

Step1: 3-Cyclobutyl-7-[[4-(1H-imidazol-1-yl)-4-oxobutyl]oxy]-2,3,4,5-tetrahydro-1H-3-benzazepine

4-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]butanoic acid (E167b) (0.90 g, 2.8 mmol) was dissolved in dimethylformamide (10 ml) and treated with 1,1'-carbonyl diimidazole (0.59 g, 3.6 mmol). After stirring at room temperature for 2.5 hours, the reaction mixture concentrated *in vacuo*. The crude residue was dissolved in dichloromethane, washed with brine and dried (sodium sulfate). The organic layer was filtered and concentrated *in vacuo* and the crude residue used directly in the next step without further purification.

Step 2: 3-Cyclobutyl-7-[[4-oxo-4-(1-piperidinyl)butyl]oxy]-2,3,4,5-tetrahydro-1H-3-benzazepine (E167)

Piperidine (0.1 ml, 1.1 mmol) was added to a stirred solution of 3-cyclobutyl-7-[[4-(1H-imidazol-1-yl)-4-oxobutyl]oxy]-2,3,4,5-tetrahydro-1H-3-benzazepine (E167, Step 1) (150 mg, 0.42 mmol) in dichloromethane (5 ml). After stirring at room temperature for 5 days the reaction mixture was concentrated *in vacuo* and the resulting residue was purified by column chromatography eluting with a mixture of .880 ammonia: ethanol: dichloromethane (1: 9: 90) to afford the title compound (E167); MS (ES+) *m/e* 371 [M+H]⁺.

Examples 168-170

Examples 168-170 (E168-E170) were prepared from Example 167 Step 1, using an analogous method to that described for Example 167 Step 2 substituting piperidine for the appropriate amine indicated in the table:

Example	Amine	LC/MS (M+H ⁺)
3-Cyclobutyl-7-[[4-oxo-4-(1-pyrrolidinyl)butyl]oxy]-2,3,4,5-tetrahydro-1H-3-benzazepine (E168)	Pyrrolidine	357
4-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-N-cyclopentylbutanamide (E169)	Cyclopentylamine	371
4-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-N-methylbutanamide (E170)	Methylamine	317

Examples 171-176

Examples 171-176 (E171-E176) were prepared from Example 123, Step 1 and the appropriate amine indicated in the table using an analogous method to that described for Example 123 Step 2 (E123):

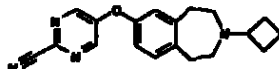
Example	Amine	LC/MS (M+H ⁺)
5-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-	Isopropylamine	381

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benzazepin-7-yl)oxy]-N-(1-methylethyl)-2-pyrazinecarboxamide (E171)		
5-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-N-(tetrahydro-2H-pyran-4-yl)-2-pyrazinecarboxamide (E172)	Tetrahydro-2H-pyran-4-amine	423
7-[[5-(1-Azetidinylcarbonyl)-2-pyrazinyl]oxy]-3-cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepine (E173)	Azetidine	379
5-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-N,N-diethyl-2-pyrazinecarboxamide (E174)	Diethylamine	395
5-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-N-[2-(methyloxy)ethyl]-2-pyrazinecarboxamide (E175)	2-(Methyloxy)ethylamine	397
5-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-N-ethyl-2-pyrazinecarboxamide (E176)	Ethylamine	367

Example 177a

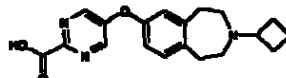
5-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-2-pyrimidinecarbonitrile (E177a)



- 5 3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-ol (E3) (1.81 g, 8.33 mmol) was dissolved in pyridine (40 ml) and sodium hydride (80% in mineral oil, 0.40 g, 10.0 mmol) was added with stirring under argon at 0 °C. The mixture was left to stir for 5 minutes. Copper (I) bromide (1.68 g, 11.7 mmol) was added and the mixture allowed to warm to room temperature over 30 minutes. 5-Bromo-2-pyrimidinecarbonitrile (D38) (2.30 g, 12.5 mmol) in pyridine (8 ml) was added and the mixture heated at 100 °C for 1 hour. The mixture was allowed to cool to room temperature and the solvent removed *in vacuo*. The crude product was purified by column chromatography, eluting with a mixture of 0.880 ammonia: methanol: dichloromethane (0.2:1.8:98) to afford the title compound (E177a); MS (ES⁺) *m/e* 321 [M+H]⁺.
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Example 177b

5-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-2-pyrimidinecarboxylic acid (E177b)



- 20 5-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-2-pyrimidinecarbonitrile (E177a) (1.22 g, 3.81 mmol) was dissolved in ethanol (20 ml), treated with 10% sodium