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CHEMICAL STUDIES ON NITROGEN HETEROCYCLIC SKELETON OF THE DAPHNIPHYLLUM ALKALOIDS

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Abstract—From a biogenetic point of view, a great variety of related alkaloids isolated from the plant *Daphniphyllaceae* are related to one another by bond formation or fission. Thus, daphnialcohol acetate (**6**), a derivative of the degradation products of daphniphylline (**1**), was subjected to von Braun degradation followed by acid-catalyzed recyclization to give an isomer (**8**) of daphnialcohol, which has a new type of nitrogen heterocyclic skeleton. Furthermore, daphnilactone-B (**3**) was converted into a daphniphylline-type compound (**19**) *via* a plausible intermediate (**21**).

The plant *Diphniphyllum macropodum* Miquel (Yuzuriha in Japanese) contains a great variety of related alkaloids, that are structurally divided into five types of nitrogen heterocyclic skeleton.[1] In particular, daphniphylline (**1**) and yuzurimine (**2**) both have been isolated as main products from the bark and leaves of the same plant.[2] Of two main groups represented by **1** and **2**, the yuzurimine group of alkaloids seem to be produced at a rather later stage in the biosynthesis of the daphniphyllum alkaloids.[3] On the other hand, daphnilactone-B (**3**) is only one main alkaloid isolated from the fruits of the plant *Daphniphyllum teijsmanni* Zollinger as well as *Daphniphyllum macropodum* Miquel.[4] From a biogenetic point of view, this alkaloid is regarded as an intermediate between daphniphylline-type and yuzurimine-type alkaloids. Furthermore, two other possible intermediates (**4** and **5**) are considered, both of which have an iso-propyl group. In the present paper, we wish to describe some important reactions concerning with nitrogen heterocyclic skeleton of these alkaloids in connection with their biogenesis as well as synthetic studies.

Daphniphylline (**1**) affords daphnialcohol acetate (**6**).[2] When treated with excess amounts of BrCN in dry benzene at room temperature for 2 days, **6** gave rise to a cyanamide (**7**; m.p. 141–143°; $C_{24}H_{36}O_2N_2$), the IR spectrum of which indicated the presence of a N–CN group (ν_{max} 2240 cm^{-1}), in 46% yield. In particular, the NMR spectrum of **7** has a broad signal at δ 5·58 (1H, br.m, Wh = 14 Hz), indicating that the newly formed tri-substituted double bond should be included in the 7-membered ring but not in the 5-membered ring. The von Braun degradation product (**7**) so far obtained was subjected to acid-catalyzed cyclization reactions under various conditions.

When heated in 6N HCl–MeOH (1:1) under reflux for 8·5 hr, **7** was converted into a new amine (**8**, m.p. 230–235°) (dec) as hydrochloride; $C_{21}H_{35}ON$ (*m/e* 317 (M^+)) in 55% yield, which was not identical with daphnialcohol (**9**). The spectral data of this base, particularly, the NMR spectrum, has no signal corresponding to an olefinic proton, but has complex signals in the region of δ 2·8–3·9 due to six protons attached to the N and O atoms. In the above reaction, acid-catalyzed intramolecular addition of an amino group, which must be formed from the N–CN group on acid hydrolysis, to the tri-substituted double bond in a possible intermediate (**10**) takes place in a manner of an anti-Markownikoff's rule. It is evident from a molecular model of **10** that steric factors operate more favourably than electronic factors in this case. This amine (**8**) with a new nitrogen heterocyclic skeleton was readily reconverted into the cyanamide (**7**) by von Braun degradation followed by acetylation with Ac_2O-pyridine. To date, a secondary amine as **11**,[5] which must be used for biogenetic type reactions, has not yet been obtained. Therefore, further studies have been carried out using daphnilactone-B (**3**)[4] which is regarded as one of the important intermediates between two main groups represented by daphniphylline (**1**) and yuzurimine (**2**), as follows.

Von Braun degradation of daphnilactone-B (**3**) with $BrCN–K_2CO_3$ in dry benzene afforded a bromocyanamide (**12**, m.p. 210° (dec);

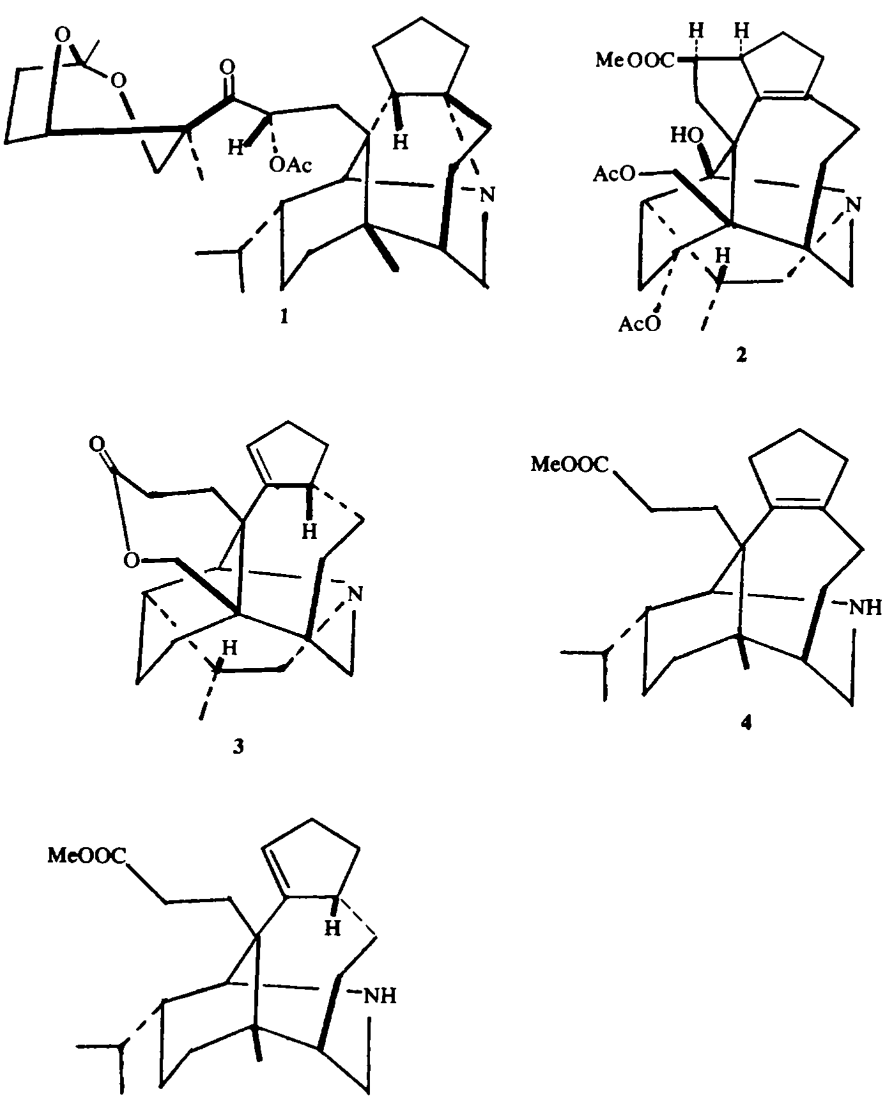
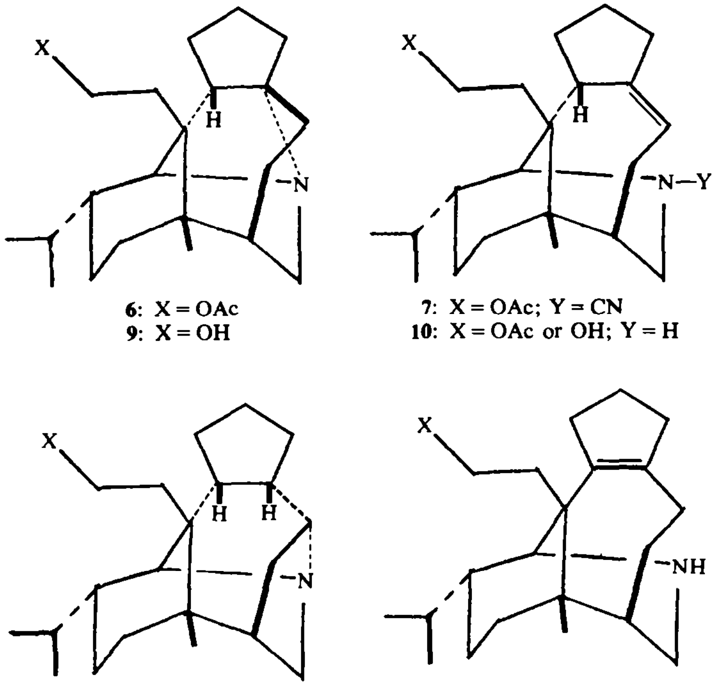


Fig 1.

$C_{23}H_{31}O_2N_2Br$) in 90% yield. Of two possible structures (**12** and **13**), which can be considered from the spectral data (ν_{max} 2240 cm^{-1} (CN) and δ 3·58 (2H, br.) due to a $-CH_2Br$ grouping), the former should be given to the von Braun degradation product on the basis of the following evidence. When treated with AgF in pyridine (room temp, 3 days), the bromocyanamide afforded an olefin (**14**, m.p. 198–200°; $C_{23}H_{30}O_2N_2$; ν_{max} 1645 cm^{-1}), whose NMR spectrum indicated the presence of $\text{Me–}\underset{|}{\text{C}}\text{=CH}_2$ grouping (δ 1·92 (3H, s), 4·96 (1H, br.s) and 5·10 (1H, br.s)). Further treatment of **14** with OsO_4 in pyridine gave a glycol (**15**), which was further treated with $NaIO_4$ to afford in good yields an oxidation product with a newly formed acetyl group (**16**, m.p. 245·5–246°; $C_{22}H_{28}O_3N_2$); ν_{max} 1720 cm^{-1} and δ 2·32 (3H, s)). A series of the above degradation reactions have been used for biosynthetic studies on daphnilactone-B (**3**).[6] Thus, the bromocyanamide (**12**) was reduced with slightly excess amounts of $NaBH_4$ to the corresponding debromocyanamide (**17**, m.p. 208–212°; $C_{23}H_{32}O_2N_2$; ν_{max} 2240 and 1735 cm^{-1}) in 50% yield.[7] However, reduction of **12** with large amounts of the same reagent afforded a diol (**18**, m.p. 200–201°; $C_{23}H_{36}O_2N_2$: ν_{max} 3340 br. and 2210 cm^{-1}) in quite high yields. In this case, the lactone grouping can be reduced quite easily, but the N–CN grouping is stable. Finally, when treated with 90% HCOOH, **17** afforded a daphniphylline-type compound (**19**, m.p. 166–168°; $C_{22}H_{33}O_2N$) in 55% yield, whose structure was con-



6: X = OAc
9: X = OH

7: X = OAc; Y = CN
10: X = OAc or OH; Y = H

8

11: X = OAc or OH

Fig 2.

firmed by its IR and NMR spectral data (ν_{max} 1730 cm^{-1}) and no NH group; δ 2·50–2·90 (4H, complex)* and 3·38 (1H, br.d, J = 12·5 Hz)) coupled with von Braun degradation of **19**, as follows. **19** reacted with BrCN–K_2CO_3 to give a new cyanamide (**20**, m.p. 233–235°; $C_{23}H_{32}O_2N_2$; ν_{max} 2240 and 1735 cm^{-1}), an isomer of **17**. The structure of this von Braun degradation product (**20**) is supported by its NMR spectrum, indicating the presence of the $H_2C\text{–}N(CN)\text{–}\underset{|}{C}H\text{–}$ grouping (δ 3·20 (1H, br.d, J = 14·0 Hz), 3·28 (1H, d, J = *ca* 2·0 Hz) and 4·12 (1H, q, J = 14·0, 7·0 Hz)) and a tri-substituted double bond (δ 5·72 (1H, br.m, Wh = 15 Hz)), which should be included in the 7-membered ring as found in the case of **7**.

In the course of the above isomerizations, a secondary amine (**21**) must be a possible intermediate, from which the daphniphylline-type compound (**20**) can be formed by protonation at the tetra-substituted double bond followed by simultaneous participation of the secondary amino group which must be produced by acid hydrolysis of the N–CN grouping in **17**.

Chemical studies on daphniphylline (**1**) as well as on daphnilactone-B (**3**) are further in progress in connection with synthetic studies on the daphniphyllum alkaloids.

EXPERIMENTAL

All m.ps were uncorrected. The IR spectra were recorded on a JASCO IR-S spectrophotometer. The NMR spectra were taken on a Nihondenshi JNM-C 60H (60 Mc) or a Varian A-60 NMR spectrometer (60 Mc) using $CDCl_3$ as solvent, unless otherwise stated. Chemical shifts are given in ppm relative to internal TMS. Coupling constants are also given in Hz (d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet). The mass spectra were obtained on a Hitachi RMU-6C mass spectrometer operating with an ionization energy of 70 eV. Column chromatography was carried out on basic alumina (Nakarai Chemical Co. Ltd., *ca* 300 mesh) or on silicic acid (Mallinckrodt, 100 mesh). TLC was performed on silica gel GF_{254} (E. Merck, A. G., Germany) using n-hexane-ether-Et_2NH, n-hexane-Et_2NH or ether-Et_2NH as solvent system.

Von Braun degradation of daphnialcohol acetate (**6**). To a soln of daphnialcohol acetate (470 mg)[2] in dry benzene (5 ml) was added a soln of BrCN (275 mg) in dry benzene (5 ml) at room temp, and then the resulting soln was stirred at room temp for 2 days. The soln was neutralized with $NaHCO_3$ aq, and then extracted with large amounts of $CHCl_3$. The extracts were washed with water, and then dried over Na_2SO_4. Removal of the solvent under reduced pressure gave an oil, which was separated by preparative TLC using n-hexane-Et_2NH (100:0·5) to give two fractions. From the more polar fraction, a white solid of a cyanamide **7** (229 mg) was obtained, m.p. 141–143° (from ligroin-ether); ν_{max} ($CHCl_3$) 2240 and

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*The signals corresponding to two protons attached to the C atoms bearing the N atom are shifted to lower field in the NMR spectrum of the hydrochloride.

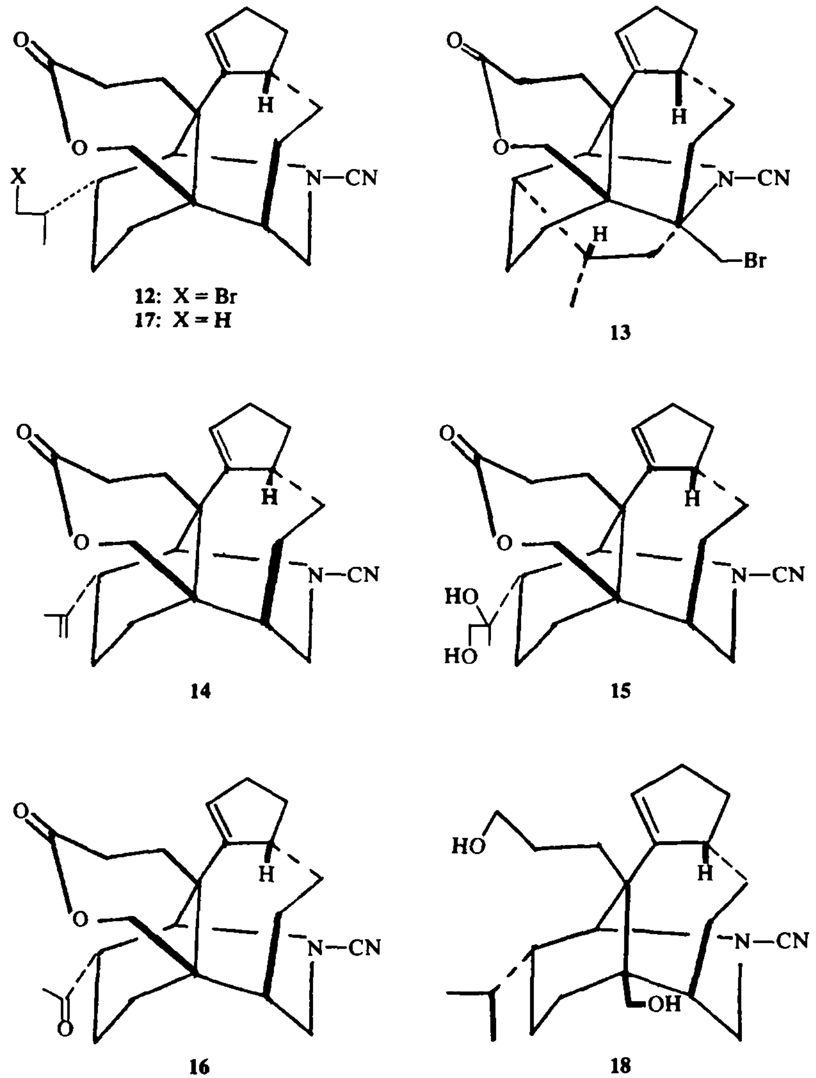
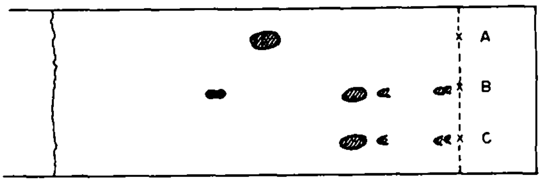


Fig 3.

1745 cm^{-1}; δ 0·95 (3H, d, J = 6·5 Hz), 1·06 (3H, d, J = 6·5 Hz), 1·12 (3H, s), 2·07 (3H, s), 2·97 (1H, d, J = 13·0 Hz), 3·46 (1H, br.s), 3·73–4·65 (3H, m) and 5·58 (1H, br.m, Wh = 14 Hz); *m/e* 384 (M^+), 369, 357, 341, 325, 311, 297 and 242 (Found: C, 75·17; H, 9·72; N, 7·38. $C_{24}H_{36}O_2N_2$ requires: C, 74·96; H, 9·44; N, 7·29%).

Cyclization of 7 *to an isomer* (8) *of daphnialcohol.* (i) 7 (70 mg) was dissolved in 6N HCl-MeOH (1:1) (7 ml), and then the resulting soln was heated under reflux for 8·5 hr. The soln was neutralized with $NaHCO_3$ aq, and then extracted with $CHCl_3$. The extracts were washed with water, and then dried over Na_2SO_4. The solvent was removed under reduced pressure to leave an oil, which was purified by preparative TLC using a mixed solvent (n-hexane - ether - Et_2NH (20:20:1·5)) to give an isomer (8) of daphnialcohol (32 mg), m.p. 230–235° (dec) (as hydrochloride) (from $CHCl_3$-ligroin' ν_{max} (film) 3400 br and 2600 br cm^{-1}; δ 0·88 (3H, s), 0·93 (3H, d, J = 6·0 Hz), 1·06 (3H, d, J = 6·0 Hz), 2·8–3·3 (3H, complex) and 3·6–3·9 (3H, complex); *m/e* 317 (M^+), 302, 286, 272, 234 and 231 (Found: C, 69·64; H, 10·29; N, 4·05. $C_{21}H_{35}ON \cdot HCl$ 1/2 H_2O requires: C, 69·20; H, 10·28; N, 3·86%).

(ii) A soln of 7 (25 mg) *in conc* H_2SO_4-H_2O (6·7:37) (2 ml) was heated under reflux for 2 hr, and then the soln was treated according to the above procedure to give an oil, the analytical TLC of which showed essentially the same pattern as found in the experiment (i), as shown below. TLC of the mixture on silica gel in n-hexane - ether - Et_2NH (20:20:1·5). A: The starting material (7); B: Experiment (i); C: Experiment (ii).



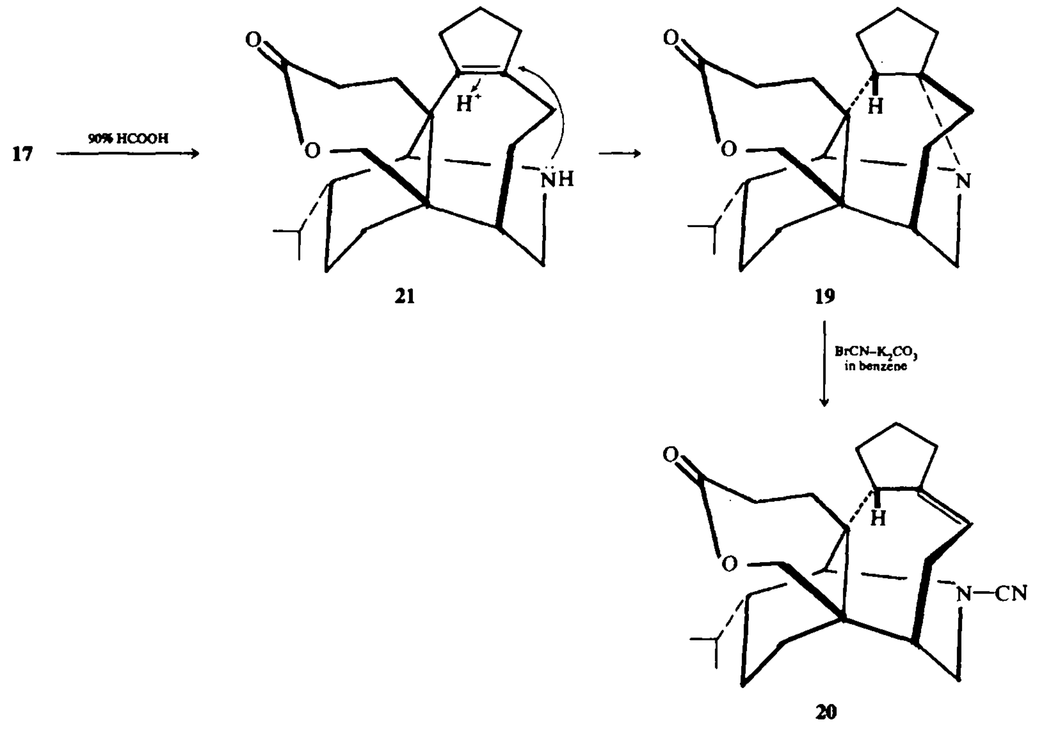


Fig 4.

Reconversion of **8** *to the cyanamide* (**7**). To a soln of **8** (10 mg) in $CHCl_3$ (1 ml) was added excess BrCN in $CHCl_3$ (1 ml), and then the resulting soln was stirred at room temp for 18 hr. The solution was neutralized with $NaHCO_3$ aq, and extracted with $CHCl_3$. The extracts were washed with water, and then dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded an oil, the preparative TLC of which gave two fractions (in n-hexane - ether - Et_2NH (20:20:1·5)). From the less polar fraction, the starting material **8** (6 mg) was obtained (IR spectrum and TLC). On the other hand, a colourless oil (*ca* 3·5 mg) was obtained from the remaining fraction. This oil was directly dissolved in Ac_2O-pyridine (1:2) (1 ml). The resulting soln was allowed to stand at room temp for 3 hr, and then concentrated under reduced pressure to give the known cyanamide **7** (*ca* 3·5 mg) (IR spectrum and TLC).

Von Braun degradation of daphnilactone-B (**3**). To a soln of daphnilactone-B (300 mg) in dry benzene (2 ml) was added a soln of BrCN (1·5 g) in dry benzene (4 ml) which was freshly prepared and passed through anhyd K_2CO_3 column before using, and then further anhyd K_2CO_3 (150 mg) was added. The mixture was stirred at room temp overnight, and then filtered. The filtrates were dissolved in benzene (*ca* 50 ml). The soln was washed successively with a lot of water and sat NaCl aq, and then dried over $MgSO_4$. The solvent was removed under reduced pressure to give white crystals which were recrystallized from n-hexane - benzene to afford colourless plates **12** (341 mg), m.p. 210°(dec); ν_{max} ($CHCl_3$) 2240 and 1735 cm^{-1}; δ 1·20 (3H, d, J = 6·0 Hz), 3·09 (1H, d, J = 13·5 Hz), 3·38 (1H, br.s), 3·58 (2H, complex), 3·70 (1H, d, J = 12·5 Hz), 4·06 (1H, q, J = 13·5, 7·5 Hz), 4·85 (1H, d, J = 12·5 Hz) and 5·87 (1H, br.s, Wh = 6·0 Hz); *m/e* 448 and 446 (M^+), 367 and 325 (Found: C, 62·24; H, 6·65; N, 6·65. $C_{23}H_{31}O_2N_2Br$ requires: C, 61·74; H, 6·98; N, 6·26%).

Dehydrobromination of **12** *with* AgF-*pyridine*. To a soln of **12** (60 mg) in dry pyridine (2 ml) was added anhyd AgF (100 mg) in one portion. The mixture, which was protected from light, was stirred at room temp for 3 days, and then poured into water and extracted with large amounts of ether. The ethereal extracts were washed successively with dil HCl aq, water, dil NaOH aq, water and sat NaCl aq, and then dried over $MgSO_4$. Removal of the solvent under reduced pressure afforded white crystals, which were recrystallized from n-hexane-benzene to give colourless needles of **14** (35 mg), m.p. 198-200°; ν_{max} ($CHCl_3$) 2240, 1735 and 1645 cm^{-1}; δ 1·92 (3H, s), 3·06 (1H, d, J = 13·5 Hz), 3·41 (1H, d, J = 3·0 Hz), 3·72 (1H, d, J = 13·0 Hz), 4·12 (1H, q, J = 13·5, 7·5 Hz), 4·87 (1H, d, J = 13·0 Hz), 4·96 (1H, br.s), 5·10 (1H, br.s) and 5·87 (1H, br.s); *m/e* 366 (M^+), 351, 335, 307 and 293 (Found: C, 75·59; H, 8·26; N, 7·83. $C_{23}H_{30}O_2N_2$ requires: C, 75·37 H, 8·25; N, 7·64%).

Oxidation of **14** *with* OsO_4. To a soln of **14** (116·5 mg) in dry pyridine (3 ml) was added a freshly prepared soln of OsO_4 (82 mg) in dry THF (4·1 ml) with stirring at room temp. In several mins the mixture was turned to dark brown and continuosly stirred at room temp overnight. To the mixture was added a soln of $NaHSO_3$ (750 mg) in water (*ca* 3 ml) with continuous stirring for 10 min (the colour of this solution turned to orange). Then, the soln was poured into water, and then extracted with large amounts of $CHCl_3$. The extracts were washed successively with dil HCl aq, dil $NaHCO_3$ aq, water and sat NaCl aq, and then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a colourless oil, which was chromatographed on silicic acid (1·4 g) using $CHCl_3$ as eluent. After a small amount of unknown oil was eluted with $CHCl_3$ (*ca* 100 ml), further elution with the same solvent gave a colourless oil of **15**, (108 mg); ν_{max} (film) 3360, 2190 and 1725 cm^{-1}; δ 1·28 (3H, s), 3·03 (1H, d, J = 14·0 Hz), 3·50 (2H, br.s), 3·65 (1H, d, J = 13·0 Hz), 3·70 (1H, br.s), 4·14 (1H, q, J = 14·0, 7·5 Hz), 4·83 (1H, d, J = 13·0 Hz) and 5·83 (1H, br.s); *m/e* 400 (M$^+$), 382, 357 and 339 (Found: *m/e* 400·2340. $C_{23}H_{32}O_4N_2$ requires: *m/e* 400·2362).

Oxidation of the glycol (**15**) *with* $NaIO_4$. To a soln of the glycol (50 mg) in freshly distilled dioxane (1 ml) was added a soln of $NaIO_4$ (50 mg) in distilled water (2 ml), and then the resulting soln was allowed to stand at room temp overnight with stirring. In the course of oxidation a white solid was precipitated. Water (30 ml) was added and then the ppt was collected by filtration. The ppt was dissolved in $CHCl_3$ and washed successively with water and sat NaCl aq, and then dried over $MgSO_4$. The solvent was removed under reduced pressure to give colourless needles of **16** (30 mg), m.p. 245·5–246° (from $CHCl_3$-benzene) ν_{max} (KBr) ν_{max} (KBr) 2190, 1730 and 1720 cm^{-1}; δ 2·32 (3H, s), 3·01 (1H, d, J = 14·0 Hz), 3·69 (1H, d, J = 13·0 Hz), 3·75 (1H, d, J = 3·0 Hz), 4·08 (1H, q, J = 14·0, 7·5 Hz), 4·80 (1H, d, J = 13·0 Hz) and 5·90 (1H, br.s); *m/e* 368 (M$^+$) and 325 (Found: C, 71·82; H, 7·55; N, 7·32. $C_{22}H_{28}O_3N_2$ requires: C, 71·71; H, 7·66; N, 7·60%).

$NaBH_4$ *Reduction of the bromo-cyanamide* (**12**). To a soln of **12** (254 mg) in anhyd DMSO (25 ml) was added a soln of $NaBH_4$ (40 mg) in anhyd DMSO (5 ml). The mixture was stirred at room temp overnight, and then poured into *ca* 30 ml cold water and extracted with a mixed solvent of n-hexane-EtOAc (1 : 1). The extracts were washed with water, and then dried over $MgSO_4$. The solvent was removed under reduced pressure to give an oil (235 mg), which was chromatographed on alumina (1 g). Elution with benzene gave a white solid, which was recrystallized from n-hexane-benzene to afford colourless needles of **17** (115 mg), m.p. 208–212°; ν_{max} ($CHCl_3$) 2240 and 1735 cm^{-1}; δ 0·98 (3H, d, J = 5·5 Hz), 1·06 (3H, d, J = 5·5 Hz), 3·05 (1H, br.d, J = 13·5 Hz), 3·41 (1H, br.s), 3·75 (1H, d, J = 13·0 Hz), 4·11 (1H, q, J = 13·5, 7·2 Hz), 4·85 (1H, d, J = 13·0 Hz) and 5·85 (1H, br.s, Wh = 5·4 Hz); *m/e* 368 (M$^+$), 355, 342, 340, 337, 326, 309, 295 and 285 (Found: C, 74·93; H, 8·65; N, 7·55. $C_{23}H_{32}O_2N_2$ requires: C, 74·96; H, 8·75; N, 7·60%).

Reduction of **12** *with large amounts of* $NaBH_4$. To a soln of **12** (100 mg) in anhyd DMSO (5 ml) was added $NaBH_4$ (100 mg). The mixture was stirred at room temp overnight, and then poured into water and extracted with a lot of $CHCl_3$. The extracts were washed successively with water and sat NaCl aq, and then dried over Na_2SO_4. The solvent was removed under reduced pressure to give an oil, which was chromatographed on alumina (1 g). Elution with benzene afforded colourless crystals (60 mg), which were recrystallized from EtOAc-$CHCl_3$ to give colourless needles of **18**, m.p. 200–201°; ν_{max} (Nujol) 3340 br. and 2210 cm^{-1}; δ 0·97 (3H, d, J = 5·6 Hz), 1·05 (3H, d, J = 5·6 Hz), 3·08 (1H, d, J = 14·0 Hz), 3·47–3·75 (4H, complex), 4·03 (1H, q, J = 14·0, 7·3 Hz), 4·15 (1H, d, J = 11·0 Hz) and 5·70 (1H, br.s); *m/e* 372 (M$^+$), 357, 355, 341, 329, 313, 303 and 289 (Found: C, 73·77; H, 10·18; N, 7·42. $C_{23}H_{36}O_2N_2$ requires: C, 74·15; H, 9·74; N, 7·52%).

Reaction of the debromocyanamide **17** *with 90%* HCOOH. A soln of **17** (100 mg) in 90% HCOOH (1 ml) was heated under reflux overnight, and then concentrated under reduced pressure to give a pale yellow oil. This oil was dissolved in water (*ca* 0·5 ml) and made basic with anhyd Na_2CO_3 (pH 9–10), and then extracted with a lot of benzene. The extracts were washed successively with water and sat NaCl aq, and then dried over $MgSO_4$. The solvent was removed under reduced pressure to afford white crystals, which were recrystallized from n-hexane-benzene to give colourless needles of a **19**, (50 mg); m.p. 166–168°; ν_{max} ($CHCl_3$) 1730 cm^{-1}; δ 0·92 (3H, d, J = 6·2 Hz), 1·00 (3H, d, J = 6·2 Hz), 2·5–2·9 (4H, complex), 3·38 (1H, br.d, J = 12·5 Hz), 3·52 (1H, d, J = 12·5 Hz) and 4·67 (1H, d, J = 12·5 Hz); *m/e* 343 (M$^+$), 328, 301, 284, 271, 266 and 228 (Found: C, 76·71; H, 9·91; N, 4·04. $C_{22}H_{33}O_2N$ requires: C, 76·92; H, 9·68; N, 4·08%).

Von Braun degradation of **19**. To a soln of **19** (47 mg) in dry benzene (1 ml) was added a soln of BrCN (*ca* 200 mg) in dry benzene (2 ml), which was passed through anhyd K_2CO_3 column before using, and further added anhyd K_2CO_3 (40 mg). Then, the mixture was stirred at room temp overnight, and then filtered. The filtrates were concentrated under reduced pressure ot give white crystals, which were dissolved in benzene (20 ml). The resulting soln was washed successively with water and sat NaCl aq, and then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a white solid, which was recrystallized from n-hexane-benzene to afford colourless needles of **20** (48 mg); m.p. 233–235°; ν_{max} ($CHCl_3$) 2240 and 1735 cm^{-1}; δ 0·98 (3H, d, J = 6·0 Hz), 1·06 (3H, d, J = 6·0 Hz), 3·02 (1H, br.d, J = 14·0 Hz), 3·28 (1H, d, J = 2·0 Hz), 3·70 (1H, d, J = 13·0 Hz), 4·12 (1H, q, J = 14·0, 7·0 Hz), 5·08 (1H, d, J = 13·0 Hz) and 5·72 (1H, br.m, Wh = 15 Hz); *m/e* 368 (M$^+$), 353, 325, 324, 309, 297 and 295 (Found: C, 74·46; H, 8·74; N, 7·72. $C_{23}H_{32}O_2N_2$ requires: C, 74·96; H, 8·75; N, 7·60%).

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REFERENCES

[1] M. Toda, H. Niwa, H. Irikawa, Y. Hirata and S. Yamamura, *Tetrahedron* **30**, 2683 (1974)

[2] H. Irikawa, N. Sakabe, S. Yamamura and Y. Hirata, *Ibid.* **24**, 5691 (1968)

[3] K. T. Suzuki, S. Okuda, H. Niwa, M. Toda, Y. Hirata and Yamamura, *Tetrahedron Letters* 799 (1973)

[4] H. Niwa, M. Toda, Y. Hirata and S. Yamamura, *Ibid.* 2697 (1972)

[5] M. Toda, Y. Hirata and S. Yamamura, *Tetrahedron* **28**, 1477 (1972); H. Irikawa, S. Yamamura and Y. Hirata, *Ibid.* **28**, 3727 (1972)

[6] H. Niwa, M. Toda, Y. Hirata, K. T. Suzuki and S. Yamamura, *Tetrahedron Letters* 2129 (1973)

[7] R. O. Hutchins, D. Hoke, J. Keogh and D. Koharski, *Ibid.* 3495 (1969)