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SYNTHESIS OF THE ENANTIOMERS OF FLAVAN-4∝-OL AND FLAVANONE

M.Rákosi, A.L.Tőkés and R.Bognár

Institut of Organic Chemistry, L.Kossuth University

and

Chemical Research Group for Antibiotics

of the Hungarian Academy of Sciences

Debrecen 10, Hungary

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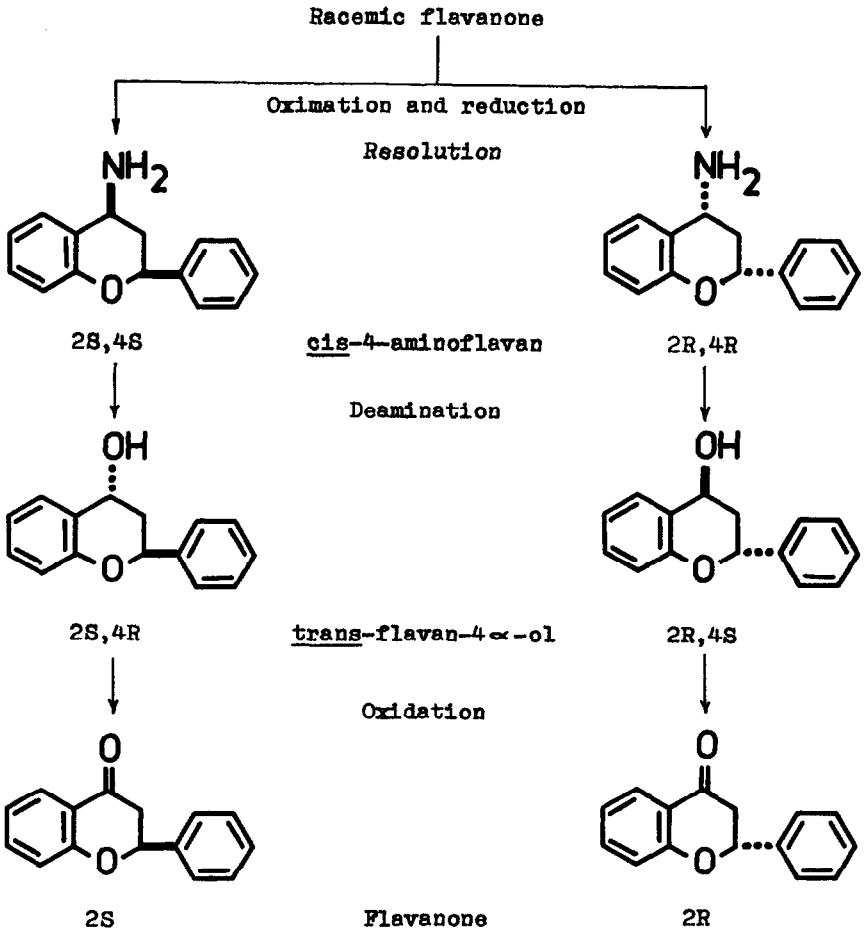
We report elsewhere (1) that racemic 4-aminoflavan, synthesized by the reduction of flavanone oxime, has been resolved through the D-(+)-camphor-10-sulphonate and dibenzoyl-D-(-)-tartrate salts. Decomposition of the diastereomeric pairs gave the two, formerly unknown, enantiomers of cis-4-aminoflavan hydrochloride [m.p. 281-283°, $[\alpha]_D$ + 28.6° (c = 0.5, ethanol); and m.p. 285-286°, $[\alpha]_D$ - 26.5° (c = 0.5, ethanol)], and from these the optically active free amines, their N-acetyl and N-benzoyl derivatives have been prepared (1).

On deamination with nitrous acid, according to the method reported by us earlier (2), the above (-)-4-aminoflavan hydrochloride yields the hitherto unknown (+)-flavan-4∝-ol [m.p. 126-127°, $[\alpha]_D$ + 16.9° (c = 0.5, ethanol), $[\alpha]_D$ + 22.1° (c = 0.22, CCl_4)], whereas (+)-4-aminoflavan hydrochloride gives (-)-flavan-4∝-ol [m.p. 127°, $[\alpha]_D$ - 10.4° (c = 0.5, ethanol), $[\alpha]_D$ - 13.2°

All new compounds gave satisfactory analyses.

($c = 0.22$, CCl_4)] (cf. ref. 5). The corresponding O-acetyl derivatives [m.p. 86-87°, $[\alpha]_D$ + 129° ($c = 0.3$, ethanol); and m.p. 85-86°, $[\alpha]_D$ - 123.5° ($c = 0.3$, ethanol)] are obtained by acetylation of the antipodes.

Sodium dichromate oxidation of the C-4 hydroxyl group of the enantiomeric flavan-4α-ols eliminated one of the two asymmetric centres giving (+)- and (-)-flavanone [m.p. 77°, $[\alpha]_D$ + 67.2° ($c = 0.35$, chloroform) and m.p. 76-77°, $[\alpha]_D$ - 64.4° ($c = 0.35$, chloroform)] in good yields. [Reported data for these compounds are m.p. 72-74°, $[\alpha]_D$ + 12.4° (benzene) (3), m.p. 76°, $[\alpha]_D$ + 52° ($c = 0.75$, chloroform) (4); and m.p. 75-76°, $[\alpha]_D$ - 9.35° (benzene) (3), m.p. 77-78°, $[\alpha]_D$ - 53.5° ($c = 2.27$, chloroform) (4)].



The stereochemistry underlying our synthetic route may be given as follows. According to NMR studies (1 , 6), (±)-4-aminoflavan prepared by the reduction of flavanone oxime is the racemic mixture of two enantiomers with cis configuration. Resolution gives, therefore, the optical antipodes 2S,4S and 2R,4R (1). Deamination of the enantiomers with nitrous acid involves inversion at C-4, and the trans (i.e. 2S,4R and 2R,4S , respectively) configurations of the two optically active flavan-4∝-ols produced were proved by IR and NMR spectrometry (5 - 12). Oxidation at the C-4 atom of the flavan-4∝-ol enantiomers gives the two optical antipodes of flavanone having only one centre of asymmetry; thus the configurations are 2S and 2R , respectively.

Optically active natural flavanones isolated so far are all levorotatory and they have identical, 2S configuration at C-2 (7). On this basis it may be assumed that the (-)-flavanone prepared by us has the 2S configuration, and for (+)-flavanone the 2R configuration seems probable. Investigations in support of this assumption are in progress. Our further work also includes the preparation of other optically active flavonoids and thiaflavonoids.

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References

(1) R.Bognár, A.L.Tőkés and M.Rákosi, "Flavonoids, XVIII. Resolution of 4-aminoflavan", Magyar Kém. Folyóirat, in press.

R.Bognár, J.W.Clark-Lewis, A.L.Tőkés and M.Rákosi, "Resolution of 4-aminoflavan into its optical isomers. Nuclear magnetic resonance spectra, configuration, and conformation of 4-aminoflavan and related flavan derivatives", Austral. J. Chem., to be published.

(2) R.Bognár, M.Rákosi, H.Fletcher, E.M.Philbin and T.S.Wheeler, Tetrahedron Letters, 4 (1959).

(3) M.Kotake and G.Nakaminami, Proc. Japan Acad., 29, 56 (1953).

(4) E.J.Corey and R.B.Mitra, J. Amer. Chem. Soc., 84, 2938 (1962).

(5) S.R.Udupa, A.Banerji and M.S.Chadha, Tetrahedron Letters, 4003 (1969); Tetrahedron, 25, 5415 (1969).

(6) B.J.Bolger, A.Hirwe, K.G.Marathe, E.M.Philbin, M.A.Vickars and C.P.Lillya, Tetrahedron, 22, 621 (1966).

(7) J.W.Clark-Lewis, Rev. Pure Appl. Chem. (Australia), 12, 96 (1962).

(8) C.P.Lillya, D.Kehoe, E.M.Philbin, M.A.Vickars and T.S.Wheeler, Chem. and Ind., 84 (1963).

(9) J.W.Clark-Lewis, T.M.Spotswood and L.R.Williams, Proc. Chem. Soc., 20 (1963).

(10) B.R.Brown and J.A.H.MacBride, J. Chem. Soc., 3822 (1964).

(11) J.W.Clark-Lewis, Austral. J. Chem., 21, 2059 (1968).

(12) G.F.Katekar and A.G.Moritz, Austral. J. Chem., 22, 2337 (1969).