

Neotame

1 Nonproprietary Names

USP–NF: Neotame

2 Synonyms

3-(3,3-Dimethylbutylamino)-*N*-(α -carboxyphenethyl)succinamic acid methyl ester; *N*-[*N*-(3,3-dimethylbutyl)-*L*- α -aspartyl]-*L*-phenylalanine 1-methyl ester; E961; *L*-phenylalanine, *N*-[*N*-(3,3-dimethylbutyl)-*L*- α -aspartyl]-1-methyl ester.

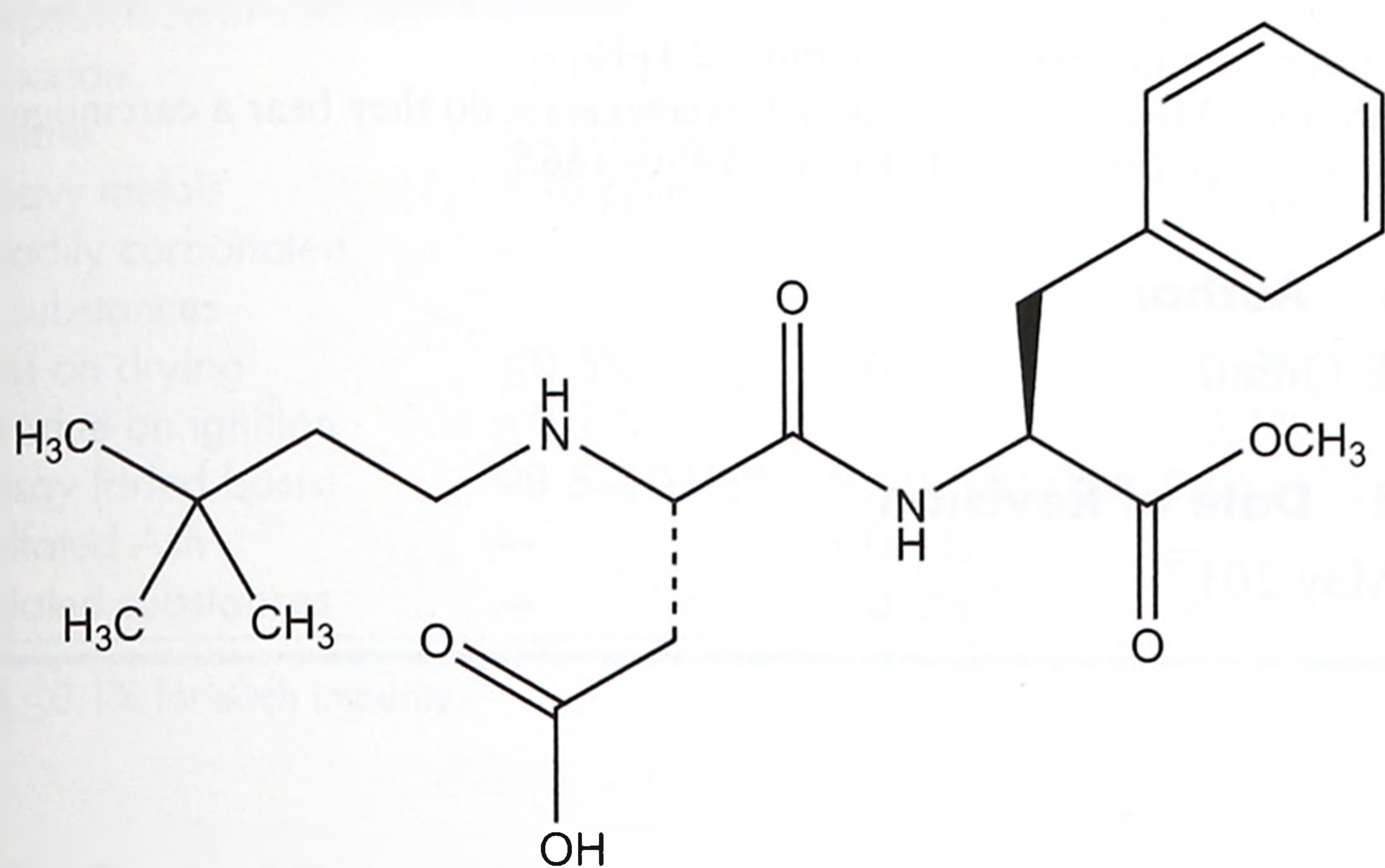
3 Chemical Name and CAS Registry Number

(3*R*)-3-(3,3-Dimethylbutylamino)-4-[[*(2R)*-1-methoxy-1-oxo-3-phenylpropan-2-yl]amino]-4-oxobutanoic acid [165450-17-9]

4 Empirical Formula and Molecular Weight

C₂₀H₃₀N₂O₅ 378.47

5 Structural Formula



6 Functional Category

Flavor enhancer; sweetening agent.

7 Applications in Pharmaceutical Formulation or Technology

Neotame is a water-soluble, nonnutritive, intense sweetening agent used in beverages and foods. It is structurally related to aspartame and is about 7000–13 000 times sweeter than sucrose, and about 30–60 times sweeter than aspartame, making it the sweetest artificial sweetener available. Neotame is said to have a ‘clean’ sweet taste in contrast to the bitter, metallic aftertaste associated with saccharin. Although neotame has approximately the same caloric value as sucrose (1.2 kJ/g) the small quantities used to achieve a desired level of sweetness in a formulation mean that it is essentially nonnutritive.

Neotame may be used in sub-sweetening quantities as a flavor enhancer, e.g. with mint or strawberry flavor.

8 Description

Neotame occurs as an odorless, white to off-white powder. It has an intense sweet taste 7000–13 000 times sweeter than sucrose depending on the matrix.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for neotame.

Test	USP 40–NF 35 S1
Identification	+
Specific optical rotation	–40.0° to –43.4°
Water	≤5.0%
Residue on ignition	≤0.2%
Lead	≤2 μg/g
Related compounds	+
Assay (anhydrous basis)	97.0–102.0%

10 Typical Properties

Acidity/alkalinity pH = 5.0–7.0 (0.5% w/v aqueous solution)

Dissociation constant

pK_{a1} = 3.01;

pK_{a2} = 8.02.

Melting point 80–83°C

Solubility see Table II.

Table II: Solubility of neotame.

Solvent	Solubility at 25°C unless otherwise stated
Ethanol	1 in 1.05
Ethyl acetate	1 in 23 at 15°C 1 in 13
Water	1 in 1 at 60°C 1 in 94 at 15°C 1 in 79 1 in 21 at 60°C

11 Stability and Storage Conditions

Neotame stability is affected by moisture, pH, and temperature. Neotame is stable in bakery products and pasteurized dairy products.

The bulk material should be stored in a well-closed container, in a cool, dry place; it is stable for up to 5 years at room temperature.

12 Incompatibilities

—

13 Method of Manufacture

Neotame is manufactured by the reaction of aspartame and 3,3-dimethylbutyraldehyde, followed by purification, drying, and milling.^(1–3)

14 Safety

Studies in animals and humans have shown that neotame is a relatively nontoxic, nonteratogenic, and noncarcinogenic substance. It is reported as safe for use during pregnancy and lactation, and by children and persons with diabetes.

Human studies in healthy and diabetic patients suggest that neotame is well-tolerated at doses up to 1.5 mg/kg body-weight daily (the highest dose studied). Following reviews of over 100

N