New Withanolides, Daturametelins C, D, E, F and G-Ac from *Datura metel* L. (Solanaceous Studies. XIV)[1)]

Kazushi SHINGU, Yoriko FURUSAWA and Toshihiro NOHARA*

Faculty of Pharmaceutical Sciences, Kumamoto University, 5-1 Oe-honmachi, Kumamoto 862, Japan. *Received December 16, 1988*

Minor new withanolides, daturametelins C, D, E, F and G-Ac, have been isolated from the methanolic extract of the fresh aerial parts of *Datura metel* L. (Solanaceae) and their structures have been determined mainly by spectroscopic means. Daturametelins E anf F are the first withanolides having a 1-one-3β-*O*-sulfate structure in ring A.

Keywords *Datura metel*; Solanaceae; withanolide; daturametelin; withametelin

In the course of our studies on the constituents of solanaceous plants, we recently reported the structural characterization of two new withanolide glucosides, daturametelins A and B (I),[2)] isolated from the methanolic extract of the fresh aerial parts of *Datura metal* L. (Solanaceae). These compounds were the first examples of withanolides possessing a glycosidic residue in the δ-lactone moiety of the molecule. Hikino *et al.*[3)] independently reported the isolation and structural determination of withametelin (II), having a novel hexacyclic structure, from the same plant. Since I occurs as a major component in the fresh plant body and is easily converted into II by the action of silica gel, we considered that II was probably an artificial product derived from I. We now report the isolation and structural characterization of five additional, related materials, daturametelins C (**1**), D (**2**), G-Ac (**3**), F (**4**) and E (**5**), from the same source.

Daturametelin C (**1**), $C_{29}H_{40}O_5$, colorless needles, mp 199—202 °C, $[\alpha]_D$ +68.7° ($CHCl_3$), showed an $(M+H)^+$ peak at *m/z* 469 in the positive fast atom bombardment mass spectrum (FAB-MS) and absorption bands at 3464 cm^{-1} (hydroxyl), 1698 cm^{-1} (α,β-unsaturated δ-lactone) and 1670 cm^{-1} (α,β-unsaturated ketone) in the infrared (IR) spectrum. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum (Table I) of **1** was similar to that of I. Signals at δ 0.77, 1.24 and 2.07 (each 3H, s) could be assigned to the three methyl groups at C-13, C-10 and C-24, respectively. By comparing the ^{1}H-NMR spectrum of **1** with those of daturametelin A tetraacetate, I-pentaacetate and II, other signals were also unambiguously attributable as follows: 3H, s, δ 3.38 (one methoxyl group), 1H, dd, *J*=4.9, 21.3 Hz, δ 2.83 and 1H, br d, *J*=21.3 Hz, δ 3.30 (H_2-4), 1H, dd, *J*=5.1, 11.7 Hz, δ 3.82 and 1H, dd, *J*=2.2, 11.7 Hz, δ 4.07 (H_2-21), 1H, d, *J*=10.6 Hz, δ 4.17 and 1H, d, *J*=10.6 Hz, δ 4.29 (H_2-27) and 1H, dt, *J*=3.5, 13.2 Hz, δ 4.50 (H-22). The lower field signals at δ 5.57 (1H, d, *J*=6.2 Hz), 5.87 (1H, ddd, *J*=1.2, 3.2, 10.0 Hz) and 6.78 (1H, ddd, *J*=2.5, 4.9, 10.0 Hz) were assignable to the olefinic protons at C-6, C-2 and C-3, respectively. The H-22 signal of II appeared as a broad singlet at δ 4.65 (1H, br s, $W_{h/2}$=8.8 Hz), while that of daturametelin A tetraacetate was a triple doublet at δ 4.41 (1H, dt, *J*=3.3, 13.2 Hz). Namely, when the hydroxymethyl group at C-20 is linked to C-24 to form a ring, the H-22 signal appears as a broad singlet, while in the absence of ring-closure (usual withanolide-type), the H-22 signal appears as a triple doublet. Since the H-22 signal was a triple doublet at δ 4.50 (1H, dt, *J*=3.5, 13.2 Hz) in the case of **1**, the side chain structure at C-17 corresponds to the latter. The ^{1}H-NMR spectrum of the enzymatic hydrolysate (**6**) derived from I showed a good accordance with that of **1** except for the chemical shift of the proton signals at C-27 and for the loss of one methyl group. That is, an AB quartet signal due to H_2-27 appeared at δ 4.29 (1H, d, *J*=10.6 Hz) and 4.17 (1H, d, *J*=10.6 Hz) in **1**, corresponding to those at δ 4.41 (1H, d, *J*=12.5 Hz) and 4.35 (1H, d, *J*=12.5 Hz) in **6**. The above result indicated that a methyl group (δ_H 3.38; δ_C 58.4) is attached to the CH_2OH group at C-25 in **1**. Therefore, the structure of **1** was presumed to be the 27-*O*-methyl ether of desgluco-daturametelin B. The carbon-13 nuclear magnetic resonance (^{13}C-NMR) data for **1** are summarized in Table II, and are consistent with the above assumed structure. Thus, the structure of **1** could be represented as (22*R*)-21,27-dihydroxy-1-oxo-witha-2,5,24-trienolide 27-*O*-methyl ether. Compound **1** might be an artifact derived from **6** during the methanolic extraction procedure.

Daturametelin D (**2**), $C_{29}H_{40}O_5$, colorless needles, mp 199.5—201.5 °C, $[\alpha]_D$ −90.6° ($CHCl_3$). EI-MS *m/z*: 468 (M^+), exhibited absorption bands at 1728 (δ-lactone) and 1664 cm^{-1} (α,β-unsaturated ketone) in its IR spectrum. In the ^{1}H-NMR spectrum there were three methyl signals at C-13 (s, δ 0.69), C-10 (s, δ 1.23) and C-24 (s, δ 1.32), one methoxyl signal at C-27 (3H, s, δ 3.38), six methylene proton signals at C-4 (1H, dd, *J*=4.7, 20.1 Hz, δ 2.83 and 1H, br d, *J*=20.1 Hz, δ 3.29), C-21 (1H, dd, *J*=3.1, 13.6 Hz, δ 3.49 and 1H, d, *J*=13.6 Hz, δ 3.91) and C-27 (1H, dd, *J*=5.5, 9.8 Hz, δ 3.77 and 1H, dd, *J*=2.7, 9.8 Hz, δ 3.99), one methine proton signal at C-22 (1H, br s, δ 4.63) and three olefinic proton signals at C-2 (1H, dt, *J*=1.6, 10.0 Hz, δ 5.87), C-3 (1H, ddd, *J*=2.5, 4.7, 10.0 Hz, δ 6.77) and C-6 (1H, d, *J*=6.2 Hz, δ 5.57). From the viewpoint of the above discussion regarding H-22, the signal due to H-22 in **2** suggested that the hydroxymethyl group at C-20 is combined with C-24 to construct a ring such as in II, which is consistent with the methyl signal at C-24 appearing at δ 1.32 (s). Furthermore, since signals due to the methylene protons at C-27 appeared as ABX type, C-25 should be a methine carbon. All signals in the ^{13}C-NMR spectrum of **2** were assigned as shown in Table II. To establish the structure of **2**, X-ray analysis was undertaken and the structure was identifide as (20*S*,22*R*,25*S*)-27-methoxy-1-oxo-21,24*R*-epoxywitha-2,5-dienolide. The methyl group at C-27 is assumed to have been artificially introduced during methanol extraction.

Daturilin,[4)] daturilinol[5)] and datumetelin[6)] were recently isolated from the same source and their structures were

TABLE I. ^{1}H-NMR Data for I, I-Ac and **1**—**7**

H	I C_5D_5N	I-Ac $CDCl_3$	II $CDCl_3$	**1** $CDCl_3$	**6** $CDCl_3$	**2** $CDCl_3$	**3** $CDCl_3$	**4** C_5D_5N	**7** $CDCl_3$	**5** C_5D_5N
2	5.99 dd (1.8, 10.0)	5.87 dd (2.0, 10.0)	5.88 dd (2.5, 9.8)	5.87 ddd (1.2, 3.2, 10.0)	5.88 dd (1.8, 9.9)	5.87 dt (1.6, 10.0)	5.87 dd (2.0, 10.0)	3.15 dd (9.5, 12.7) 3.26 dd (5.7, 12.7)	2.64 dd (5.3, 12.8) 2.73 dd (9.7, 12.8)	3.16 d (12.8) 3.24 dd (5.7, 12.7)
3	6.73 ddd (2.5, 4.7, 10.0)	6.74 ddd (2.3, 5.1, 10.0)	6.77 ddd (2.5, 5.1, 9.8)	6.78 ddd (2.5, 4.9, 10.0)	6.78 ddd (2.6, 5.1, 9.9)	6.77 ddd (2.5, 4.7, 10.0)	6.77 ddd (2.6, 4.9, 10.0)	5.07 m	3.86 m	*b)*
4	2.75 dd (4.7, 21.1) 3.22 br d (21.1)	2.83 dd (5.1, 21.6) 3.29 br d (21.6)	2.84 dd (5.1, 20.4) 3.30 dt (2.5, 20.4)	2.83 dd (4.9, 21.3) 3.30 br d (21.3)	2.83 dd (5.1, 21.2) 3.29 dd (2.6, 21.2)	2.83 dd (4.7, 20.1) 3.29 br d (20.1)	2.83 dd (4.9, 21.4) 3.29 br d (21.4)	2.89 br t (12.9) 3.08 dd (5.5, 12.9)	2.55 br d (6.6)	2.89 br t (11.4) 3.10*a)*
6	5.51 d (5.9)	5.57 d (5.9)	5.58 d (5.8)	5.57 d (6.2)	5.57 d (5.9)	5.57 d (6.2)	5.57 d (6.2)	5.47 d (5.1)	5.62 d (6.6)	5.50 br s
18	0.76 s	0.76 s	0.71 s	0.77 s	0.77 s	0.69 s	0.69 s	0.52 s	0.69 s	0.72 s
19	1.21 s	1.23 s	1.22 s	1.24 s	1.24 s	1.23 s	1.22 s	1.20 s	1.29 s	1.21 s
21	4.03 d (7.4) 4.07 d (7.4)	4.23 dd (4.4, 10.3) 4.36 d (10.3)	3.73 dd (3.0, 12.7) 3.95 d (12.7)	3.82 dd (5.1, 11.7) 4.07 dd (2.2, 11.7)	3.84 dd (4.8, 11.6) 4.08 d (11.6)	3.49 dd (3.1, 13.6) 3.91 d (13.6)	3.86 d (13.9) 3.72 dd (3.9, 13.9)	3.76 dd (3.2, 13.2) 3.87 d (13.2)	3.72 dd (3.1, 13.6) 3.90 d (13.6)	4.01 dd (3.7, 9.7) 4.26 d (9.7)
22	4.56 d (12.1)	4.46 br d (10.8)	4.65 br s ($W_{h/2}$=8.8)	4.50 dt (3.5, 13.2)	4.50 dt (3.5, 13.2)	4.63 br s	4.58 br s ($W_{h/2}$=8.8)	4.66 br s	4.65 br s	4.61 br d (13.2)
27	4.58 d (11.9) 4.56 d (11.9)	4.46 br d (10.8) 4.59 d (10.8)	6.02 br s 6.76 br s	4.17 d (10.6) 4.29 d (10.6)	4.35 d (12.5) 4.41 d (12.5)	3.77 dd (5.5, 9.8) 3.99 dd (2.7, 9.8)	3.97 dd (3.3, 9.5) 4.24*a)*	6.02 s 6.87 s	6.02 s 6.75 s	4.32 d (10.6) 4.48 d (10.6)
28	2.08 s	2.05 s	1.44 s	2.07 s	2.04 s	1.32 s	1.30 s	1.48 s	1.43 s	2.02 s
1′	4.85 d (10.6)	4.64 d (8.1)					4.35 d (8.1)			
2′		4.94 dd (8.1, 9.6)					4.97 dd (8.1, 9.8)			
3′		5.20 t (9.6)					5.18 t (9.8)			
4′		5.07 t (9.6)					5.04 t (9.8)			
5′		3.69 dt (2.6, 9.6)					3.66 ddd (2.6, 4.7, 9.8)			
6′		4.20 m					4.13 dd (2.6, 12.4) 4.25 dd (4.7, 12.4)			
OMe				3.38 s		3.38 s				3.36 s
OAc		1.99 s 2.01 s 2.02 s 2.03 s 2.07 s 2.08 s					1.99 s 2.09 s 2.06 s 2.02 s			

400 MHz; δ, multiplicity (J in Hz). *a)* Its J value could not be calculated clearly owing to overlapping with other signals. *b)* Hidden by the H_2O signal.

characterized as (20*S*,22*S*)-1-oxo-21,24*S*-epoxywitha-2,5,25-trienolide, (20*S*,22*S*)-27-hydroxy-1-oxo-21,24*S*-epoxywitha-2,5-dienolide and (20*S*, 22*S*)-27-methoxy-1-oxo-21,24*S*-epoxywitha-2,5-dienolide, respectively, by Ahmad *et al.* Among them, datumetelin possesses the same plane structure as **2**, but it differs from **2** in the configurations at C-22 and C-24. Detailed discussion of the X-ray analysis of **2** and the stereo-differences in these compounds will be given in a separate paper.

Daturametelin G-Ac (**3**), $C_{42}H_{56}O_{14}$, an amorphous powder, $[\alpha]_D$ −48.4° ($CHCl_3$), was obtained as an acetyl derivative in order to achieve a facile separation. By comparison of the ^{1}H-NMR spectrum of **3** with that of **2**, the following signals could be assigned: three methyl groups at C-13 (s, δ 0.69), C-10 (s, δ 1.22) and C-24 (s, δ 1.30), the methylene proton signals at C-4 (1H, dd, J=4.9, 21.4 Hz, δ 2.83 and 1H, br d, J=21.4 Hz, δ 3.29), the olefinic proton signals at C-2 (1H, dd, J=2.0, 10.0 Hz, δ 5.87), C-3 (1H, ddd, J=2.6, 4.9, 10.0 Hz, δ 6.77) and C-6 (1H, d, J=6.2 Hz, δ 5.57). The broad singlet signal at δ 4.58 ($W_{h/2}$=8.8 Hz) was assigned to H-22, and the signal shape showed that the hydroxymethyl group at C-20 had combined with C-24 in the lactone ring moiety and formed a ring such as that in II. Furthermore, the ^{1}H-NMR spectrum of **3** indicated the existence of the per-*O*-acetyl β-glucopyranosyl moiety [δ 3.66 (1H, ddd, J=2.6, 4.7, 9.8 Hz, H-5′), 4.13 (1H, dd, J=2.6, 12.4 Hz, H-6′), 4.25 (1H, dd, J=4.7, 12.4 Hz, H′-6′), 4.35 (1H, d, J=8.1 Hz, H-1′), 4.97 (1H, dd, J=8.1, 9.8 Hz, H-2′), 5.04 (1H, t, J=9.8 Hz, H-4′), 5.18 (1H, t, J=9.8 Hz, H-3′)]. Accordingly, it was assumed that **3** possessed the

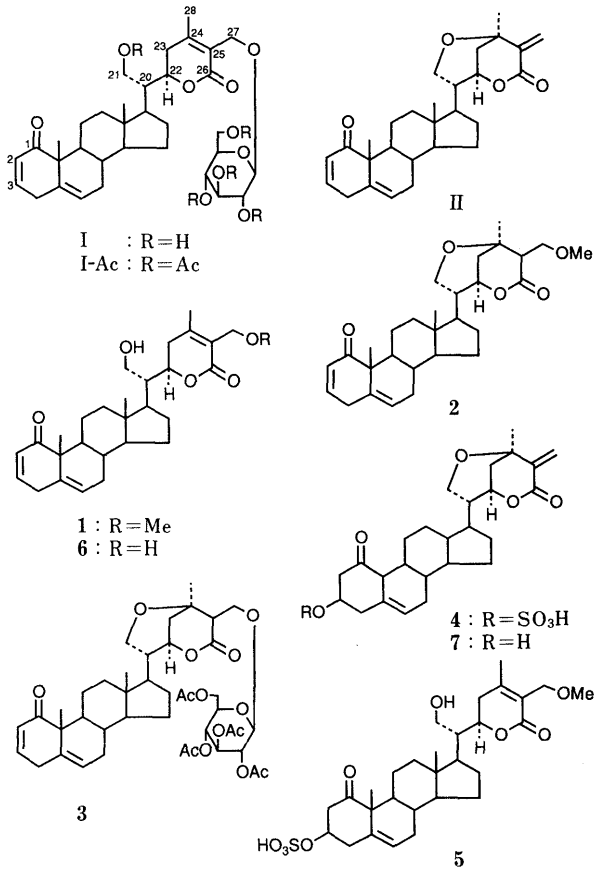
TABLE II. ^{13}C-NMR Data for II and **1**—**3** ($CDCl_3$), I, **4** and **5** (Pyridine-d_5)

C	I	II	1	2	3	4	5
1	203.9	204.5	204.3	204.2	204.2	210.4	210.3
2	127.9	128.0	127.9	128.0	128.0	39.3	39.0
3	145.9	145.0	145.2	145.0	145.1	73.9	74.2
4	33.6	33.4	33.5	33.5	33.5	31.3	31.4
5	136.3	135.9	136.0	136.0	136.0	135.7	136.0
6	124.8	124.5	124.6	124.5	124.7	125.9	126.1
7	31.1	30.7	30.7	30.7	30.8	30.0	29.9
8	33.4	33.2	33.3	33.2	33.3	32.0	33.4
9	43.5	42.8	42.9	42.9	42.9	42.8	43.1
10	50.8	50.4	50.5	50.7	50.5	47.7	52.9
11	24.1	23.6	23.7	23.6	23.6	22.9	22.9
12	39.3	39.6	39.2	39.7	39.7	39.7	39.2
13	42.6	42.5	42.3	42.6	42.6	42.8	42.8
14	56.3	56.0	56.1	56.0	56.0	56.1	56.3
15	24.5	24.0	24.2	24.1	24.1	24.2	24.4
16	27.1	26.5	27.2	26.3	26.4	26.6	27.2
17	47.2	47.6	46.3	47.8	47.9	46.1	47.2
18	12.4	12.7	12.2	12.7	12.8	12.5	12.3
19	19.0	18.9	18.9	18.9	19.0	19.0	18.9
20	46.0	39.9	45.3	39.9	40.4	40.5	45.9
21	58.9	60.4	59.7	60.1	59.8	60.7	58.9
22	77.9	75.8	77.9	76.1	In solv.	75.8	78.0
23	33.3	33.2	32.7	33.2	30.5	33.2	32.1
24	157.9	69.2	157.3	69.1	70.6	69.8	157.5
25	123.1	138.9	123.3	50.5	51.1	140.4	124.0
26	166.2	165.2	165.7	171.8	172.4	165.2	166.1
27	63.4	129.7	65.7	70.8	70.8	129.0	66.0
28	20.5	25.6	20.4	26.9	24.9	25.6	20.2
27-OMe			58.4	58.7			57.9
glc-1	104.6				101.8		
2	75.0				71.2		
3	78.4				72.4		
4	71.4				68.6		
5	78.4				71.9		
6	62.8				61.9		

per-*O*-acetyl glucopyranosyl group in place of the methyl group at C-27 in **2**. The ^{13}C-NMR spectrum of **3** was identical with that of **2** except for a small difference in the carbon signals of C-23 and C-28. Therefore, the structure of **3** could be represented as shown in the formula.

Daturametelin F (**4**), $C_{28}H_{38}O_8S$, an amorphous powder, $[\alpha]_D$ +5.0° (pyridine), neg. FAB-MS *m/z*: 533 $[M-H]^-$, showed strong absorption bands due to a hydroxyl group (3468 cm^{-1}), carbonyl group and δ-lactone moiety (1716 cm^{-1}), vinyl group (1626 cm^{-1}) and an *S-O* functional group (1226 cm^{-1}) in the IR spectrum.[7] By comparing the ^{1}H-NMR spectrum of **4** with that of II, we could assign three methyl group signals at C-13 (δ0.52), C-10 (δ1.20) and C-24 (δ1.48), the methylene proton signal at C-21 (1H, dd, J=3.2, 13.2 Hz, δ3.76 and 1H, d, J=13.2 Hz, δ3.87), the methine proton signal at C-22 (1H, br s, δ4.66), the olefinic proton signal at C-6 (1H, d, J=5.1 Hz, δ5.47) and the vinyl proton signals at C-27 (1H, s, δ6.02 and 1H, s, δ6.87). Moreover, the ^{1}H–^{1}H correlation spectroscopy (COSY) NMR spectrum led to the assignments of H_2-4 (1H, br t, J=12.9 Hz, δ2.89 and 1H, dd, J=5.5, 12.9 Hz, δ3.08), H_2-2 (1H, dd, J=9.5, 12.7 Hz, δ3.15 and 1H, dd, J=5.7, 12.7 Hz, δ3.26) and H-3 (1H, m, δ5.07) adjacent to an oxygen-bearing carbon. The presence of the sulfate group on the C-3 hydroxyl group was confirmed chemically and spectroscopically as follows. Compound **4** showed high polarity (*Rf* 0.28, solvent, $CHCl_3$: MeOH : H_2O = 8 : 2 : 0.2) on thin layer chromatography (TLC). On treatment of **4** with pyridine–dioxane,[8] the reaction mixture including the hydrolysate (**7**) was positive to the potassium rhodizonate reagent.[9] In the ^{1}H-NMR spectrum of **7**, a signal due to the hydroxy methine proton at C-3 was shifted to the higher field side (δ5.07 in **4**; δ3.86 in **7**). Furthermore, on treatment with pyridine–acetic anhydride, **4** changed into II. These results supported the 3-*O*-sulfate structure, whose configuration was determined to be β-one from the coupling constants between H-3 (m) and H_2-2, and between H-3 and H_2-4. A comparative study of the ^{13}C-NMR spectrum of **4** with that of II revealed the following facts. 1) The chemical shifts except for C-1—4 and C-10 on the A-ring in the ^{13}C-NMR spectrum of **4** showed good coincidence with those of II (Table II). 2) The C-1 signal at δ204.5 in II was shifted to δ210.4 in **4**, the sp^2 carbons of C-2 and C-3 in **1**—**3** disappeared in **4**, and the C-3 in **4** changed into an oxygen-bearing carbon. Therefore, the structure of **4** was concluded to be as shown in the formula.

Daturametelin E (**5**), an amorphous powder, $[\alpha]_D$ +25.8° (MeOH), showed an analogous ^{1}H-NMR pattern with that of **1**. A comparative ^{1}H-NMR study of **5** with **1** allowed assignments of the following signals: H_3-18 (s, δ0.72), H_3-19 (s, δ1.21), H_3-28 (s, δ2.02), MeO-27 (s, δ3.36), H_2-21 (1H, dd, J=3.7, 9.7 Hz, δ4.01, and 1H, d, J=9.7 Hz, δ4.26), H_2-27 (1H, d, J=10.6 Hz, δ4.32 and 1H, d, J=10.6, δ4.48), H-22 (1H, br d, J=13.2 Hz, δ4.61) and H-6 (1H, br s, δ5.50). Since the ^{1}H-NMR signals between δ2.8 and 3.3 in **5** were in good accordance with those in **4**, the existence of the 1-one-3β-hydroxyl structure in the steroid was suggested. Moreover, the ^{13}C-NMR spectrum indicated the sulfate group to be linked to the C-3 hydroxyl



group, as in **4**. The chemical shifts for C-1—19 and C-20—28 in the ^{13}C-NMR spectrum of **5** showed a good coincidence with those of **4** and **1**, respectively. Therefore, the structure of **5** was concluded to be as shown in the formula.

Daturametelins E (**5**) and F (**4**) are the first withanolides possessing the 1-one-3β-*O*-sulfate group on ring A. According to Glotter *et al.*,[10] in the formation of the substitution pattern of rings A and B in the withanolides, hydroxylation at C-1 takes place from the rear, less hindered side of the molecule, in the first step, and in the next step, the intermediate 5-ene-1α,3β-diol is selectively oxidized to the corresponding ketone, which undergoes β-elimination to give the common 2,5-dien-1-one structure. The 3-*O*-derivatives such as **4** and **5** are regarded as important intermediates in the biosynthesis of withanolides.

Experimental

All melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. The optical rotations were measured with a JASCO DIP-360 automatic digital polarimeter. The IR spectra were recorded with a Hitachi IR spectrometer, model 270—30. The ^{1}H- and ^{13}C-NMR spctra were measured with a JEOL JNM-GX 400 NMR spectrometer and chemical shifts are given on a δ (ppm) scale with tetramethylsilane as an internal standard. The electron inpact (EI)- and FAB-MS were measured with JEOL JMS-01SG and DX-300 spectrometers. The FAB-MS were taken in a glycerol matrix containing NaI. TLC was performed on precoated Kieselgel 60 F_{254} plates (Merck) and detection was achieved by spraying 10% H_2SO_4 followed by heating or by spraying the potassium rhodizonate reagent. Column chromatography was carried out on Kieselgel (70—230 mesh and 230—400 mesh, Merck).

Extraction and Separation The fresh aerial parts of *Datura metel* L. (Solanaceae) (1.7 kg), harvested at the herb garden in Kumamoto Univ. in September 1986, were extracted with MeOH and the extract was separated into the $CHCl_3$–MeOH soluble portion (19.3 g) and the water-soluble portion (24.7 g). A part (15.4 g) of the $CHCl_3$–MeOH soluble portion was subjected repeatedly to column chromatography over silica gel using $CHCl_3$:MeOH:H_2O = 1:0:1→8:2:0.1→0:1:0 to give daturametelins C (**1**, 20.7 mg), D (**2**, 60.1 mg), E (**5**, 9.6 mg), F (**4**, 30 mg) and G-Ac (**3**, 8.2 mg); compound **3** was difficult to isolate and was converted to the acetyl derivative to facilitate separation.

Daturametelin C (1) Colorless needles from $CHCl_3$–MeOH, mp 199.0—202.0 °C. $[\alpha]_D^{25}$ +68.7° (c=0.49, $CHCl_3$). FAB-MS *m/z*: 469 $(M+H)^+$, 419, 267, 154, 136, 107, 91. IR ν_{max}^{KBr} cm^{-1}: 3464, 1698, 1670 (sh), 1640 (sh), 1402, 1384, 1246, 1192, 1090, 754.

Enzymic Hydrolysis of Daturametelin B (I) A mixture of I (200 mg) and β-glucosidase (from almond, Sigma Co., Ltd.) in a solution of AcOH–AcONa buffer (pH 4.5) was incubated at 38 °C for 6 h. The products were purified by silica gel column chromatography to afford compound **6** (9.7 mg) together with the starting material.

Daturametelin D (2) Colorless needles from $CHCl_3$–MeOH, mp 199.5—201.5 °C. $[\alpha]_D^{26}$ −90.6° (c=0.68, $CHCl_3$). EI-MS *m/z*: 468 (M^+), 436, 423, 386, 365, 268, 267, 253, 227, 225, 173, 171, 159, 155, 147, 145, 143, 135, 133, 131, 129, 122, 121, 107, 105. IR ν_{max}^{KBr} cm^{-1}: 1728, 1682, 1664, 1466, 1384, 1352, 1300, 1234, 1172, 1058.

Daturametelin G-Ac (3) An amorphous powder, $[\alpha]_D^{27}$ −48.4° (c=0.42, $CHCl_3$).

Daturametelin F (4) An amorphous powder, $[\alpha]_D^{20}$ +5.0° (c=0.42, pyridine). Neg. FAB-MS *m/z*: 533 $(M-H)^-$. EI-MS *m/z*: 436 $(M^+ - HO_3SOH)$, 408, 354, 331, 313, 262, 239, 237. IR ν_{max}^{KBr} cm^{-1}: 3468, 1716, 1626, 1386, 1226.

Solvolysis of 4 A solution of **4** (5 mg) in pyridine–dioxane (4:1, v/v, 1.5 ml) was heated on a water bath at 80 °C for 5 h. The reaction mixture was evaporated to dryness *in vacuo* and the residue was subjected to preparative thin layer chromatography on silica gel (solvent, *n*-hexane:acetone=2:1, v/v) to afford a hydrolysate **7** (1 mg).

Treatment of 4 with Acetic Anhydride and Pyridine A solution of **4** (7 mg) in pyridine–acetic anhydride (4:3, v/v, 3 ml) was heated on a water bath at 80 °C for 2 h and the reaction mixture was chromatographed on silica gel (*n*-hexane:EtOAc=3:1, v/v) to afford a compound identical with II (1.1 mg). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, s, H_3-18), 1.22 (3H, s, H_3-19), 1.57 (3H, s, H_3-28), 2.82 (1H, dd, J=5.3, 20.6 Hz, H-4), 3.29 (1H, br d, J=21.6 Hz, H′-4), 3.73 (1H, dd, J=3.1, 13.4 Hz, H-21), 3.93 (1H, d, J=13.2 Hz, H′-21), 4.65 (1H, br s, H-22), 5.57 (1H, d, J=6.2 Hz, H-6), 5.87 (1H, dd, J=1.8, 9.9 Hz, H-2), 6.02 (1H, s, H-27), 6.76 (1H, s, H′-27), 6.78 (1H, m, H-3).

Daturametelin E (5) An amorphous powder, $[\alpha]_D^{28}$ +25.8° (c=0.69, MeOH).

Acknowledgements We would like to express our thanks to Dr. Y. Ida, School of Pharmaceutical Sciences, Showa University, for his valuable advice.

References and Notes

1) Part XIII: S. Yahara, M. Ohtsuka, K. Nakano and T. Nohara, *Chem. Pharm. Bull.*, **37**, 1802 (1989).
2) K. Shingu, T. Kajimoto, Y. Furusawa and T. Nohara, *Chem. Pharm. Bull.*, **35**, 4359 (1987).
3) Y. Oshima, A. Bagchi, H. Hikino, S. C. Sinha, M. Shahai and A. B. Ray, *Tetrahedron Lett.*, **26**, 1852 (1987).
4) S. Siddiqui, N. Sultana, S. S. Ahmad and S. I. Haider, *Phytochemistry*, **26**, 2641 (1987).
5) T. Mahmood, S. S. Ahmad and S. Siddiqui, *Heterocycles*, **27**, 101 (1988).
6) T. Mahmood, S. S. Ahmad and A. Fazal, *Planta Medica*, **54**, 468 (1988).
7) I. Kitagawa, M. Kobayasi and T. Sugawara, *Chem. Pharm. Bull.*, **26**, 1852 (1978).
8) I. Kitagawa and M. Kobayashi, *Chem. Pharm. Bull.*, **26**, 1864 (1978).
9) *a*) D. P. Burma, *Anal. Chim. Acta*, **9**, 513 (1953); *b*) J. J. Schneider and M. L. Lewbart, *J. Biol. Chem.*, **222**, 787 (1956).
10) E. Glotter, I. Kirson, D. Lavie and A. Abraham, "Bioorganic Chemistry," ed. by E. E. van Tamelen, Academic Press, New York, 1978, Vol. II, pp. 57—95.