

## Enantiomerism in Natural Procyanidin Polymers: Use of Epicatechin as a Chiral Resolution Reagent

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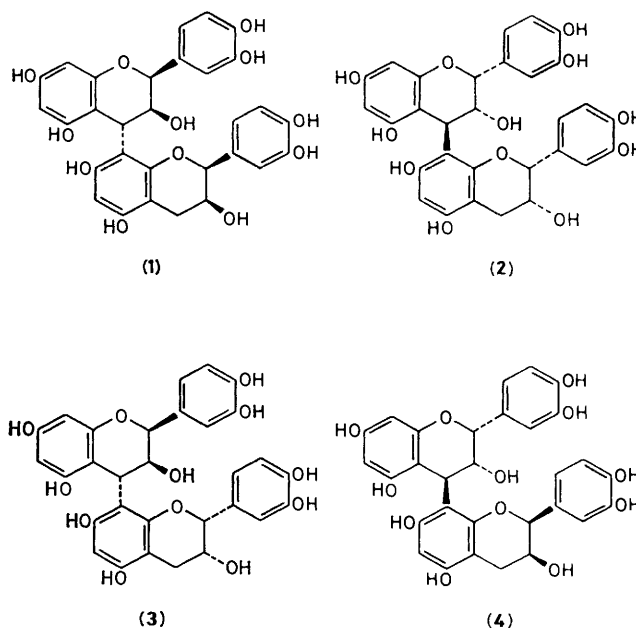
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Procyanidin polymers isolated from *Palmae* species contain 2,3-*cis* 5,7,3',4'-tetrahydroxyflavan-3-ol units predominantly of the abnormal (2*S*,3*S*) configuration, but also containing about 25% of units with a (2*R*,3*R*) configuration; the proportion of each enantiomer was determined by the stereo- and regio-specific condensation of each unit's carbocation with (2*S*,3*S*)-(+) or (2*R*,3*R*)-(−)-epicatechin and resolution of the diastereoisomeric C(4)–C(8) linked epicatechin dimers.

Procyanidins normally consist of 5,7,3',4'-tetrahydroxyflavan-3-ol units with a 2*R* configuration.<sup>1</sup> The occurrence in the family *Palmae* of (2*S*,3*S*)-(+)-epicatechin<sup>2</sup> and the dimer *ent*-procyanidin B2 (**1**)<sup>3</sup> is therefore exceptional, and prompted us to investigate the polymeric procyanidins of these plants. In particular, the leaves of *Phoenix canariensis* yielded a procyanidin (PC) polymer, shown by <sup>13</sup>C n.m.r. spectroscopy<sup>4</sup> to consist exclusively of 2,3-*cis*-PC units. The polymer exhibited a strong negative specific rotation,  $[\alpha]_{578}^{30} -91^\circ$  (*c* 0.8 in water), which is consistent<sup>4</sup> with the expected 2*S* configuration. This value may be contrasted with the strong positive specific rotation,  $[\alpha]_{578}^{30} +174^\circ$ , possessed by polymers consisting exclusively of 2,3-*cis*-PC units with a 2*R* configuration.<sup>4</sup> The difference in magnitude of the specific rotations is consistent with the palm polymer being partly racemic. Computation based on the additive effect of chiroptical contributions from each enantiomer<sup>5</sup> showed that the ratio of 2*S*:2*R* units is 73:27.

Confirmation of this estimate required cleavage of the polymer into constituent units and their chiral resolution. This was facilitated by the known ready cleavage of polymeric procyanidins in mild acid solution to form the monomeric 4-carbocations,<sup>4</sup> with retention of configuration, followed by their stereo- and regio-specific condensation<sup>6,7</sup> with (2*R*,3*R*)-(−)-epicatechin to form the dimeric diastereoisomers (**2**) and (**3**). Chiral resolution was effected by separation of the dimers by reverse-phase h.p.l.c.<sup>8</sup> to give procyanidin B2 (**2**),<sup>†</sup>  $[\alpha]_{578}^{30} +24.5^\circ$  (*c* 0.20 in methanol–water, 1:1 v/v) and (**3**),  $[\alpha]_{578}^{30} -182^\circ$  (*c* 0.15 in methanol–water, 1:1 v/v). Measurement of the relative amounts of (**2**) and (**3**) by h.p.l.c. gave a ratio of 76:24 for 2*S*:2*R*, in close agreement with the value calculated from the specific rotation.

Similar regiospecific capture by (2*S*,3*S*)-(+)-epicatechin of the carbocation generated by acid treatment of a polymer



containing 2*R* 2,3-*cis*-PC units, yielded, almost exclusively, the dimer (**4**),  $[\alpha]_{578}^{30} +187^\circ$  (*c* 0.23 in methanol–water, 1:1 v/v), the enantiomer of (**3**). Finally, reaction of the *P. canariensis* tannin with (2*S*,3*S*)-(+)-epicatechin yielded (**4**), and the last theoretically possible diastereoisomer of procyanidin B2, (**1**),  $[\alpha]_{578}^{30} -23.9^\circ$  (*c* 0.19 in methanol–water, 1:1 v/v); the two dimers were resolved by h.p.l.c., and thus provided a further estimate of 2*S*:2*R*, from the relative amounts of (**1**) and (**4**), of 73:27.

Conformational differences, readily apparent from molecular models, probably account for the ready resolution of the diastereoisomeric pairs of dimers by h.p.l.c. Such differences were observed in the <sup>1</sup>H n.m.r. spectra of the deca-acetates, where the chemical shift of 8-H in the most shielded conformer

<sup>†</sup> Structures of all compounds in this study were supported by satisfactory analytical and spectroscopic data.

of (3) and (4) was at  $\delta$  6.4, intermediate between that of the C(4)–C(6) linked dimer, procyanidin B5,  $\delta$  6.6, and the highly shielded position displayed by (1) and (2),  $\delta$  6.0.

The above is the first chiral resolution of procyanidin units, and the first synthesis of the four theoretically possible diastereoisomers of a C(4)–C(8) linked procyanidin dimer with the same relative configuration of C-2, C-3, and C-4.

The authors thank Drs. R. H. Newman and H. Wong for n.m.r. spectra.

Received, 26th October 1981; Com. 1256

### References

- 1 E. Haslam in 'The Flavonoids,' eds. J. B. Harborne, T. J. Mabry, and H. Mabry, Chapman and Hall, London, 1975, p. 510.
  - 2 F. Delle Monache, F. Ferrari, A. Poce-Tucci, and G. B. Marini-Bettolo, *Phytochemistry*, 1972, **11**, 2333.
  - 3 F. Delle Monache, F. Ferrari, and G. B. Marini-Bettolo, *Gazz. Chim. Ital.*, 1971, **101**, 387.
  - 4 Z. Czochanska, L. Y. Foo, R. H. Newman, and L. J. Porter, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2278.
  - 5 P. Salvadori and F. Ciardelli, in 'Fundamental Aspects and Recent Developments in ORD and CD,' eds. F. Ciardelli and P. Salvadori, Heyden, London, 1973, p. 6.
  - 6 E. Haslam, *J. Chem. Soc., Chem. Commun.*, 1974, 594.
  - 7 J. J. Botha, D. Ferreira, and D. G. Roux, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1235.
  - 8 R. W. Hemingway, L. Y. Foo, and L. J. Porter, *J. Chem. Soc., Chem. Commun.*, 1981, 320.
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