Pergamon

Tetrahedron Letters, Vol. 35, No. 40, pp. 7415-7416, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01548-1

A Novel Doubly-Linked Proteracacinidin Analogue from *Acacia caffra*

Elfranco Malan[1], Ashika Sireeparsad[1], Johann F.W. Burger[2], and Daneel Ferreira[2]

[1]Department of Chemistry, University of Durban-Westville, Private Bag X54001, Durban, 4000 South Africa
[2]Department of Chemistry, University of the Orange Free State, P.O. Box 339, Bloemfontein, 9300 South Africa

Abstract A new proteracacinidin analogue with a unique double linkage, ent-oritin-(4β→7, 5→6)-epioritin-4α-ol was isolated from the heartwood of *Acacia caffra*.

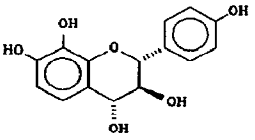
Proteracacinidin oligomers until very recently were unknown and the first two biflavonoids in this proanthocyanidin class were isolated from *Acacia galpini*[1,2]. A considerable number of doubly linked (A-type) proanthocyanidins were isolated from various sources[3], all of them have in common an ether linkage from C-2 and a carbon-carbon bond from C-4 of the T-unit to variable positions on the B-unit.

The new proteracacinidin type compound (3) has a unique 4β→7 ether linkage as well as a rare carbon-carbon bond, between the A- and D-rings (5→6), the latter bonding-type was first observed in compounds from *Prosopis glandulosa*[4]. The ^{1}H NMR (C_6D_6) spectrum of the derivative (4) showed the presence of eight acetoxyl groups (Table 1) and an AA'BB' substitution pattern for both the B- and E-rings. The chemical shifts of the H-2,6 doublets of both the B- and E-rings were differentiated using the H-2(C) and H-2(F) resonances as reference signals in a decoupling experiment. Similarly the C- and F-rings both exhibited AMX heterocyclic systems with coupling constants reminiscent of a 2,3-*trans*-3,4- *trans*-($J_{2,3}$ = 4.5; $J_{3,4}$ = 6.0 Hz) and a 2,3-*cis*-3,4-*cis* configuration ($J_{2,3}$ = 1.5; $J_{3,4}$ = 4.0 Hz) for the C- and F-rings respectively[5]. The relative stereochemistry was confirmed by an NOE experiment, adapted to avoid INDOR effects associated with long-range scalar coupling, showing a significant association between H-2(C) and H-4(C) (6.7%) and between H-2(F) and H-4(F) (7.2%), indicating that these protons occupy the same side of the heterocyclic ring.

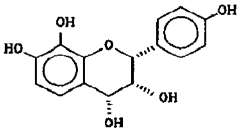
The chemical shift of H-5(D) (δ 7.55) was assigned *via* its NOE association (7.6%) with H-4(F). No association could be found between the singlet at δ 7.24 and H-4(C) and hence its assignment as H-6(A). NOE difference spectroscopy showed a strong association (15.2%) between H-6(A) and H-5(D) and the conspicuous absence of association between either H-3(C) or H-4(C) to H-5(D) which then unambiguously indicates the biphenyl linkage between C-5(A) and C-6(D) in derivative (4).

The presence of only eight acetoxyl signals in the ^{1}H NMR spectrum of the derivative (4) suggested that two of the oxygen functionalities of the presumed flavan-3,4-diol precursors [enantiomer of (1)] and (2) could be involved in the C-4(C) and C-7(D) bond. FAB-MS (m/z 896) confirmed the molecular ion required by the molecular formula of $C_{46}H_{40}O_{19}$.

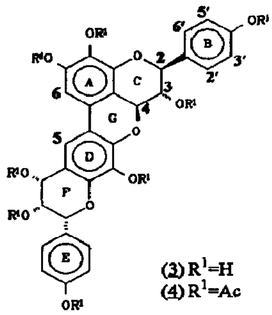
The CD spectrum of (4) exhibits a positive cotton effect ($[\theta]_{250}$ 1.5×10^5) which indicated a 4β(C) linkage and thus 4*S* absolute stereochemistry. When taken in conjunction with ^{1}H NMR coupling constants this indicates 2*S*, 3*R*, 4*S* absolute configuration for the ABC-moiety. Both oritin-4α-ol (1) and epioritin-4α-ol (2) with 2*R*, 3*S*, 4*R*- and 2*R*, 3*R*, 4*R*-absolute configurations occur abundantly in the heartwood, the latter constituting the most likely biogenetic precursor to the lower unit of the novel



(1)



(2)



(3) R^1=H
(4) R^1=Ac

Table 1. ^1H NMR data (300MHz) of Compound (2) in C_6D_6/296K

Ring	H	ppm/splitting/J-value
A	6	7.24,s
B	2,6 3,5	7.18,d,8.5 6.97,d,8.5
C	2 3 4	5.20,d,4.5 5.98,dd,4.5,6.0 4.75,d.6.0
D	5	7.55,s
E	2,6 3,5	7.29,d,9.0 7.04,d,9.0
F	2 3 4	4.98,br.s,1.5 5.85,dd,1.5,4.0 6.30,d,4.0
	OAc	1.45,1.55,1.67,1.71,1.81,1.82, 1.83,2.03(each s)

oligoflavanoid (3). The proposed absolute stereochemistry of the DEF-unit stems from such a conjecture. Compound (3) represents the first proanthocyanidin where the interflavanyl linkages are presumably established by a combined one (5→6 bond) and two-electron (7-0→4 bond) process.

From Dreiding models it is evident that for the G-ring of (3) to form, the C-ring conformation changes from the well-known sofa to a distorted chair (O_1-C_1-C_3-C_4) with the G-ring then in a twisted half-boat. Despite these conformational deviations, the 'central core' of the molecule comprising the A-, C-, G-, D-, and F-rings exhibits a remarkable degree of planarity which is atypical amongst condensed tannin analogues.

Acknowledgements Financial support by the Research Committee of the University of Durban-Westville, the 'Sentrale Navorsingsfonds' of the University of the Orange Free State and by the Foundation for Research Development, Pretoria is gratefully acknowledged.

References and Notes

1. Malan E.; Sireeparsad, A. *Phytochemistry*, 1994, manuscript no. 4407, in the press.
2. Malan, E.; Roux, D.G. *Phytochemistry*, 1975, 14, 1835.
3. The Chemistry of A-type proanthocyanidins was extensively reviewed by L.J. Porter in The Flavonoids, Advances in Research since 1980. (J.B. Harborne, ed.) Chapman and Hall, London, 1988, pp. 21-62, and in The Flavonoids, Advances in Research since 1988 (J.B. Harborne, ed.) Chapman and Hall, London, 1993, 23-55.
4. Young, E.; Brandt, E.V.; Young, D.A.; Ferreira, D.; Roux, D.G. *J. Chem. Soc., Perkin Trans. 1*, 1986, 1737.
5. Van Zyl, P.W.; Steynberg, J.P.; Brandt, E.V.; Ferreira, D. *Magn. Reson. Chem.*, 1993, 31, 1057.

(*Received in UK* 26 *May* 1994; *revised* 4 *August* 1994; *accepted* 12 *August* 1994)