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Isolation of Some New Tryptoquivaline-related Metabolites from *Aspergillus fumigatus*[1]

Mikio Yamazaki, Emi Okuyama, and Yukio Maebayashi

Research Institute for Chemobiodynamics, Chiba University[2]

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The structures of tryptoquivaline L, M and N, which were newly isolated from the fungus, *Aspergillus fumigatus*, have been elucidated as **1**, **3** and **11**, respectively. Concomitantly, the previously proposed structures of tryptoquivaline C (**9**) and D (**4**) have been revised to **10** and **8**. The exchange of the hydrogen on C-12 during epimerization of the dextrorotatory tryptoquivalines was demonstrated by means of a deuterium NMR spectral study.

Keywords——structure; tryptoquivaline; tryptoquivaline C; tryptoquivaline D; tryptoquivaline L; tryptoquivaline M; tryptoquivaline N; *Aspergillus fumigatus*; fungal metabolite

The isolation and structure elucidation of eight tryptoquivaline-related metabolites from *Aspergillus fumigatus*, tryptoquivalines C–J, have already been reported from our laboratory.[3,4] In this brief report, the structure elucidation of tryptoquivalines L, M and N, which have been newly isolated from the same fungus, is described. A revision of the structures of tryptoquivalines C and D is also presented.

Among the three newly isolated metabolites, tryptoquivaline L(FTL, **1**) was obtained as colorless leaflets, $C_{23}H_{20}N_4O_5$ (M^+ *m/e* 432.1457), mp 265—268°, $[\alpha]_D^{23}$ −229°. The spectral data for FTL (**1**) resemble those of the other tryptoquivalines, suggesting that FTL (**1**) is a tryptoquivaline-related compound. In the proton nuclear magnetic resonance (PMR) spectrum of FTL (**1**), a singlet due to the aromatic proton on C-26 appeared at 8.53 ppm, two singlets due to the methyl groups attached to C-15 appeared at 1.26 and 1.36 ppm, and a hydroxyl singlet appeared at 8.74 ppm (disappeared on addition of D_2O). These findings suggested that FTL (**1**) has a structure similar to that of tryptoquivaline G(FTG, **2**), $C_{23}H_{20}N_4O_5$ (M^+ *m/e* 432.1411), $[\alpha]_D^{11}$ +215° which appeared the signals of one aromatic

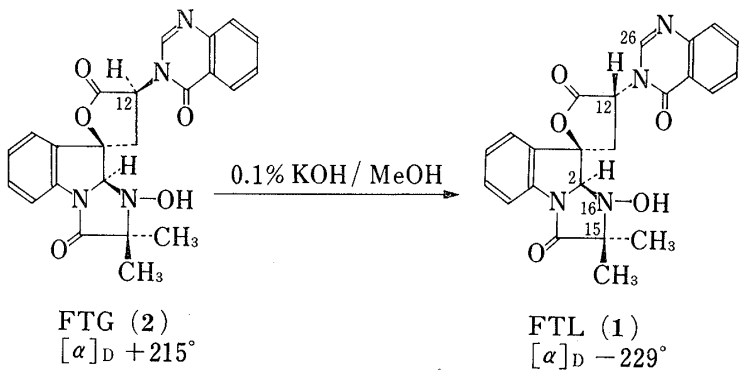


Fig. 1. Epimeric Conversion of FTG to FTL by Dilute Alkali

1) This study was reported in part at 98th Annual Meeting of the Pharmaceutical Society of Japan (Okayama, 1978).
2) Location: *1-8-1, Inohana, Chiba, 280, Japan.*
3) M. Yamazaki, H. Fujimoto, and E. Okuyama, *Chem. Pharm. Bull.* (Tokyo), **25**, 2554 (1977).
4) M. Yamazaki, H. Fujimoto, and E. Okuyama, *Chem. Pharm. Bull.* (Tokyo), **26**, 111 (1978).

proton, two methyl and one hydroxyl groups in the PMR spectrum.[4] FTG (**2**) was found to be converted to FTL (**1**), indicating that **1** is a stereoisomer of FTG (**2**).

Tryptoquivaline M (FTM, **3**) was obtained as colorless plates, $C_{28}H_{28}N_4O_7$ (M^+ *m/e* 532.1932), mp 157—164°, $[\alpha]_D^{24}$ −154°. The spectral data for FTM (**3**) were quite similar to those of tryptoquivaline D (FTD, **8**), $C_{28}H_{28}N_4O_7$, mp 224—225°, $[\alpha]_D^{28}$ +115°. All the signals in the PMR spectrum of FTD (**8**) were observed in the spectrum of FTM (**3**), although the chemical shifts of the protons attached to C-12 and 13 (γ-lactone) were slightly different from those of FTD. Since the optical rotation of FTM (**3**) was opposite to that of FTD (**8**), FTM (**3**) was supposed to be a stereoisomer of FTD. The revised structure of FTD (**8**) is used here, though it has been previously proposed to be **4**. The reasons for the revision will be discussed later (see Table I).

When FTD (**8**), which is dextrorotatory, was treated with 0.1% KOH in methanol, a desacetyl product (epidesacetyl-FTD, **5**) was obtained. This product (**5**) was levorotatory and was easily acetylated with acetic anhydride and acetic acid to afford a monoacetate (**6**), $C_{28}H_{28}N_4O_7$ (M^+ *m/e* 532), mp 135—139°, $[\alpha]_D^{23}$ −161°, and a diacetate (**7**), $C_{30}H_{30}N_4O_8$ (M^+ *m/e* 574), amorphous, $[\alpha]_D^{21}$ −148° (see Chart 1). The monoacetate (**6**) was first supposed to be identical with FTM, *i-e.* a diastereoisomer of FTD. However, direct comparison of **6** with FTM (**3**) indicated that these two compounds were not identical, whereas the diacetate (**7**) was identical with FTM-acetate, which was obtained from FTM itself on acetylation.

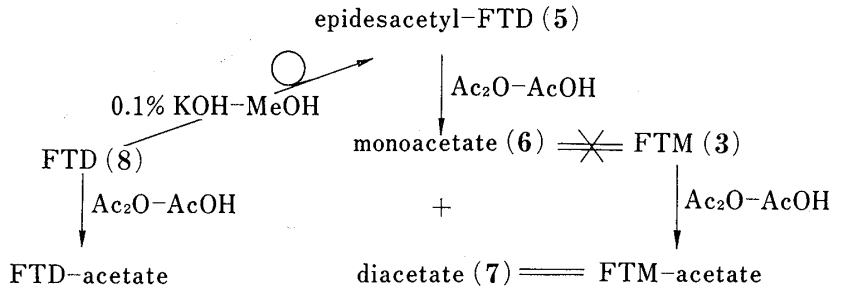
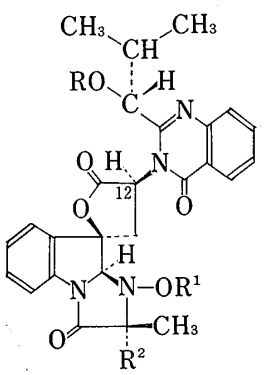
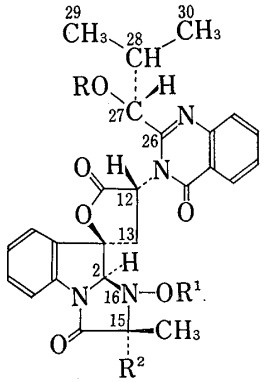


Chart 1



	R	R^1	R^2
FTD=nortryptoquivaline[6] (**8**):	Ac	H	H
FTD-acetate :	Ac	Ac	H
FTC=tryptoquivaline[5] (**10**):	Ac	H	CH_3
FTC-acetate :	Ac	Ac	CH_3



	R	R^1	R^2
epidesacetyl-FTD (**5**):	H	H	H
epidesacetyl-FTD-monoacetate (**6**) :	H	Ac	H
epidesacetyl-FTD-diacetate (**7**) :	Ac	Ac	H
FTM (**3**) :	Ac	H	H
FTM-acetate :	Ac	Ac	H
epidesacetyl-FTC-diacetate :	Ac	Ac	CH_3

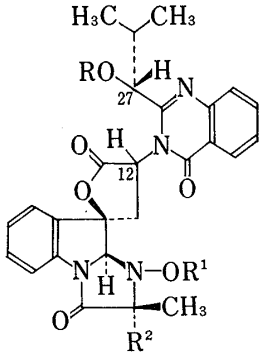
Fig. 2. Structures of FTC, FTD and Their Epimeric Derivatives

In the PMR spectrum of the monoacetate (**6**), a broad signal of the methine proton attached to C-27 was observed at 4.86 ppm. A coupling of the signal to the signals of C(27)–OH at 4.40 ppm and C(28)–H at 2.20 ppm was observed. On D_2O treatment, the signal of the hydroxyl proton at 4.40 ppm disappeared, and sharpening of the broad signal of C(27)–H occurred. Accordingly, it is suggested that the hydroxyl group attached to C-27 might be free and the hydroxyl attached to the nitrogen atom (N-16) might be acetylated. The structure of the monoacetate of epidesacetyl-FTD was therefore proposed to be **6**.

Table I lists the chemical shifts of the methine protons attached to C-27 of some FTD-related compounds. The signals of C(27)–H, were observed around 5.50 ppm when the hydroxyl group on C-27 was acetylated (*e.g.*, in FTD-acetate, epidesacetyl-FTD-diacetate (**7**), FTM-acetate). On the other hand, the signals were shifted to around 4.8 ppm when the hydroxyl group was free (*e.g.*, in epidesacetyl-FTD-monoacetate (**6**), epidesacetyl-FTC).

Table I. PMR Spectral Data for C(27)-H of FTD–related Compounds

	Structure			Chemical shift ppm (coupling const. Hz)
	R	R^1	R^2	
FTD (incorrect, **4**)	H	Ac	H	——
FTD (revised, **8**)	Ac	H	H	5.61 (doublet, 9)
FTD–acetate	Ac	Ac	H	5.50 (doublet, 9)
Epidesacetyl–FTD monoacetate (**6**)	H	Ac	H	4.86 (br. doublet, 4)
Epidesacetyl–FTD diacetate (**7**)	Ac	Ac	H	5.65 (doublet, 9)
FTM (**3**)	Ac	H	H	5.54 (doublet, 10)
FTM–acetate	Ac	Ac	H	5.65 (doublet, 9)
FTC (incorrect, **9**)	H	Ac	CH_3	——
FTC (revised, **10**)=tryptoquivaline	Ac	H	CH_3	5.59 (doublet, 9)
Epidesacetyl–FTC	H	H	CH_3	4.60 (doublet, 4)



The hydroxyl group on C-27 of FTM (**3**) should therefore be acetylated (a doublet of C(27)–H appeared at 5.54 ppm) and the structure of FTM should be **3**, *i.e.*, an isomer of the monoacetate (**6**) of epidesacetyl-FTD with regard to the position of the acetyl group (see Chart 1). Thus, the structure of FTD (**4**) proposed previously[3] seemed to be in conflict with the PMR data (a doublet of C(27)–H appeared at 5.61 ppm). The position of the acetoxyl group should be at position-27 in FTD, and the structure of FTD should thus be revised to **8**.

As reported previously,[3] tryptoquivaline C(FTC, **9**) was isolated together with FTD (**8**), and the structure **9** for FTC was proposed at the same time by analogy with that of FTD. FTD was postulated to be a nor-derivative of FTC from the basis of the spectral data. FTC was thought to have a structure analogous to that of tryptoquivaline (**10**), which is a tremorgenic toxin isolated from the fungus, *Aspergillus clavatus*. The structure of tryptoquivaline (**10**) was determined by x-ray analysis of the methanolysis product obtained from **10** by

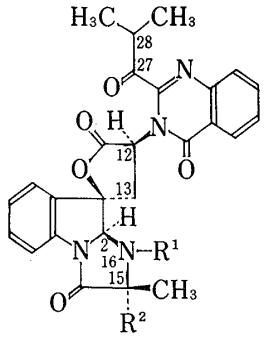
Clardy *et al.*[5] The physicochemical properties of FTC are very similar to those of tryptoquivaline (**10**), although they are not entirely identical, as shown in Table II. However the acetates derived from both FTC and tryptoquivaline (**10**) were found to be identical in direct comparison. FTC was thus assumed to be an isomer of **10** with regard to the position of the acetyl group, although the PMR data for C(27)–H were in conflict with our conclusion (a doublet appeared at 5.61 ppm in the spectrum of FTC) at the time.

Table II. Comparison of Physicochemical Properties of FTC and Tryptoquivaline

	FTC[a]	Tryptoquivaline[b]
mp	215—217° (decomp)[c] (recryst. from MeOH)	153—155° (recryst. from hexane–CH_2Cl_2)
$[\alpha]_D$	+168° ($CHCl_3$)	+142° ($CHCl_3$)
PMR δ ppm in $CDCl_3$	3.03 (1H, dd, 14, 10), 3.20 (1H, dd, 14, 10), 2.67 (1H, m), 4.99 (1H, s), 5.59 (1H, d, 9), 5.67 (1H, t, 10), 7.33—7.93 (7H, m), 8.22 (1H, d, 8), 7.08 (1H, s, disappeared with D_2O)	3.10 (1H, d, 10), 3.15 (1H, d, 10), 2.63 (1H, m), 5.00 (1H, s), 5.61 (1H, d, 9), 5.70 (1H, t, 10), 7.12—7.90 (7H, m), 8.22 (1H, d, 8), 3.63 (1H, br), 4.04 (1H, br)

a) M. Yamazaki *et al.*, *Tetrahedron Lett.*, **1976**, 2861.
b) J. Clardy *et al.*, *J. Am. Chem. Soc.*, **97**, 663 (1975).
c) When recrystallized from hexane–CH_2Cl_2, mp 231—232°.

It may be concluded now that the proposed structure of FTC (**9**) is incorrect and should be revised to **10**, in the same way as for FTD. Direct comparison of FTC with a sample of tryptoquivaline (**10**) provided by Prof.Büchi, however, has not clearly confirmed their identity. However, FTD was completely identical with nortryptoquivaline (**8**) provided by Prof.Büchi. The reason for the difference observed between FTC and tryptoquivaline (**10**) is not clear.



	R^1	R^2
FTN (**11**):	H	H
FTI (**12**):	OH	CH_3

Fig. 3. The Structures of FTN (**11**) and I (**12**)

Tryptoquivaline N(FTN, **11**), $C_{26}H_{24}N_4O_5$ (M^+ *m/e* 472), mp 193—197°, $[\alpha]_D^{23}$ +127°, showed an ultraviolet (UV) spectrum different from those of other tryptoquivaline-related compounds but similar to that of tryptoquivaline I(FTI, **12**).[4]

In the PMR spectrum of FTN (**11**) in $CDCl_3$, two doublets of the methyl protons (C-29 and 30) at 1.26 and 1.30 ppm (3H, doublet, J=7 Hz) and a multiplet of the methine proton (C-28) at 4.08 ppm (1H, multiplet) appeared. The chemical shift of the signal at 4.08 ppm seemed to be lowered by about 1.5 ppm in comparison with those of the other compounds. This finding indicates that a carbonyl group may be present at position 27 in the side chain of FTN (**11**), as in FTI (**12**) (Fig. 3). The appearance of a methyl doublet at 1.55 ppm (3H, doublet, J=7 Hz) and a methine quartet at 4.12 ppm (1H, quartet, J=7 Hz) in the PMR spectrum of FTN (**11**) indicated the presence of only one methyl group at position 15 in this compound. A signal at 3.05 ppm (1H, br.singlet), which disappeared on treatment with D_2O, was assigned to N(16)–H. This signal shifted to 3.78 ppm in the spectrum in DMSO-d_6,

5) J. Clardy, J.P. Springer, G. Büchi, K. Matsuo, and R. Wightman, *J. Am. Chem. Soc.*, **97**, 663 (1975).

and on irradiation of this signal, sharpening of the broad doublet of the methine proton attached to C-2(1H, br.doublet, $J=7$ Hz) at 5.45 ppm was observed. The structure of FTN was thus proposed to be **11**. It was comfirmed subsequently that FTN (**11**) was identical with deoxynortryptoquivalone, which was recently isolated from *Aspergillus clavatus* by Büchi *et al.*[6]

The structures of the eleven tryptoquivaline-related metabolites from *Aspergillus fumigatus* have thus all been elucidated. Among them, tryptoquivalines C, D, E, G, I, J and N are dextrorotatory, and F, H, L and M are levorotatory. We have found that FTF, H, and L are the stereoisomers of J, E and G, respectively and each of the former can be derived from the corresponding latter isomer by treatment with diluted alkali.[4] We have also demonstrated that FTC affords a deacetylated epimer by the same treatment.[3]

When FTD (**8**) was treated with 0.1%KOH in deuteriomethanol, a desacetyl product labeled with deuterium was obtained. This product was levorotatory, and was acetylated to afford a diacetate (**13**), $C_{30}DH_{29}N_4O_8$ (M^+ *m/e* 575). In the PMR spectrum of the diacetate (**13**), no signal assignable to the methine proton on C-12 was observed. On the other hand, in the deuterium NMR spectrum of this compound (**13**), an intense signal of deuterium at C-12 was observed at 6.26 ppm, as shown in Fig. 4. These findings indicate that an exchange of the hydrogen attached to C-12 may occur on epimerization of FTD with alkali.

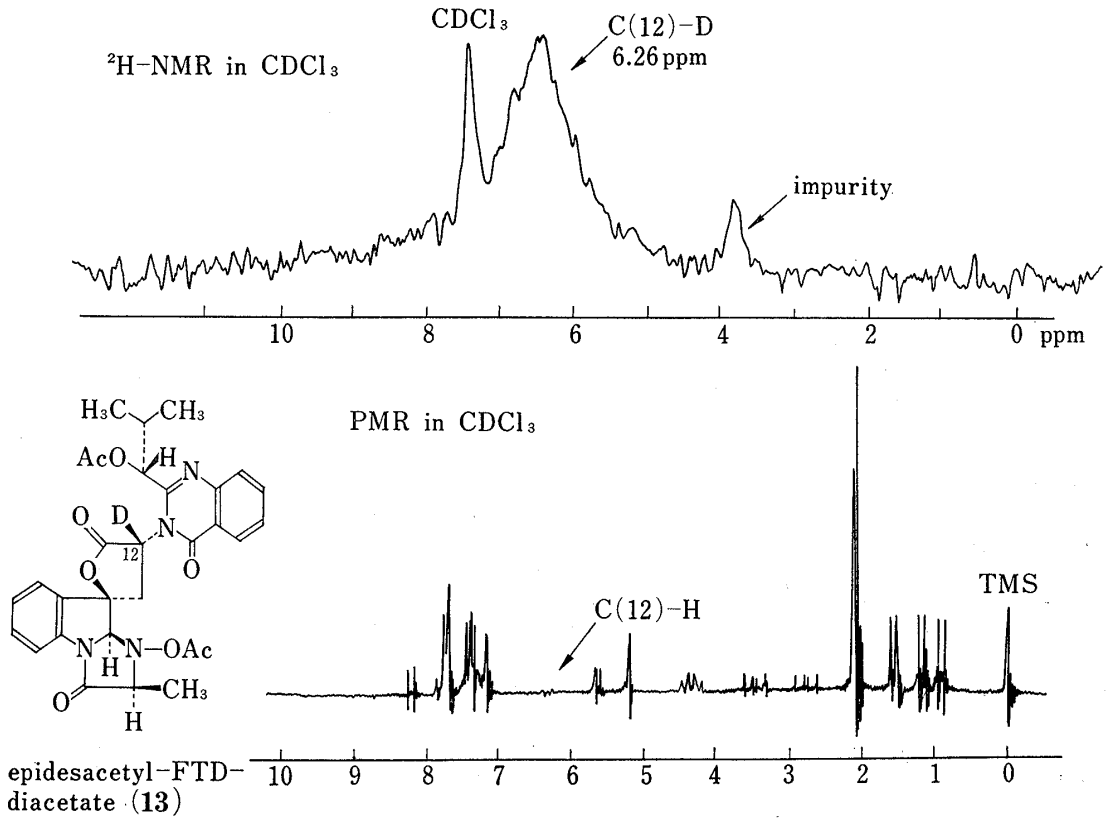


Fig. 4. PMR and ^{2}H-NMR Spectra of Epidesacetyl-FTD-diacetate

The configuration at C-12 in FTM (**3**) and epidesacetyl-FTD (**5**) should be *R*, since an *S*-configuration at C-12 in FTD has already been demonstrated.[3] It may therefore be concluded that the configuration at C-12 of FTG (**2**), which is dextrorotatory, should be *S* and that of FTL (**1**), which is levorotatory, should be *R*. In the PMR spectra of the levorotatory compounds, a slight change of the pattern of ABX-type signals of $-CH_2-CH$ (C-12 and 13) was observed, probably due to the change of configuration on C-12.

6) G. Büchi, K.C. Luk, B. Kobbe, and J.M. Townsend, *J. Org. Chem.*, **42**, 244 (1977).

Experimental

All melting points are uncorrected. Optical rotation was measured on a Yanagimoto Or-50 automatic polarimeter. UV, IR and NMR spectra were measured with Hitachi 323, Hitachi EPI-G3, and JEOL JNM PS-100 machines, respectively (chemical shifts are shown in ppm from Me_4Si added as an internal standard). Mass spectra were measured on a JEOL JMS OlSG-2 macine equipped with a JMA 2000 mass data analysis system, and ORD with a JASCO ORD/CD J-20 unit. The plates used for thin-layer chromatography were coated with Merck Kieselgel GF_{254} (0.25 mm thickness).

Isolation of Tryptoquivalines L (FTL, 1), M (FTM, 3) and N (FTN, 11)——The residual extract of *Aspergillus fumigatus* IFM 4482, from which the eight tryptoquivalines, FTC to J, had previously been isolated, was further chromatographed on a column of silica gel (Wakogel C-200) packed with benzene. FTL (1) and N (11) were obtained from the fraction eluted with benzene–acetone (30: 1) and M (3) was obtained from the fraction eluted with $CHCl_3$ by subsequent purification using preparative TLC.

FTL (1), (0.058% yield): Colorless leaflets (from acetone), $C_{23}H_{20}N_4O_5$ (M^+ *m/e* 432.1457, Calcd. 432.1434), mp 265—268°, $[\alpha]_D^{23}$ −229° (*c*=0.03, DMSO). UV λ_{max}^{MeOH} nm (ε): 216 (sh 33900), 226 (33000), 231 (sh 30800), 252 (sh 17400), 264 (sh 12300), 274 (sh 8400), 290 (sh 3700), 302 (3000), 315 (2400). IR ν_{max}^{KBr} cm^{-1}: 3230, 1784, 1749, 1670, 1616, 1485, 1260, 1200. NMR (in DMSO-d_6) δ: 1.26 (3H, singlet), 1.36 (3H, singlet), 3.03 (1H, doublet of doublets, *J*=13 and 10), 3.43 (1H, doublet of doublets, *J*=13 and 10), 5.21 (1H, singlet), 5.57 (1H, triplet, *J*=10), 7.24—8.00 (7H, multiplet), 8.23 (1H, doublet, *J*=8), 8.53 (1H, singlet), 8.74 (1H, singlet, disappeared with D_2O). MS *m/e* (%): 432 (M^+ 76), 286 (13), 269 (15), 256 (16), 242 (28), 229 (100), 199 (16), 188 (27), 173 (13), 147 (39), 130 (26).

FTM (3), (0.03% yield): Colorless plates (from MeOH–H_2O), $C_{28}H_{28}N_4O_7$ (M^+ *m/e* 532.1932, Calcd. 532.1959), mp 157—164°, $[\alpha]_D^{24}$ −154° (*c*=0.50, $CHCl_3$). UV λ_{max}^{MeOH} nm (ε): 228 (32700), 232 (30700), 255 (15400), 278 (9300), 305 (2900), 317 (2700). IR ν_{max}^{KBr} cm^{-1}: 3400, 1788, 1725, 1678, 1600, 1480, 1464, 1210. NMR (in $CDCl_3$) δ: 0.92 (3H, doublet, *J*=6), 1.04 (3H, doublet, *J*=6), 1.55 (3H, doublet, *J*=7), 2.16 (3H, singlet), 2.68 (1H, doudlet of doublets, *J*=11 and 10), 2.74 (1H, multiplet), 3.65 (1H, doublet of doublets, *J*=11 and 10), 4.15 (1H, quartet, *J*=7), 5.22 (1H, singlet), 5.54 (1H, doublet, *J*=10), 5.87 (1H, triplet, *J*=10), 6.86 (1H, broad singlet), 7.12—7.88 (7H, multiplet), 8.24 (1H, doublet, *J*=8). MS *m/e* (%): 532 (M^+ 100), 261 (33), 255 (23), 215 (50), 214 (22), 201 (56), 130 (19).

FTN (11), (0.063% yield): Colorless needles (from MeOH), $C_{26}H_{24}N_4O_5$ (M^+ *m/e* 472.1770, Calcd. 472.1747), mp 193—197°, $[\alpha]_D^{23}$ +127° (*c*=0.06, DMSO). UV λ_{max}^{MeOH} nm (ε): 232 (32300), 251 (sh 17900), 291 (9000), 320 (sh 6100). IR ν_{max}^{KBr} cm^{-1}: 3360, 1780, 1722, 1705, 1680, 1607, 1481, 1250. NMR (in $CDCl_3$) δ: 1.26 (3H, doublet, *J*=7), 1.30 (3H, doublet, *J*=7), 1.55 (3H, doublet, *J*=7), 3.03 (1H, doublet of doublets, *J*=13 and 10), 3.05 (1H, disappeared with D_2O), 3.31 (1H, doublet of doublets, *J*=13 and 10), 4.08 (1H, multiplet), 4.12 (1H, quartet, *J*=7), 5.34 (1H, singlet), 5.46 (1H, triplet, *J*=10), 7.04—7.80 (7H, multiplet), 8.24 (1H, doublet, *J*=8). MS *m/e* (%): 472 (M^+ 100), 444 (22), 256 (40), 243 (17), 228 (48), 217 (44), 199 (17), 186 (20), 174 (44), 158 (24), 146 (38), 130 (35).

Epimerization of Tryptoquivaline G (FTG, 2) to Tryptoquivaline L (FTL, 1)——FTG (2), (50 mg) was treated with 0.1% KOH–MeOH (3 ml) for 35 min. The reaction mixture was poured into cold water to obtain a white precipitate, which was collected and washed with water until the washings became neutral. The procuct was levorotatory and was shown to be identical to FTL (1) on TLC and by comparison of IR, NMR and ORD spectra.

Acetylation of Tryptoquivaline M (FTM, 3)——FTM (3), (30 mg) was stirred in a mixture of Ac_2O (1 ml) and AcOH (1 ml) at room temperature for 26 hr. The reaction mixture was poured into cold water and extracted with ether. The extract solution was evaporated down *in vacuo*, and an amorphous product was obtained (32 mg). The product showed one clear spot on TLC and was identical with **7**, which was prepared from FTD (**8**) by treatment with alkali followed by acetylation, on TLC and in the IR and NMR spectra.

Deacetylation (Epimerization) of Tryptoquivaline D (FTD, 8)——FTD (**8**), (100 mg) was stirred in a solution of 0.1% KOH in MeOH at room temperature for 15 min. The reaction mixture was poured into cold water (25 ml), acidified with HCl and extracted with ether. After removal of the extract solution by evaporation *in vacuo*, the residual yellow amorphous material (98 mg) was acetylated without further purification by standing for 17 hr at room temperature in a mixture of Ac_2O and AcOH. On purification by preparative thin-layer chromatography (TLC) on silica gel plates with benzene–acetone (6: 1), two products, mono- (**6**), (41 mg) and diacetylated (**7**), (38 mg) were obtained.

Monoacetate (**6**): Colorless crystals (from MeOH–H_2O), $C_{28}H_{28}N_4O_7$ (M^+ *m/e* 532), mp 135—139°, $[\alpha]_D^{23}$ −161° (*c*=0.10, MeOH). UV λ_{max}^{EtOH} nm (ε): 217 (sh 40600), 227 (41700), 232 (sh 39500), 255 (sh 16800), 265 (sh 13300), 276 (sh 10800), 307 (3800), 319 (3000). IR λ_{max}^{KBr} cm^{-1}: 3450, 1785, 1730, 1678, 1609, 1596, 1475, 1203. NMR (in $CDCl_3$) δ: 0.84 (3H, doublet, *J*=6), 1.21 (3H, doublet, *J*=6), 1.53 (3H, doublet, *J*=7), 2.15 (3H, singlet), 2.20 (1H, multiplet), 2.77 (1H, doublet of doublets, *J*=12 and 10), 3.53 (1H, doublet of doublets, *J*=12 and 10), 4.24 (1H, quartet, *J*=7), 4.40 (1H, broad singlet, disappeared with D_2O), 4.86 (1H, broad doublet, *J*=4, sharpened with D_2O), 5.20 (1H, singlet), 5.89 (1H, triplet, *J*=10), 7.21—7.86 (7H, multiplet), 8.23 (1H, doublet, *J*=8). MS *m/e* (%): 532 (M^+ 4), 472 (18), 454 (83), 411 (11), 367 (22), 254 (30), 236 (40), 201 (100), 197 (40), 169 (97), 130 (23), 128 (28).

Diacetate (7): Colorless amorphous material, $C_{30}H_{30}N_4O_8$ (M^+ *m/e* 574), $[\alpha]_D^{21}$ −148° (*c*=0.28, $CHCl_3$). UV λ_{max}^{MeOH} nm (*ε*): 228 (30600), 233 (sh 29100), 269 (8700), 278 (sh 8100), 307 (3000), 319 (2400). IR ν_{max}^{KBr} cm^{-1}: 1785, 1738, 1680, 1608, 1597, 1474, 1207. NMR (in $CDCl_3$) *δ*: 0.97 (3H, doublet, *J*=6), 1.18 (3H, doublet, *J*=6), 1.54 (3H, doublet, *J*=7), 2.13 (3H, singlet), 2.14 (3H, singlet), 2.46 (1H, multiplet), 2.80 (1H, doublet of doublets, *J*=13 and 10), 3.46 (1H, doublet of doublets, *J*=13 and 10), 4.27 (1H, quartet, *J*=7), 5.24 (1H, singlet), 5.65 (1H, doublet, *J*=9), 6.29 (1H, triplet, *J*=10), 7.22—7.84 (7H, multiplet), 8.21 (1H, doublet, *J*=8). MS *m/e* (%): 574 (M^+ 5), 532 (13), 514 (35), 470 (25), 455 (13), 261 (48), 254 (100), 210 (83), 201 (57), 182 (55), 176 (35), 169 (18), 149 (20), 141 (11), 130 (16).

Epimerization of Tryptoquivaline D (FTD, 8) in CD_3OD——FTD (8), (100 mg) was stirred in 0.1% KOH-CD_3OD (5 ml) at room temperature for 15 min. Deacetyl-FTD labeled with deuterium was obtained after treatment of the reaction mixture in the manner described above. The product was acetylated again without purification and a diacetate (13), (32 mg) was obtained.[7]

Diacetate (13): Colorless amorphous material, $C_{30}DH_{29}N_4O_8$ (M^+ *m/e* 575). NMR (in $CDCl_3$) *δ*: 0.95 (3H, doublet, *J*=7), 1.16 (3H, doublet, *J*=7), 1.53 (1H, doublet, *J*=7), 2.10 (3H, singlet), 2.13 (3H, singlet), 2.46 (1H, multiplet), 2.74 (1H, doublet, *J*=13), 3.42 (1H, doublet, *J*=13), 4.23 (1H, quartet, *J*=7), 5.16 (1H, singlet), 5.59 (1H, doublet, *J*=10), 7.10—7.72 (7H, multiplet), 8.14 (1H, doublet, *J*=8). MS *m/e* (%): 575 (M^+ 1), 533 (4), 515 (12), 471 (11), 456 (7), 261 (33), 255 (100), 211 (75), 201 (41), 183 (48), 176 (21), 169 (23), 142 (12), 130 (14).

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7) The acetate of deuteriotryptoquivaline D (13 mg) was also obtained together with 13 as a product of this reaction.