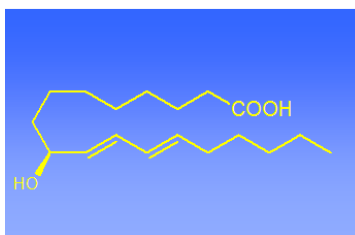


Lipid of the Month: January 2009

Dimorphecolic acid



Dimorphecolic acid was isolated in 1960 by Wolff *et al.* (1) from seeds of *Dimorphotheca aurantiaca* and assigned the structure 9-hydroxy-10(*E*),12(*E*)-octadecadienoic acid.

Subsequent studies demonstrated that the chiral carbon had the "*S*" absolute configuration (2). Also the related 9(*S*)-hydroxy-10(*E*),12(*Z*)-octadecadienoic acid (9-HODE) has been isolated from natural sources, and in order to distinguish the 12(*E*) and 12(*Z*) compounds the former is sometimes referred to as β -dimorphecolic acid and the latter α -dimorphecolic acid. Several total syntheses of these compounds have been described (see ref. 3 and references cited therein).

Biosynthesis of α -dimorphecolic acid takes place by reduction of the corresponding hydroperoxide (9-HPODE), which is formed from linoleic acid in the presence of 9-lipoxygenases. The reduction step can be accomplished by a peroxidase and an electron donor, or by a peroxygenase-catalyzed coupled reduction/oxidation. β -Dimorphecolic acid, on the other hand, is not a lipoxygenase product (4). It is formed from oleic acid by action of two unusual desaturases which are present in developing seeds of *Dimorphotheca sinuata* (5). These enzymes, DsFAD2-1 and DsFAD2-2, are both non-heme diiron proteins related to the common plant oleate desaturase (FAD2), which converts oleate to linoleate. DsFAD2-1 was found to introduce an *E* double bond at the Δ^{12} position of oleate thus producing the linoleic acid isomer 9(*Z*),12(*E*)-octadecadienoic acid. Further conversion of this compound by DsFAD2-2 involved a) elimination of a hydrogen from C-11, b) isomerization of the Δ^9 double bond to the Δ^{10} position and c) capture of OH from the Fe(III)-O-Fe(IV)-OH group of

the enzyme to create the final 9(*S*)-hydroxy-10(*E*),12(*E*) partial structure.

The diiron cluster present in FAD2 type desaturases has significant catalytic potential. Not only does it catalyze introduction of a double bond in the Δ^{12} position, but depending on its amino acid environment it can also introduce a hydroxyl group at C-12, an epoxide group at C-12/C-13, or a triple bond at C-12/C-13 (6-9). It seems likely that the 15(*R*)-hydroxylinoleic acid present in oat seeds (10) is biosynthesized in an analogous way by a homolog of linoleate Δ^{15} desaturase.

The biological properties of β -dimorphecolic acid are not well studied, however, α -dimorphecolic acid (9-HODE) serves as a ligand for G2A, a stress-inducible G protein-coupled receptor in human keratinocytes, and may play a proinflammatory role in skin under oxidative conditions (11). Furthermore, 9-HODE as well as 13-HODE and 15-deoxy- $\Delta^{12,14}$ -prostaglandin J_2 activate peroxisome proliferator-activated receptor- γ (PPAR γ), which has important roles in *e.g.* lipid and carbohydrate metabolism (12).

Dimorphecolic acid (O-1802-10g) from Lipidox is isolated from seeds of *Dimorphotheca sinuata*. Also available is α -dimorphecolic acid (O-1802-10b) and the above-mentioned compounds 9(*Z*),12(*E*)-octadecadienoic acid (A-1802-1b) and 15(*R*)-hydroxylinoleic acid (O-1802-3d).

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