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Syntheses of Pterocarpans. III.[*1] Synthetic Analogues of Neodulin[*2]

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4',5'-Dimethoxy-2'-hydroxyfurano[3'',2'':6,7]isoflavone was obtained from isoelliptol isoflavone by selective demethylation with boron tribromide. The treatment of the 2'-hydroxyisoflavone with sodium borohydride in absolute alcohol - tetrahydrofuran afforded 8,9-dimethoxyfurano[3',2':2,3]pterocarpan. 8,9-Dimethoxyfurano[2',3':3,4]pterocarpan was prepared from elliptol isoflavone by a similar procedure.

(−)-Neodulin was isolated from *Neorautanenia edulis* C. A. Sm. by Van Duuren.1) Its structure was identified as 8,9-methylenedioxyfurano[3',2':2, 3]pterocarpan (I) on the basis of degradative studies and the results of spectral analyses. Recently, I was derived from dehydroneotenone (II), a naturally-occurring furano[3'',2'':6,7]isoflavone, by Brink *et al.*;2) further the present authors achieved the total syntesis of II.3) These facts confirmed the chemical structure of neodulin to be I. An analogue of I containing *ortho*-dimethoxyl groups instead of a methylenedioxy group, 8,9-dimethoxyfurano[3',2':2,3]pterocarpan (III), is a commonly-occurring type in coumestans and rotenoids. The present paper will describe the synthesis of III by a modification of the procedure reported earlier.4,5)

The selective demethylation of dihydroisoelliptol isoflavone (2',4',5'-trimethoxy-4'',5''-dihydrofurano[3'',2'':6,7]isoflavone (IV)6) with either boron tribromide or anhydrous aluminum chloride in acetonitrile4,7) afforded 4',5'-dimethoxy-2'-hydroxy-4'',5''-dihydrofurano[3'',2'':6,7] isoflavone (V), which then gave a mono-acetate by the usual method. The reduction of the 2'-hydroxydihydroisoflavone V with sodium borohydride in absolute alcohol - tetrahydrofuran, followed by cyclization with hydrochloric acid, gave 8,9-dimethoxy-4',5'-dihydrofurano[3',2':2,3]pterocarpan (VI). The dehydrogenation of the dihydrofuranoisoflavone IV with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (D. D.Q.) or with 10% Pd-C gave isoelliptol isoflavone (2', 4', 5' - trimethoxyfurano[3'', 2'':6,7]isoflavone) (VII), which had been previously obtained from IV with *N*-bromosuccinimide.6) By a procedure similar to that used for IV, VII gave the desired furanopterocarpan III *via* 4',5'-dimethoxy-2'-hydroxyfurano[3'',2'':6,7]isoflavone (VIII). The catalytic hydrogenation of III afforded dihydrofuranopterocarpan VI.

8, 9 - Dimethoxyfurano[2', 3', : 3, 4]pterocarpan (IX), an isomer of III, was also obtained from elliptol isoflavone (X)8) *via* 2'-hydroxy-4',5'-di-

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[*1] Part II: K. Fukui and M. Nakayama, This Bulletin, **42**, 1408 (1969).

[*2] Presented at the Ube Local Meeting (November, 1966) and the 21st Annual Meeting (Osaka, April, 1968) of the Chemical Society of Japan.

1) B. L. Van Duuren, *J. Org. Chem.*, **26**, 5013 (1961).

2) C. v. d. M. Brink, J. J. Dekker, E. C. Hanekom, D. H. Meiring and G. J. H. Rall, *J. S. African Chem. Inst.*, **18**, 21 (1965); *Chem. Abstr.*, **63**, 14834h (1965).

3) K. Fukui and M. Nakayama, *Experientia*, **20**, 668 (1964); This Bulletin, **41**, 2733 (1968).

4) K. Fukui, M. Nakayama and T. Harano, *ibid.*, **42**, 233 (1969).

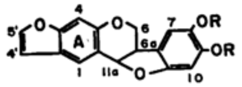
5) V. K. Kalra, A. S. Kukla and T. R. Seshadri, *Indian J. Chem.*, **5**, 607 (1967).

6) K. Fukui, M. Nakayama, A. Tanaka and S. Sasatani, This Bulletin, **38**, 845 (1965).

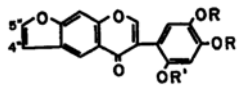
7) a) K. Aghoimurthy, A. S. Kukla and T. R. Seshadri, *J. Indian Chem. Soc.*, **38**, 914 (1961); b) V. K. Kalra, A. S. Kukla and T. R. Seshadri, *Indian J. Chem.*, **5**, 287 (1967); c) K. Fukui, M. Nakayama and T. Harano, *Experientia*, **23**, 613 (1967).

8) K. Fukui, M. Nakayama and M. Hatanaka, This Bulletin, **36**, 872 (1963).

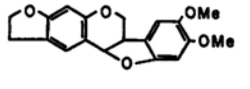
methoxyfurano[2″,3″:7,8]isoflavone (XI).⁹⁾



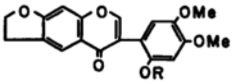
I R-R=CH$_2$
III R=Me



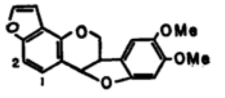
II R-R=CH$_2$, R'=Me
VII R=R'=Me
VIII R=Me, R'=H



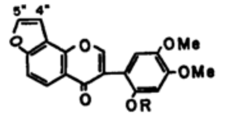
VI



IV R=Me
V R=H

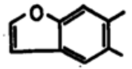


IX

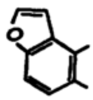


X R=Me
XI R=H

The NMR spectra of the two isomeric furanopterocarpans, III and IX, and the dihydrocompound VI are shown in Figs. 1—3 and Table 1.*3 In the spectra of these compounds the signals at δ 3.2—4.5 (3H, complex multiplets) and at δ 5.3—5.7 (1H, multiplet) can be assigned to the C-6 and C-6a, and the C-11a protons, respectively; the signals are fully consistent with the formulation of the pterocarpan system on the basis of the analyses previously reported.⁴⁾ Furthermore, a set of one-proton signals at δ 6.80 and 6.48 (each, 1H, singlet) in the spectrum of III (Fig. 1), which closely resemble those in the spectra of VI and IX, can be assigned to the aromatic protons at C-7 and C-10 respectively. The remaining two signals, those of aromatic protons at δ 7.70 (1H, singlet) and 7.07 (1H, doublet, J=1 Hz), can be attributed to the protons at C-1 and C-4 respectively in view of their small coupling constants.¹⁰⁾ However, in the spectrum of IX, the corresponding signals were found at δ 7.43 (1H, doublet) and 7.16 (1H, broad doublet) and formed an AB-type (J_{AB}=8.5 Hz), indicating that the two protons are oriented in *ortho* positions (C-1 and C-2) to one another. These facts show that the structures of III and IX belong to the linear ring system (A) and the angular ring system (B) respectively. From these results, it is apparent that the linear or angular pattern of furanopterocarpans can be determined easily by analyzing the NMR pattern of the aromatic protons of the A-ring. A long-range coupling is observed between the aromatic proton at C-4 or C-2 (broad singlet) and the β-furano-proton at C-4′ (double doublet or broad singlet) in the



(A)



(B)

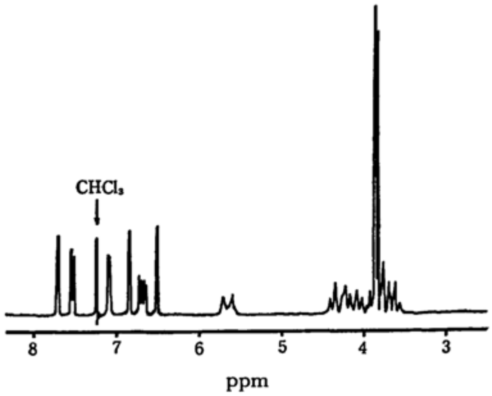


Fig. 1. NMR spectrum of III.

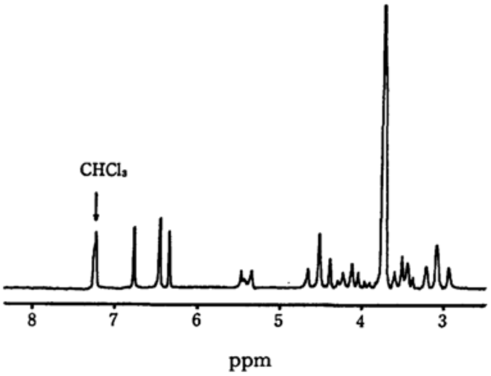


Fig. 2. NMR spectrum of VI.

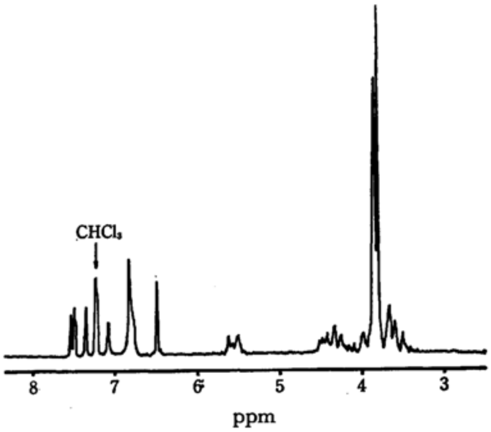


Fig. 3. NMR spectrum of IX.

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9) V. Chandrashekar, M. Krishnamurti and T. R. Seshadri, *Tetrahedron,* **23**, 2505 (1967).

*3 The NMR spectra were measured with a Varian A-60 spectrometer and a Hitachi R-20 spectrometer, using tetramethylsilane as the internal standard (δ-value in CDCl$_3$).

10) H. S. Gutowsky, C. H. Holm, A. Saika and G. A. Williams, *J. Am. Chem. Soc.,* **79**, 4596 (1957).

TABLE 1. NMR DATA OF PTEROCARPANS[*3,4]

Proton		Compound		
		III	VI	IX
Arom.	C-1	7.70_{s}	7.27_{s}	7.43_{d} $(J=8.5)$
	C-2			7.16_{bd} $(J=8.5)$
	C-4	7.07_{d} $(J=1.0)$	6.47_{s}	
	C-7	6.80_{s}	6.79_{s}	6.82_{s}
	C-10	6.48_{s}	6.35_{s}	6.50_{s}
Furan	C-4′	6.68_{dd} $(J=2.0,\ 1.0)$	3.13_{t} $(J=8.0)$	6.82_{bs}
	C-5′	7.52_{d} $(J=2.0)$	4.55_{t} $(J=8.0)$	7.52_{d} $(J=2.0)$
Ring	C-11a	5.63_{m}	5.45_{m}	5.57_{m}
	C-6—C-6a	3.3—4.5_{m}	3.2—4.3_{m}	3.3—4.5_{m}
$OC\underline{H}_3$		3.78_{s}	3.80_{s}	3.80_{s}
		3.81_{s}	3.83_{s}	3.83_{s}

[*4] s=singlet; bs=broad singlet; d=doublet; bd=broad doublet; t=triplet; m=multiplet

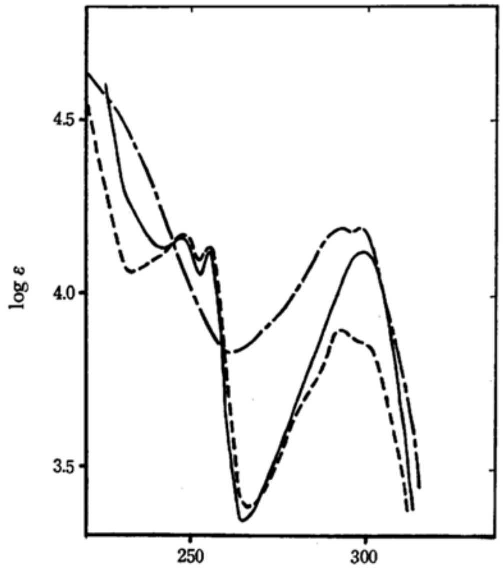

Fig. 4. UV spectra of III (——), VI (– – –) and IX (–·–·–) in ethanol solution.

furanopterocarpans, III and IX. Similar observations have been reported in several earlier reports.[11)] This phenomenon also appears as a double doublet at the C-4′′ proton of acetyl derivatives of the furanoisoflavones, VIII and XI.

The ultraviolet spectra of the furanopterocarpan, III, and its dihydro compound, VI, are shown in Fig. 4. The former contains two absorption maxima, at *ca.* 25 mμ and at *ca.* 300 mμ, while the latter contains only one maximum, at *ca.* 300 mμ. The strong absorption in the region *ca.* 250 mμ is characteristic of the benzofuran grouping, as has previously been noted by the present authors and by others.[3,12)]

Experimental[*5]

4′,5′-Dimethoxy-2′-hydroxy-4′′,5′′-dihydrofurano-[3′′,2′′:6,7]-isoflavone (V). *a) With Boron Tribromide.* A solution of boron tribromide in anhydrous methylene chloride (5 m*l*) was added, at room temperature, to a solution of the isoflavone IV[6)] (1.0 g) in the same solvent (200 m*l*), and then allowed to stand overnight in the dark. After the solution had been poured into water, the separated solid was collected and washed with water. The product was recrystallized from ethanol to give V as light yellow needles; mp 204—205°C; yield, 0.8 g. It showed a negative ferric chloride reaction. IR: 1623 cm^{-1} (C=O). UV: λ_{max} mμ (log ε); 264 (3.92), 306 (4.10).

Found: C, 66.96; H, 4.81%. Calcd for $C_{19}H_{16}O_6$: C, 67.07; H, 4.75%.

b) With Aluminum Chloride. A mixture of IV (1.2 g) and anhydrous aluminum chloride (4.0 g) in anhydrous acetonitrile (30 m*l*) was refluxed for 12 hr. The solvent was removed as far as possible, and then the residue was treated with 10% hydrochloric acid. The separated solid was collected, washed with water, and recrystallized from ethanol to give V, mp 203—204°C, which was identical with the sample obtained in a); yield, 1.05 g.

The acetate: hot acetic anhydride - anhydrous sodium acetate method; mp 196—197°C (colorless needles from ethanol). IR: 1752, 1643 cm^{-1} (C=O). UV: λ_{max}

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11) a) J. A. Elvidge and R. G. Foster, *J. Chem. Soc.*, **1963**, 590; b) E. A. Abu-Mustafa and M. B. E. Fayez, *Can. J. Chem.*, **45**, 325 (1967); c) K. Fukui, M. Nakayama and S. Tanaka, This Bulletin, **42**, No. 7 (1969), in press.

12) a) K. Fukui, M. Nakayama and K. Okazaki, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **87**, 1096 (1966); b) D. K. Chatterjee, R. M. Chatterje and K. Sen, *J. Org. Chem.*, **29**, 2467 (1964).

[*5] All the melting points are uncorrected. The infrared spectra were measured in Nujol, while the ultraviolet spectra were measured in ethanol, unless otherwise stated.

mμ (log ε); 276 (4.17), 307 (4.17). NMR:[*3,4] δ 8.06_s (C-5); 7.80_s (C-2); 6.83_s, 6.73_s, 6.68_s (C-8,3′,6′); 4.79_t (J=8.0, C-5′′); 3.91_s (6H, $OC\underline{H}_3$), 3.33_t (J=8.0, C-4′′); 2.15_s (3H, $OCOC\underline{H}_3$).

Found: C, 65.99; H, 4.73%. Calcd for $C_{21}H_{18}O_7$: C, 65.96; H, 4.75%.

8,9 - Dimethoxy - 4′,5′ - dihydrofurano[3′,2′ : 2,3]-pterocarpan (VI). A solution of sodium borohydride (600 mg) in absolute ethanol (15 m*l*) was added, drop by drop, to a solution of the above isoflavone V (500 mg) in anhydrous tetrahydrofuran (80 m*l*). The reaction mixture was then kept for 60 hr at room temperature while being stirred. After acetone (20 m*l*) had been added to decompose the excess reducing agent, the solvent was removed under reduced pressure. The residue was treated with 10% hydrochloric acid, and then the separated solid was collected, washed with water and recrystallized from ethanol to give VI as colorless plates; mp 174—175°C; yield, 400 mg. IR: 1624, 1598, 1498 cm^{-1} (phenyl). UV: λ_{max} mμ (log ε); 294 (4.19), 298 (4.19); ($CHCl_3$) 299.5 (4.08).

Found: C, 69.92; H, 5.51%. Calcd for $C_{19}H_{18}O_5$: C, 69.92; H, 5.56%.

Isoelliptol Isoflavone (2′,4′,5′-Trimethoxyfurano-[3′′,2′′: 6,7]isoflavone) (VII). *A) With 10% Pd-C.* A mixture of IV (1.7 g) 10% palladium-charcoal (300 mg), and diphenyl ether (30 m*l*) was refluxed for 12 hr. The catalyst was then filtered off, and the solvent removed by steam distillation. The resulting precipitate was collected and recrystallized from ethanol to give VII as colorless needles; mp 191—192°C (lit. mp 190—190.5°C[6]; mp 191°C[13]); yield, 1.0 g. This was identical with an authentic sample obtained from IV by the *N*-bromosuccinimide method.[6]

b) With D.D.Q. A mixture of IV (1.0 g), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (700 mg), and absolute benzene (70 m*l*) was refluxed for 20 hr. After the solution had then been cooled, the precipitated hydroquinone derivative was filtered off and the solvent was removed as far as possible. The residual solid was recrystallized from ethanol to give a mixture of two compounds as colorless needles; mp 190—199°C; yield, 700 mg. The mixture (500 mg) was chromatographed on a silica gel column (12 g); subsequent elution with chloroform - *n*-hexane gave the desired isoflavone, VII (mp 190—191°C), which was identical with the sample derived by the above-described method; yield, 100 mg. Further elution with the same solvent gave the starting isoflavone, IV (mp 200—201°C; 400 mg).

3′,4′-Dimethoxy-2′-hydroxyfurano[3′′,2′′: 6,7]isoflavone (VIII). A mixture of VII (500 mg), boron tribromide (130 mg), and methylene chloride (20 m*l*) was treated by a method similar to that used for IV. The crude product was recrystallized from ethanol to give VIII as light yellow needles; mp 212—213°C (lit,[13] mp 200—201°C); yield, 400 mg. This was identical with an authentic sample obtained from VII by the aluminum chloride - acetonitrile method.[13] IR: 1620 cm^{-1} (C=O). UV: λ_{max} mμ (log ε); 239 (4.56), 260_{sh}[*6] (4.36), 304 (4.15).

Found: C, 67.50; H, 4.44%. Calcd for $C_{19}H_{14}O_6$: C, 67.45; H, 4.17%.

The acetate: hot acetic anhydride - anhydrous sodium acetate method; mp 216—217°C (colorless needles from ethanol). IR: 1745, 1643cm^{-1} (C=O). UV: λ_{max} mμ (log ε); 239 (4.53), 306 (4.02). NMR:[*3,4] δ 8.55_s (C-5); 7.94_s (C-2); 7.59_{bs} (C-8); 7.75_d (J=2.5, C-5′′); 6.90_{dd} (J=2.5, 1.0, C-4′′); 6.89_s (C-6′); 6.73_s (C-3′); 3.90_s (6H, $OC\underline{H}_3$); 2.13_s (3H, $OCOC\underline{H}_3$).

Found: C, 66.41; H, 4.33%. Calcd for $C_{21}H_{16}O_7$: C, 66.31; H, 4.24%.

8,9-Dimethoxyfurano[3′,2′:2,3]pterocarpan (III). A mixture of VIII (350mg), sodium borohydride (400mg), and absolute tetrahydrofuran - ethanol (4 : 1, 50m*l*) was treated by a method similar to that used for V. The crude product was recrystallized from ethanol to give III as colorless needles; mp 172—173°C; yield, 200mg. IR: 1617, 1586, 1535, 1510, 1500cm^{-1} (phenyl); ($CHCl_3$) 1620, 1590, 1520, 1493cm^{-1} (phenyl). UV: λ_{max} mμ (log ε); 247 (4.24), 255 (4.12), 299 (4.12); ($CHCl_3$) 250 (4.05), 256.5 (4.06), 302 (4.10).

Found: C, 70.28; H, 5.01%. Calcd for $C_{19}H_{16}O_5$: C, 70.36; H, 4.98%.

Hydrogenation of III. Furanopterocarpan III (300 mg) was hydrogenated in ethyl acetate (40 m*l*) over 10% Pd-C (600 mg) at atmospheric pressure and at room temperature. The catalyst was then filtered off, and the solvent was removed under reduced pressure. The residue was dissolved in benzene. The benzene solution was washed with a 5% aqueous sodium hydroxide solution and then with water. The evaporation of the dried solution and the chromatography of the resulting solid on silica gel with chloroform - *n*-hexane (1 : 1) gave colorless crystals, which were then recrystallized from ethanol to give VI; mp 174—175°C; yield, 150 mg. This was identical with the sample derived by the method described above.

4′,5′- Dimethoxy-2′-hydroxyfurano[2′′,3′′: 3,4]isoflavone (XI). 2′-Hydroxyisoflavone XI was prepared, according to the directions of Seshadri,[9] from elliptol isoflavone, X.[8] Recrystallization from ethanol gave XI; mp 207—208°C (lit.[9] mp 204—205°C).

Found: C, 67.57; H, 4.27%. Calcd for $C_{19}H_{14}O_6$: C, 67.45; H, 4.17%.

The acetate: hot acetic anhydride - anhydrous sodium acetate method; mp 205—206°C (colorless needles from ethanol). IR: 1770, 1744, 1637 cm^{-1} (C=O). UV: λ_{max} mμ (log ε); 230 (4.53), 247_i[*7] (4.48), 312_{sh}[*6] (3.81). NMR:[*3,4] 8.12_d (J=9.0, C-5); 7.97_s (C-2); 7.73_d (J=2.0, C-5′′); 7.55_d (J=9.0, C-6); 7.13_{bs} (C-4′′) 6.87_s (C-6′); 6.72_s (C-3′); 3.90_s (6H, $OC\underline{H}_3$); 2.13_s ($OCOC\underline{H}_3$, 3H).

Found: C, 66.27; H, 4.40%. Calcd for $C_{21}H_{16}O_7$: C, 66.31; H, 4.24%.

8,9-Dimethoxyfurano[2′,3′: 3,4]pterocarpan (IX). A mixture of XI (150 mg), sodium borohydride (200 mg), and absolute tetrahydrofuran - ethanol (6 : 1, 35 m*l*) was treated by a method similar to that used for V. The crude product was recrystallized from ethanol to give IX as colorless prisms; mp 180—181°C; yield, 70 mg. IR: 1613, 1596, 1492 cm^{-1} (phenyl). UV: λ_{max} mμ (log ε); 247.5 (4.17), 255.5 (4.13), 292.5 (3.90); ($CHCl_3$) 251 (4.12), 256 (4.12), 292.5 (3.89), 300_i[*7] (3.86).

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13) V. Chandrashekar, M. Krishnamurti and T. R. Seshadri, *Curr. Sci. (India)*, **36**, 623 (1967); *Chem. Abstr.*, **68**, 59402q (1968).

[*6] sh=shoulder.

[*7] i=inflection point.

Found: C, 70.19; H, 5.08%. Calcd for $C_{19}H_{16}O_5$: C, 70.36; H, 4.98%.

The authors wish to express their thanks to Professor Shô Itô, Tohoku University, for his NMR measurements, and to Miss Toshiko Hiwaki, of this laboratory, for her microanalyses and her measurements of the ultraviolet spectra.