nm; PMR: Table I), which was found to be identical with a compound (**6**) derived from bisnorquassin (**7**)[6] by methylation with diazomethane.[7] These transformations along with the spectral data described above lead to the structure **3** (except the configurations at C-12 and C-13) for the lactone (**3**).

An assignment of the methyl signals in the PMR spectra of a number of nigakilactones and nigakihemiacetals has been reported.[8] The method utilized for these bitter principles was applied to the present investigation. The result is summarized in Table I. A comparison between the data for **3** and **4** shows that an introduction of a hydroxyl group at C-13β causes downfield shifts (Δ+0.26 and Δ+0.22 ppm) of the signals due to methyl groups at C-8 and C-13, respectively, in accordance with the published data.[8] The hydroxyl group at C-13 of **3** must therefore be in a β-configuration.

Oxidation of the known nigakilactone N (**8**; $C_{21}H_{30}O_7$)[1c] with chromium trioxide in pyridine gave a ketone (**9**),[9] $C_{21}H_{28}O_7$ (M^+ at *m/e* 392), amorphous solid, ν_{max}^{Nujol} 3450, 1725, 1700, and 1625 cm^{-1}; λ_{max}^{MeOH} 264 nm (ε 3000), which was then treated with bismuth trioxide in acetic acid at 100° to afford **6**. The lactone (**3**) was found to be not identical with **9**. This leads to a 12α-hydroxyl configuration for the lactone (**3**); the structure of the lactone (**3**) should be represented by **3**. The structure (**1**) follows for nigakihemiacetal E.

The spectral data of nigakihemiacetal F (**2**), $C_{22}H_{34}O_6$ (M^+ at *m/e* 394), mp 211°, $[\alpha]_D$ +92° (EtOH), ν_{max}^{Nujol} 3470, 1680, and 1635 cm^{-1}, λ_{max}^{EtOH} 270 nm, ε 4800; PMR (Table I), suggest that **2** is a compound closely related to the known nigakihemiacetal C (**10**).[1b,3] This was shown by the formation of **2**[10] on methylation of **10** with methanolic hydrogen chloride. The structure (**2**) is therefore given for nigakihemiacetal F.[11] In the PMR spectrum of **2**, the C-16 proton appears at δ 4.76 as a multiplet ($W_{1/2}$ 5 Hz). The methoxyl group at C-16 is suggested to be in a β(axial)-configuration.

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[5] Bismuth trioxide is a reagent known to be able to transform α-ketols into α-diketones (or diosphenols). The reaction resulted in a formation of **6**, though our initial aim was to obtain a 12-keto derivative of **3**.

[6] C.G. Casinovi, V. Bellavita, G. Grandolini, and P. Ceccherelli, *Tetrahedron Letters*, **1965**, 2273.

[7] Casinovi, *et al.* (ref 6) reported the formation of a dimethylated product (quassin) by treatment of **7** with diazomethane. In our case, the same treatment resulted in the formation of **6** along with quassin as a minor product.

[8] T. Murae, T. Ikeda, A. Sugie, T. Nishihama, T. Tsuyuki, and T. Takahashi, *Bull. Chem. Soc. Japan*, **46**, 3621 (1973).

[9] An alternative structure with an 11α-hydroxyl and a 12-ketone group can be excluded, as the structure of this type would show a UV absorption maximum at *ca.* 272 nm due to a hydrogen bonding between the hydroxyl group at C-11α and a carbonyl group at C-1 (ref. 1).

[10] The other isomer (at C-16) of **2** was not obtained.

[11] Nigakihemiacetal F might be an artifact produced during isolation.