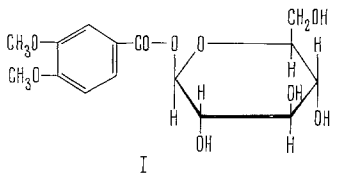
at *m/e* 167 (M-Me), 139 (*m/e* 167-CO), 165 (M-OH), 137 ($M\text{-}\overset{+}{O} \equiv$ C-OH), 122 (*m/e* 167-COOH), 121 and 45 ($\overset{+}{O} \equiv$ C-OH). An analysis of the spectral data indicated the presence of -COOH and -OMe groups only in the acid, which was subsequently identified as veratric acid by comparison of mp, mixture mp, and superimposable IR-spectrum with an authentic sample. The glucoside does not contain any free reducing group, is sparingly soluble in water (due to ester linkage), is easily hydrolyzed by emulsin, and exhibits a high negative specific optical rotation. On the basis of this evidence, the glucoside is assigned the structure (I), veratroyl β-D-glucoside and is named as *Tecomin*, as it appears to be new[7].



I

Zusammenfassung. Isolierung und Strukturaufklärung eines neuen Esterglukosides aus der Rinde von *Tecomella undulata*.

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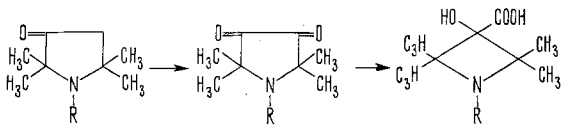
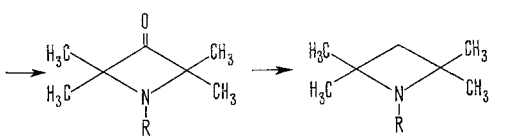
Synthesis of 2,2,4,4-Tetramethyl-Azetidine

For a number of years we have been working on the synthesis and pharmacological activities of compounds containing tetramethylated heterocyclic amines, like 2, 2, 6, 6-tetramethyl-piperidine, 1, 2, 5, 6-tetrahydro-2, 2, 6, 6-tetramethyl-pyridine, 2, 2, 5, 5-tetramethyl-pirrolidine and 2, 2, 5, 5-tetramethyl-pyrroline[1,a-f]. In order to complete these lines of research, it was found interesting to have also the unknown 2, 2, 4, 4-tetramethyl-azetidine (XI). As starting compound 1-acetyl-3-hydroxy-2, 2, 4, 4-tetramethyl-3-azetidincarboxylic acid (IV)[2,3], was used in preliminary experiments.



I R = H
II R = COC_6H_5
III R = COC_6H_5
IV R = $COCH_3$
V R = COC_6H_5



VI R = $COCH_3$
VII R = COC_6H_5
VIII R = $COCH_3$
IX R = COC_6H_5
X R = $CH_2C_6H_5$
XI R = H

Compound (VI) was obtained by oxidative decarboxylation of (IV); by reducing the ketogroup a compound identified as (VIII) was obtained. This compound readily underwent hydrolysis under alkaline conditions, but the desired 2, 2, 4, 4-tetramethyl-azetidine was not obtained. Ring opening with development of NH_3, acetic acid and a branched unsaturated hydrocarbon occurred. Since it was necessary to avoid the final hydrolysis of the compound, we protected the cyclic nitrogen by a benzoyl group, which, by reduction, becomes a benzilic group and can thus easily be removed by catalytic hydrogenation. Using this method it was possible to obtain 2, 2, 4, 4-tetramethyl-azetidine. All the compounds were isolated, purified, and their structure assigned by IR- and NMR-spectra (Table).

1-acetyl-2, 2, 4, 4-tetramethyl-3-azetidinone (VI) was obtained according to CHEN et al.[3], by boiling for 5 h the 1-acetyl-3-hydroxy-2, 2, 4, 4-tetramethyl-3-azetidincarboxylic acid (IV)[2,3] with $Pb(CH_3COO)_4$ in CCl_4 (Yield 82%[4], b.p. 106–108 °C/16 mm Hg, mp 41–42 °C; Anal. Calc. for $C_9H_{15}NO_2$ (169.2) C 63.88 H 8.94 *N* 8.28, Found C 62.76 H 8.88 *N* 8.29).

$$\nu_{CO\ ketone} = 1820\ cm^{-1};\quad \nu_{CO\ amide} = 1648\ cm^{-1}.$$

1-acetyl-2, 2, 4, 4-tetramethyl-azetidine (VIII) was obtained by heating the compound (VI) with hydrazine hydrate and KOH in triethylenglicol at 160 °C[5], and subsequently distillation (Yield 65%, b.p. 95–97 °C/16 mm Hg; Anal. Calc. for $C_9H_{17}NO$ (155.2) C 69.65 H 11.04 *N* 9.02, Found C 69.98 H 10.97 *N* 9.03).

$$\nu_{CO\ amide} = 1640\ cm^{-1}.$$

In order to obtain 2, 2, 4, 4-tetramethyl-azetidine by hydrolysis of (VIII), the following experiments were performed: a) acid hydrolysis by boiling with HCl 6*N*: no modifications took place. b) Alkaline hydrolysis by boiling 5 h with KOH 30%[6]. Under these conditions the unmodified compound, together with potassium acetate and molecular fragments not further identified (during the reaction there is development of NH_3) were obtained. c) Alkaline hydrolysis, by heating with anhydrous KOH at 220 °C followed by distillation, gave NH_3, CH_3COOK

[1] a) Belg. Pat. 697,242; b) Belg. Pat. 702,780; c) Belg. Pat. 702,535; d) Belg. Pat. 702,778; e) Belg. Pat. 702,781 (To ERASME); f) Belg. Pat. 724,007 (To CIRM).
[2] C. SANDRIS and G. OURISSON, Bull. Soc. chim. Fr. (*1958*), 354.
[3] T. CHEN, T. SANNJIKI, H. KATO and N. M. OHTA, Bull. chem. Soc. Japan *40*, 2398 (1967).
[4] In [2] there were obtained only small quantities of (VI), in [3] with a Yield of 37%.
[5] US 3020288 (May-Baker Ltd) – CA *57*, 3416g (1962).
[6] In [2] hydrolysis experiments of 2,2,5,5 tetramethyl-3-pirrolidinone were made but without success.

and an unidentified aliphatic unsaturated hydrocarbon (b.p. 78–80 °C).

According to SANDRIS and OURISSON[2] it was possible to obtain the 1-benzoyl-2, 2, 5, 5-tetramethyl-3-pyrrolidinone (II) from 2, 2, 5, 5-tetramethyl-3-pirrolidinone (I), using benzene, in the presence of triethylamine (Yield 79%, b.p. 143–145 °C/0.25 mm Hg, mp 55–57 °C. Anal. Calc. for $C_{15}H_{19}NO_2$ (245.3) C 73.44 H 7.80 *N* 5.71, Found C 72.93 H 7.68 *N* 5.69).

$$\nu_{CO\ ketone} = 1758\ cm^{-1};\quad \nu_{CO\ amide} = 1628\ cm^{-1}.$$

1-benzoyl-2, 2, 5, 5-tetramethyl-3, 4-pyrrolidindione (III) was prepared by oxidation of (II) using SeO_2, in aqueous dioxane, at 80 °C (Yield 58%[6], mp 112–114 °C; Anal. Calc. for $C_{15}H_{17}NO_3$ (259.3) C 69.48 H 6.60 *N* 5.40, Found C 68.88 H 6.69 *N* 5.37).

$$\nu_{CO\ ketone} = 1782\text{–}1769\ cm^{-1};\quad \nu_{CO\ amide} = 1640\ cm^{-1}.$$

1-benzoyl-3-hydroxy-2, 2, 4, 4-tetramethyl-3-azetidincarboxylic acid (V) was obtained by heating the compound (III) in aqueous solution of KOH 20%, until boiling. (Yield 91%, mp 253–255 °C (dec.); Anal. Calc. for $C_{15}H_{19}NO_4$ (277.3) C 64.97 H 6.60 *N* 5.05, Found C 65.32 H 7.01 *N* 5.05).

$$\nu_{OH} = 3419\ cm^{-1};\quad \nu_{CO\ ketone} = 1690\ cm^{-1};$$
$$\nu_{CO\ amide} = 1550\ cm^{-1}.$$

1-benzoyl-2, 2, 4, 4-tetramethyl-3-azetidinone (VII) was prepared by oxidation of (V) with $Pb(CH_3COO)_4$ in $CHCl_3$ (Yield 97%, b.p. 120–123 °C/0.4 mm Hg; mp 61–63 °C; Anal. Calc. for $C_{14}H_{17}NO_2$ (231.3) C 72.69 H 7.40 *N* 6.05, Found C 73.11 H 7.38 *N* 6.07).

$$\nu_{CO\ ketone} = 1825\ cm^{-1};\quad \nu_{CO\ amide}\ 1625\ cm^{-1}.$$

1-benzoyl-2, 2, 4, 4-tetramethyl-azetidine (IX) was obtained by a method similar to that used for (VI) (Yield 64%, mp 103–105 °C; Anal. Calc. for $C_{14}H_{19}NO$ (217.3) C 77.49 H 8.82 *N* 6.45; Found C 76.36 H 8.68 *N* 6.48).

$$\nu_{CO\ amide} = 1620\ cm^{-1}.$$

1-benzyl-2, 2, 4, 4-tetramethyl-azetidine (X) prepared by reduction of (IX) with $LiAlH_4$, in ethyl ether, was isolated, as the chlorhydrate. (Yield 96%, mp 174–176 °C; Anal. Calc. for $C_{14}H_{21}N \cdot HCl$ (239.8) C 70.06 H 9.40 *N* 5.83 Cl 14.77. Found C 70.54 H 9.38 *N* 5.84 Cl 14.63).

2, 2, 4, 4-tetramethyl-azetidine (XI) was obtained by hydrogenolysis of (X). HCl, in ethanol, in the presence of Pd/C 10%, and isolated as chlorhydrate. (Yield 82%, mp 198–200 °C; Anal. Calc. for $C_7H_{15}N \cdot HCl$ (149.6) C 56.20 H 10.78 *N* 9.36 Cl 23.68; Found C 56.41 H 10.66 *N* 9.38 Cl 23.65).

Chemical shifts, ppm (τ)[a]

		ϕ	$-CH_3$	$-CH_2$	-NH-	-OH-
II	CCl_4	2.70 s	8.50[b] s 8.72[c] s	7.5 s	–	–
III	CCl_4	2.68 s	8.52[d] s	–	–	–
V	DMSO(d_6)	2.60 s	8.35 b 8.78 b	–	–	3.00[e] b
VII	CCl_4	2.62 s	8.52 s	–	–	–
IX	CCl_4	2.69 s	8.60 b	8.10 s	–	–
X	CCl_4	2.85 m	8.90 s	6.45[f] s 8.30[g] s	–	–
XI	CCl_4	–	8.80 s	8.10 s	7.53[h] s	–

[a] The NMR-spectra were recorded on Perkin Elmer R 12, at 60 MHz. [b] 6 protons of methyl groups vicinal to –CO– function. [c] 6 protons of methyl groups vicinal to $-CH_2-$. [d] 12 protons of methyl groups vicinal to –CO– function. [e] The assignement is uncertain, but the structure of the compound was confirmed by IR-spectra. [f] $-CH_2-$ of benzylic group. [g] $-CH_2-$ of heterocyclic ring. [h] This signal is removed completely when few drops of D_2O are added to CCl_4. s, single; m, multiple; b, very broad peak.

Riassunto. La 2, 2, 4, 4-tetrametil-azetidina (XI), è stata preparata per la prima volta con ottime rese, a partire da 2, 2, 5, 5-tetrametil-3-pirrolidone (I), attraverso i seguenti intermedi: 1-benzoil-2, 2, 5, 5-tetrametil-3-pirrolidone (II), 1-benzoil-2, 2, 5, 5-tetrametil-3, 4-pirrolidindione (III), acido 1-benzoil-3-idrossi-2, 2, 4, 4-tetrametil-3-azetidin-carbossilico (V), 1-benzoil-2, 2, 4, 4-tetrametil-3-azetidinone (VII), 1-benzoil-2, 2, 4, 4-tetrametil-azetidina (IX) e 1-benzil-2, 2, 4, 4-tetrametil-azetidina (X).

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Modification of Digitalis Inotropism by a Lactam Derivative

The importance of the unsaturated lactone ring for typical effects of cardiotonic steroids has been well documented[1, 2]. Recently, derivatives of such steroids have been synthesized with specific changes in the group located at the C-17 position[3–7]. One of these compounds, acetylisodigitoxigeninic lactam, reduces the effects of a subsequent dose of a standard cardenolide lactone.

Ammonolysis of digitoxigenin **1** in methanol solution affords lactol amide **2a**[8] (55%) mp 271–273°, $[\alpha]_D^{20}$ – 5° (*c* 1, pyridine) and lactol **2b**, mp 201–203°, $[\alpha]_D^{20}$, +44° (*c*, 1, pyridine), concomitantly formed in 14% yield. That **2a** and **2b** differ only in the orientation of the hydroxyl group at C-21 is shown by oxidation (CrO_3-pyridine) of either lactol to the same lactone **5**, mp 284–286°, $[\alpha]_D^{20}$ – 3°