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Acid-catalyzed rearrangements of flavans to novel benzofuran derivatives.

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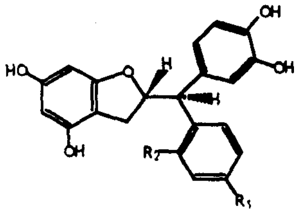
The objective of this work was to define. reactions that occur when proanthocyanidins arid their derivatives are reacted in the presence of acidcatalysts. Pure compounds (either as the free phenols, the methyl ether, or the methyl ether-acetate derivatives) were isolated by a variety of chromatographic methods. Proof of their structure was based mainly on 2D-NMR as well as high-resolution MS and CD experiments. Some of the results of these experiments are summarized here.

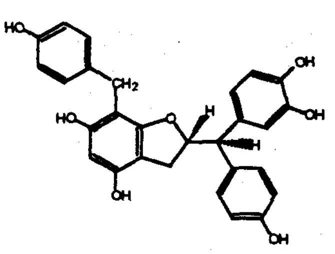
Reaction of (+)-catechin with phenol and either sulfuric or hydrochloric acid catalysts (Peng, Conner, Hemingway, 1997) gave 2-[(3,4-dihydroxyphenyl)(4-hydroxyphenyl)methyl]-2,3-dihydro-4,6-benzofurandiol (1) as previously reported from similar reactions catalyzed by Lewis acids (Mitsunaga, Abe, Ohara, 1994). In addition, the 2-hydroxyphenyl derivative (2) resulting from *ortho* condensation of phenol at $C\text{-}2_C$ was isolated. The product 2-[3,4-dihydroxyphenyl)(4-hydroxyphenyl)methyl]-2,3-dihydro-7-(4-hydroxyphenyl)methyl-4,6-benzofurandiol (3) resulting From liberation of formaldehyde and condensation of *p*-hydroxybenzyl alcohol on the pbloroglucinol A-ring was also obtained. An appreciation for the high reactivity of the phlorogucinol A-ring is obtained by the isolation of a product in which catechin competed for the $C\text{-}2_C$ carbocation even though the mole ratio of phenol to catechin was about 40: 1. Subsequent reaction of phenol at C-2 of the lower unit and two dehydration ring closures resulted in the formation of 2-(1,3,5-trihydroxyphenyl)-methyl-3-(3,4-dihydroxyphenyl)-6-[(3,4-dihydroxyphenyl)(4-

hydroxyphenyl)methyl]-2,3,5,6-tetrahydrobenzo-[1,2-b,5,4-b’]-difuran-4-ol (4).



(1) R1 = OH; R2 = H

(2) R1 = H; R2 = OH



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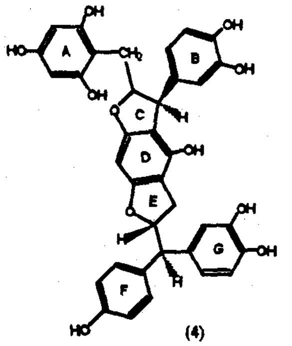
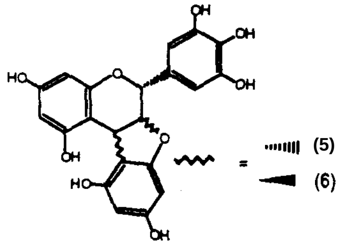
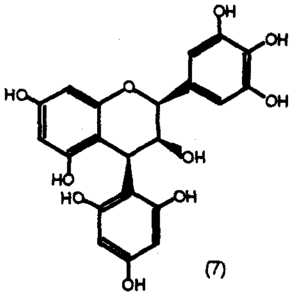


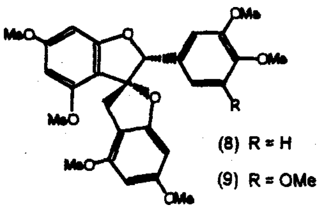
(4)

A series of novel benzofuran derivatives was obtained from reaction of a prodelphinidin polymer with phloroglucinol at 105 “C for 24 and 48 hours using acetic acid as a catalyst (Steynberg, Steynberg, Hemingway, Ferreira, McGraw, 1997). The stereochemistry of the two [1]benzofuro[2,3-c]chromenes (5) and (6) isolated suggested that a phenohc hydroxy group of the phloroglucinol unit displaced the protonated 3 hydroxy of the pyran ring in an S_N2 dehydration. Further experiments suggested that may not be required. Perhaps the most important product isolated from these experiments was the 2S all-*cis* phloroglucinol adduct (7) demonstrating inversion of the stereochemistry at C-2$_C$ when reaction conditions are pushed to long times at high temperature. Most surprising was the formation of **(2*R*,3*R*)-2-(3,4-dimethoxyphenyl)-4,4',6,6'-tetramethoxy-3,2'-spirobi[2,3-dihydro[1]benzofuran]** (8) and the **3,4,5-trimethoxy** analogue from the prodelphinidins (9). These rearrangement reactions explain why higher yields of flavan-4-phloroglucinol adducts are not obtained by prolonged heating with acetic acid.





(7)



(8) R = H

(9) R = OMe

References

MITSUNAGA, T., ABE, I., OHARA, S. 1994, The Chemical Structure and Stereochemistry of Phenol Adduct Compounds Derived from (+)-Catechins Upon Phenolation. Mokuzai Gakkaishi, 40: 100-106.

PENG, W., CONNER, A.H., HEMINGWAY, R.W. 1997, Phenolation of (+)-Catechin with Mineral Acids. II Identification of New Reaction Products, *J. Wood Chem. Technol.* 17(4):341-360.

STEYNBERG, P.J, STEYNBERG, J.P., HEMINGWAY, R.W., FERREIRA, D., McGraw, G.W. 1997, Acid-Catalyzed Rearrangements of Flavan-4-Phloroglucinol Derivatives to Novel 6-Hydroxyphenyl-6a, 11 b-Dihydro-6H-[1]Benzofuro[2,3-c]-Chromenes and Hydroxyphenyl-3,2'-Spirobi[dihydro[1]Benzofurans. *J. Chem. Soc. Perkin Trans. I*, :2395-2403.