Tetrahedron Letters No.27, pp. 3199-3202, 1966. Pergamon Press Ltd.
Printed in Great Britain.

STEREOCHEMISTRY OF ISOFLAVAN-4-OLS

A.S.R. Anjaneyulu, M. Gopala Rao, L. Ramachandra Row
and C. Sri Krishna
Department of Chemistry, Andhra University, Waltair, India

(Received 9 May 1966)

NMR study of 7-methoxy and 7,4'-dimethoxy isoflavan-4-ols (I m.p. 138-40°, II m.p. 141-43°), reverses our earlier observation[1] that the 4-OH could be equatorial in these compounds. These isoflavan-4-ols (I,II) were obtained by the action of $NaBH_4$ on the corresponding isoflavones. They suffer ready dehydration in presence of protonic reagents even below 50°.

Analysis of NMR spectrum (Table I) of 7,4'-dimethoxy isoflavan-4-ol (II) suggests an ABXY system giving $J_{AX}=3.5$, $J_{AY}=1.2$, $J_{BY}=-0.2$, $J_{AB}=10.3$, $J_{XY}=3.4$ c/s. Similar analysis was obtained for the 7-methoxy analogue (I). $J_{AX}=12.0$, $J_{BX}=3.2$, $J_{AY}=1.4$, $J_{BY}=-0.2$, $J_{AB}=10.4$, $J_{XY}=3.1$ c/s. In both cases A=2axH, B=2eqH, X=3axH and Y=4eqH.

From the above, the two isoflavan-4-ols (I,II) are 3,4-*cis* compounds so that with 3-aryl group equatorial, the 4-OH is axial. This is also consistant with the dehydration data[1]. Earlier, Inoue et al.[2,3] also suggested 3,4-*cis* configuration for these isoflavan-4-ols (I & II) solely on a consideration of the mechanism of catalytic reduction.

TABLE I

NMR spectra of isoflavan-4-ols and 6,4'-$(OMe)_2$flavan-4-ol. τ -values

	Compound	Aromatic protons				$H_{2A,2B,4}$		Methoxyl		H_3	4-OH
I.	7-OMe	$H_{3'4'5'}$	$H_{2'6'}$	H_5	$H_{6'8}$			7	4'		
	isoflavan-4-ol	2.70	2.77*	3.38	3.56	5.14-5.84*		6.24	---	6.59*-	8.22
			2.85	3.44						6.89	
			2.9								
II.	7,4'-$(OMe)_2$	$H_{3'5'}$	$H_{2'6'}$								
	isoflavan-4-ol	2.80,	3.06*	3.41	3.60	5.25-6.06*		6.25	6.22	6.58*-	8.09
		2.90	3.19	3.45						6.96	
			3.23								
III.	6,4'-$(OMe)_2$	$H_{2'6'}$	$H_{3'5'}$	$H_{5,7,8}$		H_2	H_4	6	4'	$H_{3A,3B}$	4-OH
	flavan-4-ol	2.58*-	2.97*	3.18*		4.98	5.00	6.25	6.20	7.30*-	7.95
		2.71	3.04	3.24						8.18	

* multiple peaks.

But the reduction of 2-substituted isoflavanones with Pt/H or $NaBH_4$ appears to give rise to the isomeric 3,4-trans isoflavan-4-ols. From a study of NMR data, Inoue et al.[4] and Micheli et al.[5] proved that the 2-methyl isoflavan-4-ols possess 4-equatorial hydroxyl ($J_{3H,4H}$=7.5[4], 10.0[4], 7.1[5] c/s). It appears, therefore, that the presence (or absence) of the 2-methyl group directs the reducing agent to attack the carbonyl group from a side that permits the formation of equatorial (or axial) 4-hydroxyl.

Further, it is interesting to note that $NaBH_4$ or Pt/H also reduces flavanones to give flavan-4β-ols with 4-eq OH[6,7,8,9]. It is, therefore, probable that the course of reduction of the flavanone carbonyl also follows a similar reaction path as in 2-methyl isoflavanones. The contribution of 7-methoxyl appears to be negligible, for, 6,4'-dimethoxy flavanone (III) also produces the 4-equatorial hydroxy compound (IV) during reduction with $NaBH_4$[10] as could be seen from the NMR data which consists of a complex ABXY spectrum in which A and B quartets overlap as well as X and Y quartets. Analysis (Table I) gives J_{AX}=11.5, J_{BX}=2.0, J_{AY}=10.5, J_{BY}=5.6, J_{AB}=13.0 c/s where A=3eqH, B=3axH, X=2H, Y=4H. In this flavan-4-ol (IV) both the substituents are equatorial.

We are highly indebted to Dr. T.M.Spotswood for running the NMR spectra and to Prof. J.W.Clark-Lewis for their analysis.

REFERENCES

1. A.S.R. Anjaneyulu, C. Sri Krishna and L. Ramachandra Row, *Tetrahedron*, **21**,2677(1965)
2. N. Inoue, *Bull.Chem.Soc.Japan*, **37**,601,606(1964)
3. N. Inoue, S. Yamaguchi and S. Fujiwara, *Bull.Chem.Soc.Japan*, **37**,588(1964)
4. N. Inoue and S. Ito, *Chem. & Ind.*, 1382(1965)
5. R.A. Micheli, A.N. Booth, A.L. Livingstone and E.M. Bickoff, *J.Medicinal Pharm.Chem.*, **5**,321(1961)
6. J.W. Clark-Lewis, T.M. Spotswood and L.R. Williams, *Proc.Chem.Soc.*, 20(1963)
7. C.P. Lillya, D. Kehoe, E.M. Philbin, M.V. Vickars and T.S. Wheeler, *Chem. & Ind.*, 84(1963)
8. C.P. Lillya, S.E. Drewes and D.G. Roux, *Chem. & Ind.*, 784(1963)
9. H.G. Krishnamurty, K.G. Sarma and T.R. Seshadri, *Current Sci.(India)*, **32**,453(1963)
10. L.R. Row, G.P. Sastry, P.V.S. Rao and M. Gopala Rao, *J.Ind.Chem.Soc.*, **40**,311(1963)

Note added:- After this paper was ready, we received a reprint from Prof.N.Inoue on the same topic which confirms our proton assignments. (S.Yamaguchi, S.Ito, A.Nakamura and N.Inoue, Bull.Chem.Soc.Japan, **38**, 2187 (1965)]