

## Product Information

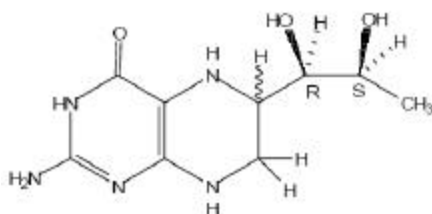
### (6R)-5,6,7,8-Tetrahydrobiopterin dihydrochloride

Product Number **T4425**

Storage Temperature  $-20\text{ }^{\circ}\text{C}$

CAS RN: 69056-38-8

Synonyms: BH<sub>4</sub>; 6R-BH<sub>4</sub>; Sapropterin; Dapropterin; 2-amino-6-(1,2-dihydroxypropyl)-5,6,7,8-tetrahydro-3H-pteridin-4-one



#### Product Description

Molecular formula: C<sub>9</sub>H<sub>15</sub>N<sub>5</sub>O<sub>3</sub> · 2HCl

Formula weight: 314.17

$[\alpha]_D^{25} = -6.6^{\circ}$  to  $-7.6^{\circ}$  (C = 1 in 0.1 N HCl).

$E^{216}_{1\%} = 15,400$  (0.1 N HCl)<sup>1</sup>

$E^{264}_{1\%} = 13,750$  (0.1 N HCl)<sup>1</sup>

Tetrahydrobiopterin is a natural cofactor for phenylalanine hydroxylase,<sup>2</sup> tyrosine hydroxylase,<sup>3</sup> tryptophan hydroxylase,<sup>4</sup> nitric oxide synthase,<sup>5</sup> and alkylglycerol monooxygenase.<sup>6</sup> Thus, it is necessary *in vivo* for the conversion of phenylalanine to tyrosine and for the production of the hormone epinephrine and of the monoamine neurotransmitters, serotonin, dopamine, and norepinephrine.<sup>7</sup> It is also involved in apoptosis and other cellular events mediated by nitric oxide production<sup>8,9</sup> and catalyzes the cleavage of alkylglycerol ethers.<sup>6</sup>

Tetrahydrobiopterin is synthesized *in vivo* from GTP by the sequential action of GTP cyclohydrolase I, pyruvoyltetrahydrobiopterin synthase, and sepiapterin reductase.<sup>5,9</sup>

During enzymatic hydroxylations or production of nitric oxide *in vivo*, tetrahydrobiopterin is oxidized to a quinonoid dihydrobiopterin intermediate that is rapidly recycled to tetrahydrobiopterin by dihydropteridine reductase and NADPH.<sup>8,10</sup>

In the absence of dihydropteridine reductase *in vivo* or in aqueous buffer *in vitro*, the quinonoid intermediate isomerizes to form 7,8-dihydrobiopterin. The latter can be reduced to tetrahydrobiopterin *in vivo* by the action of dihydrofolate reductase and NADPH.<sup>1</sup>

Some forms of phenylketonuria are due to deficiencies in tetrahydrobiopterin production and can be potentially treated with tetrahydrobiopterin instead of a low phenylalanine diet.<sup>11</sup>

Tetrahydrobiopterin can be produced from 7,8-dihydrobiopterin *in vitro* by enzymatic reduction with dihydrofolate reductase and NADPH<sup>7</sup> or by catalytic reduction with H<sub>2</sub> in the presence of PtO<sub>2</sub>.<sup>10</sup> Review articles on tetrahydrobiopterin are available.<sup>12,13</sup>

#### Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

#### Preparation instructions

The product is soluble in oxygen-free water (20 mg/ml).

#### Storage and Stability

Tetrahydrobiopterin is very hygroscopic. The product should be stored desiccated and protected from light at  $-20\text{ }^{\circ}\text{C}$ . Under these conditions the product is stable for 3 years.

Tetrahydrobiopterin reacts with oxygen, especially in neutral and alkaline solutions. Due to oxidation, tetrahydrobiopterin solutions become yellow, but are relatively stable at  $-20\text{ }^{\circ}\text{C}$ . Solutions in 0.1 N HCl are stable for several weeks at  $-20\text{ }^{\circ}\text{C}$ . Its half-life in 0.1 M phosphate buffer, pH 6.8, is ~16 minutes at room temperature and it is completely destroyed in 90 minutes.<sup>1,10</sup> In neutral phosphate or HEPES buffer, the primary breakdown product is 7,8-dihydrobiopterin with some loss of the alkyl sidechain to form 7,8-dihydropterin. In neutral Tris, bicine, or bicarbonate buffer, 7,8-dihydropterin is the major breakdown product.<sup>14,15</sup>

## References

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NDH,PHC,MAM 02/06-1

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