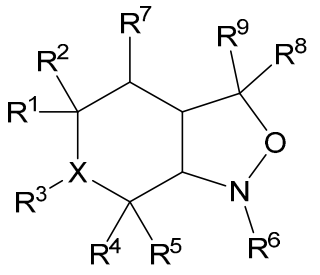
Claims

1. Non-medical method of modulating of transient receptor potential channel melastatin member 8 (TRPM8) comprising bringing the receptor into contact with a compound of formula (Ia), a salt or solvate thereof



(Ia)

wherein

X is C,

R^3 is selected from hydrogen, C_1-C_6 alkyl, C_1-C_7 alkyl substituted with one or two OH groups, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkyl substituted with one or two OH groups, C_5-C_7 cycloalkenyl, C_5-C_7 cycloalkenyl substituted with one, two or three C_1-C_3 alkyl groups, and phenyl;

R^1 is selected from hydrogen,

C_1-C_6 alkyl,

C_1-C_7 alkyl substituted with one or two OH groups,

C_3-C_7 alkenyl,

phenyl optionally substituted with up to five substituents selected from the group consisting of halogen, C≡N, NO_2, C_1-C_6 alkyl, C_1-C_6 alkyl comprising up to 5 halogen atoms, C_1-C_6 alkyloxy, C_1-C_6 alkyloxy comprising up to 5 halogen atoms, C_3-C_7 cycloalkyl, –C(O)O-R^{10} wherein R^{10} is selected from hydrogen and C_1-C_3 alkyl, and –SR^{11} wherein R^{11} is selected from hydrogen and C_1-C_3 alkyl,

naphthyl optionally substituted with up to five substituents selected from the group consisting of halogen, C≡N, NO_2, C_1-C_6 alkyl, C_1-C_6 alkyl comprising up to 5 halogen atoms, C_1-C_6 alkyloxy, C_1-C_6 alkyloxy comprising up to 5 halogen atoms, C_3-C_7 cycloalkyl, –C(O)O-R^{10} wherein R^{10} is selected from hydrogen and C_1-C_3 alkyl, and –SR^{11} wherein R^{11} is selected from hydrogen and C_1-C_3 alkyl, and

C_5-C_{10} mono- or bicyclic aryl wherein 1 or 2 C-atoms are replaced by a hetero atom independently selected from sulfur, nitrogen, and oxygen, optionally substituted with up to three substituents selected from the group consisting of halogen, C≡N, NO_2, C_1-C_6 alkyl, C_1-C_6 alkyl comprising up to 5 halogen atoms, C_1-C_6 alkyloxy, C_1-C_6 alkyloxy comprising up to 5 halogen atoms, C_3-C_7 cycloalkyl, –C(O)O-R^{10} wherein R^{10} is selected from hydrogen and C_1-C_3 alkyl, and –SR^{11} wherein R^{11} is selected from hydrogen and C_1-C_3 alkyl;

R^2 is selected from hydrogen and methyl;

R^4, R^5, and R^7 are independently selected from hydrogen and C_1-C_6 alkyl;

R^6 is selected from hydrogen, C_1-C_6 alkyl, and C_3-C_7 cycloalkyl;

R^8 and R^9 are independently selected from hydrogen, and C_1-C_6 alkly, or

R^8 and R^9 form together with the C-atom to which they are attached a 3, 4, 5, 6, or 7- membered cycloalkyl ring.

2. Non-medical method according to claim 1 wherein the compound of formula (Ia), a salt or solvate thereof is a compound, wherein R^3 is selected from hydrogen, C_1-C_6 alkyl, C_1-C_7 alkyl substituted with one or two OH groups, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkyl substituted with one or two OH groups, C_5-C_7 cycloalkenyl, C_5-C_7 cycloalkenyl substituted with one, two or three C_1-C_3 alkyl groups, and phenyl.

3. Non-medical method according to claim 1 wherein the compound of formula (Ia) is selected from the group consisting of 4-methyl-3-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 4-methoxy-3-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1-ethyl-5-(2-methoxyphenyl)-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 5-(2-methoxyphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(3,5-difluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1,3,3,5,7-pentamethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 5-(5-chloro-2-methylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 3-(1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazol-5-yl)-4-methoxybenzonitrile; 5-(2,5-

dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 3-(1-ethyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazol-5-yl)-4-methylbenzonitrile; 5-(5-fluoro-2-methylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-5-(2-methoxyphenyl)-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 3-chloro-5-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 3-(1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 5-(3,4-difluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 3-(1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazol-5-yl)-4-methylbenzonitrile; 5-(2-methoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 2-methyl-5-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; methyl 4-methyl-3-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzoate; 1-isopropyl-3,3,5,7-tetramethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 5-(3-fluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-phenyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,7-trimethyl-5-phenyloctahydrobenzo[c]isoxazole; 5-(4-chloro-2-methylphenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 5-(2,4-dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(4-fluoro-2-methylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(2,5-difluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-ethyl-3,3,5,7-tetramethyl-5-phenyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(p-tolyl)octahydrobenzo[c]isoxazole; 1-isopropyl-3,3,5,7-tetramethyl-5-phenyloctahydrobenzo[c]isoxazole; 1,3,3,7-tetramethyl-5-phenyloctahydrobenzo[c]isoxazole; 1-isopropyl-5-(2-methoxyphenyl)-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(2-fluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 4-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 3-methyl-4-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 5-(2,4-difluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(2,5-dimethoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(2,3-dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(2,4,5-trimethylphenyl)octahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(4-(methylthio)phenyl)octahydrobenzo[c]isoxazole; 2-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 5-(3-methoxyphenyl)-

1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(3-chloro-2-methylphenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(naphthalen-2-yl)octahydrobenzo[c]isoxazole; 5-(2,4-dimethylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 4-methyl-3-(1,3,3,7-tetramethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1,3,3,7-tetramethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(2-ethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(m-tolyl)octahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(5-methylthiophen-3-yl)octahydrobenzo[c]isoxazole; 1-ethyl-3,3,7-trimethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(2-ethylphenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(2,6-dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(benzo[d][1,3]dioxol-5-yl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-5-(6-methoxypyridin-2-yl)-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(5-chloro-2-methylphenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 5-butyl-1,3,3-trimethyloctahydrobenzo[c]isoxazole; 5-(2,4-dimethoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,7-trimethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 1-isopropyl-3,3,7-trimethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(5-fluoro-2-methylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(3,5-dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 1,3,3-trimethyl-6-(4-methylcyclohex-3-en-1-yl)octahydrobenzo[c]isoxazole; 5-(3-fluoro-5-(trifluoromethyl)phenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3-dimethyl-5-propyloctahydrobenzo[c]isoxazole; 1,3,3-trimethyl-5-pentyloctahydrobenzo[c]isoxazole; 1-ethyl-3,3,5,7-tetramethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 5-(3,5-dimethylphenyl)-1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(2,5-dimethylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5,7-diethyl-1-isopropyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(2-methyl-5-(trifluoromethyl)phenyl)octahydrobenzo[c]isoxazole; 1-ethyl-3,3-dimethyl-5-propyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-propyloctahydrobenzo[c]isoxazole; 1,3,3-trimethyl-5-

propyloctahydrobenzo[c]isoxazole; 2-methyl-3-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1,3,3,7-tetramethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 5-butyl-1-ethyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 5-(4-fluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(furan-3-yl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazol-1-ium chloride; 1,3,3,5,7-pentamethyl-5-(naphthalen-1-yl)octahydrobenzo[c]isoxazole; 5-(2-ethoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(3-chloro-2-methylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(6-methoxypyridin-2-yl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(5-methylthiophen-2-yl)octahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(4-methylpyridin-3-yl)octahydrobenzo[c]isoxazole; 1-ethyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(2-ethylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-butyl-1-isopropyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 1-ethyl-3,3,5,7-tetramethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(4-fluoro-2-methylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-5,7-dimethylhexahydro-1H-spiro[benzo[c]isoxazole-3,1'-cyclopentane]; 1,5,7-triethyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,5,7-tetramethyl-5-propyloctahydrobenzo[c]isoxazole; 6-isopentyl-1,4,4,8-tetramethyloctahydro-2H-benzo[d][1,3]oxazine; 5-(3,5-dimethoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5,7-diethyl-1,3,3-trimethyloctahydrobenzo[c]isoxazole; 1-isopropyl-5-(4-methoxyphenyl)-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(3-isopropylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3-trimethyl-6-phenyloctahydrobenzo[c]isoxazole; 5-ethyl-1-isopropyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(2-(methylthio)phenyl)octahydrobenzo[c]isoxazole; 1,5,7-trimethylhexahydro-1H-spiro[benzo[c]isoxazole-3,1'-cyclopentane]; 5-ethyl-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(4-methoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,4,5,7-hexamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(pyridin-3-

yl)octahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole hydrochloride; 5-(4-fluoro-2-methoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(4-fluorophenyl)-1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 4-methyl-2-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1,3,3,5-tetramethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 6-isopentyl-1,4,4,8-tetramethyloctahydro-2H-benzo[d][1,3]oxazin-2-one; 1-isopropyl-3,3,5,7-tetramethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-isopentyl-1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 2-chloro-5-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 5-(4-(tert-butyl)phenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(4-(tert-butyl)phenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(4-(tert-butyl)phenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; and 1,3,3,6-tetramethyloctahydrobenzo[c]isoxazole, or a salt or solvate thereof.

4. A non-medical method of inducing a cooling sensation in a human or animal comprising contacting the human or animal with a compound of formula (Ia), or a salt or solvate thereof, as defined in claim 1 to 3.

5. A non-medical method of achieving a cooling effect on the skin or mucosa comprising contacting the skin or mucosa with a product comprising one or more compounds of formula (Ia) as defined in claim 1 to 3.

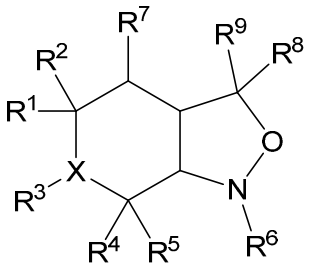
6. A consumer product comprising one or more compounds of formula (Ia) as defined in claim 1 to 3.

7. A pharmaceutical composition comprising one or more compounds of formula (Ia) as defined in claim 1 to 3.

8. The compound of formula (Ia) as defined in claim 1 to 3, for use in providing cooling sensation.

9. The compound of formula (Ia) as defined in claim 1 to 3 for use as medicament.

10. A composition comprising a cool sensation wherein the composition comprises a compound of formula (Ia)



(Ia)

wherein

X is C,

R^3 is selected from hydrogen, C_1-C_6 alkyl, C_1-C_7 alkyl substituted with one or two OH groups, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkyl substituted with one or two OH groups, C_5-C_7 cycloalkenyl, C_5-C_7 cycloalkenyl substituted with one, two or three C_1-C_3 alkyl groups, and phenyl;

R^1 is selected from hydrogen,

C_1-C_6 alkyl,

C_1-C_7 alkyl substituted with one or two OH groups,

C_3-C_7 alkenyl,

phenyl optionally substituted with up to five substituents selected from the group consisting of halogen, C≡N, NO_2, C_1-C_6 alky, C_1-C_6 alkyl comprising up to 5 halogen atoms, C_1-C_6 alkyloxy, C_1-C_6 alkyloxy comprising up to 5 halogen atoms, C_3-C_7 cycloalkyl, –C(O)O-R^{10} wherein R^{10} is selected from hydrogen and C_1-C_3 alkyl, and –SR^{11} wherein R^{11} is selected from hydrogen and C_1-C_3 alkyl,

naphthyl optionally substituted with up to five substituents selected from the group consisting of halogen, C≡N, NO_2, C_1-C_6 alkyl, C_1-C_6 alkyl comprising up to 5 halogen atoms, C_1-C_6 alkyloxy, C_1-C_6 alkyloxy comprising up to 5 halogen atoms, C_3-C_7 cycloalkyl, –C(O)O-R^{10} wherein R^{10} is selected from hydrogen and C_1-C_3 alkyl, and –SR^{11} wherein R^{11} is selected from hydrogen and C_1-C_3 alkyl, and

C_5-C_{10} mono- or bicyclic aryl wherein 1 or 2 C-atoms are replaced by a hetero atom independently selected from sulfur, nitrogen, and oxygen, optionally substituted with up to three substituents selected from the group consisting of halogen, C≡N, NO_2, C_1-C_6 alkyl, C_1-C_6 alkyl comprising up to 5 halogen atoms,

C_1-C_6 alkyloxy, C_1-C_6 alkyloxy comprising up to 5 halogen atoms, C_3-C_7 cycloalkyl, –C(O)O-R^{10} wherein R^{10} is selected from hydrogen and C_1-C_3 alkyl, and –SR^{11} wherein R^{11} is selected from hydrogen and C_1-C_3 alkyl;

R^2 is selected from hydrogen and methyl**;**

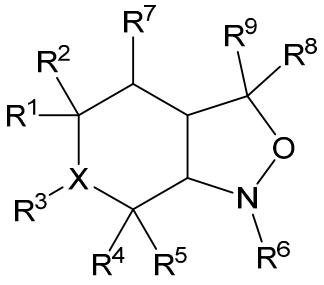
R^4, R^5, and R^7 are independently selected from hydrogen and C_1-C_6 alkyl;

R^6 is selected from hydrogen, C_1-C_6 alkyl, and C_3-C_7 cycloalkyl;

R^8 and R^9 are independently selected from hydrogen, and C_1-C_6 alkly, or

R^8 and R^9 form together with the C-atom to which they are attached a 3, 4, 5, 6, or 7- membered cycloalkyl ring.

11. A compound of formula (Ia), a salt or solvate thereof



(Ia)

wherein

X is C,

R^3 is selected from hydrogen, C_1-C_6 alkyl, C_1-C_7 alkyl substituted with one or two OH groups, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkyl substituted with one or two OH groups, C_5-C_7 cycloalkenyl, C_5-C_7 cycloalkenyl substituted with one, two or three C_1-C_3 alkyl groups, and phenyl;

R^1 is selected from hydrogen,

C_1-C_6 alkyl,

C_1-C_7 alkyl substituted with one or two OH groups,

C_3-C_7 alkenyl,

phenyl optionally substituted with up to five substituents selected from the group consisting of halogen, C≡N, NO_2, C_1-C_6 alkyl, C_1-C_6 alkyl comprising up to 5 halogen atoms, C_1-C_6 alkyloxy, C_1-C_6 alkyloxy comprising up to 5 halogen

atoms, C_3-C_7 cycloalkyl, –C(O)O-R^{10} wherein R^{10} is selected from hydrogen and C_1-C_3 alkyl, and –SR^{11} wherein R^{11} is selected from hydrogen and C_1-C_3 alkyl, naphthyl optionally substituted with up to five substituents selected from the group consisting of halogen, C≡N, NO_2, C_1-C_6 alkyl, C_1-C_6 alkyl comprising up to 5 halogen atoms, C_1-C_6 alkyloxy, C_1-C_6 alkyloxy comprising up to 5 halogen atoms, C_3-C_7 cycloalkyl, –C(O)O-R^{10} wherein R^{10} is selected from hydrogen and C_1-C_3 alkyl, and –SR^{11} wherein R^{11} is selected from hydrogen and C_1-C_3 alkyl, and

C_5-C_{10} mono- or bicyclic aryl wherein 1 or 2 C-atoms are replaced by a hetero atom independently selected from sulfur, nitrogen, and oxygen, optionally substituted with up to three substituents selected from the group consisting of halogen, C≡N, NO_2, C_1-C_6 alkyl, C_1-C_6 alkyl comprising up to 5 halogen atoms, C_1-C_6 alkyloxy, C_1-C_6 alkyloxy comprising up to 5 halogen atoms, C_3-C_7 cycloalkyl, –C(O)O-R^{10} wherein R^{10} is selected from hydrogen and C_1-C_3 alkyl, and –SR^{11} wherein R^{11} is selected from hydrogen and C_1-C_3 alkyl;

R^2 is selected from hydrogen and methyl;

R^4, R^5, and R^7 are independently selected from hydrogen and C_1-C_6 alkyl;

R^6 is selected from hydrogen, C_1-C_6 alkyl, and C_3-C_7 cycloalkyl;

R^8 and R^9 are independently selected from hydrogen, and C_1-C_6 alkly, or

R^8 and R^9 form together with the C-atom to which they are attached a 3, 4, 5, 6, or 7- membered cycloalkyl ring.

12. A compound according to claim 12 wherein R^1 is not hydrogen.

13. A compound according to claim 11 selected from the group consisting of of 4-methyl-3-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 4-methoxy-3-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1-ethyl-5-(2-methoxyphenyl)-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 5-(2-methoxyphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(3,5-difluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1,3,3,5,7-pentamethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 5-(5-chloro-2-methylphenyl)-1,3,3,5,7-

pentamethyloctahydrobenzo[c]isoxazole; 3-(1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazol-5-yl)-4-methoxybenzonitrile; 5-(2,5-dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 3-(1-ethyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazol-5-yl)-4-methylbenzonitrile; 5-(5-fluoro-2-methylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-5-(2-methoxyphenyl)-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 3-chloro-5-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 3-(1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 5-(3,4-difluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 3-(1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazol-5-yl)-4-methylbenzonitrile; 5-(2-methoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 2-methyl-5-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; methyl 4-methyl-3-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzoate; 1-isopropyl-3,3,5,7-tetramethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 5-(3-fluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-phenyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,7-trimethyl-5-phenyloctahydrobenzo[c]isoxazole; 5-(4-chloro-2-methylphenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 5-(2,4-dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(4-fluoro-2-methylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(2,5-difluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-ethyl-3,3,5,7-tetramethyl-5-phenyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(p-tolyl)octahydrobenzo[c]isoxazole; 1-isopropyl-3,3,5,7-tetramethyl-5-phenyloctahydrobenzo[c]isoxazole; 1,3,3,7-tetramethyl-5-phenyloctahydrobenzo[c]isoxazole; 1-isopropyl-5-(2-methoxyphenyl)-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(2-fluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 4-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 3-methyl-4-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 5-(2,4-difluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(2,5-dimethoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(2,3-dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(2,4,5-trimethylphenyl)octahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(4-

(methylthio)phenyl)octahydrobenzo[c]isoxazole; 2-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 5-(3-methoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(3-chloro-2-methylphenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(naphthalen-2-yl)octahydrobenzo[c]isoxazole; 5-(2,4-dimethylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 4-methyl-3-(1,3,3,7-tetramethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1,3,3,7-tetramethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(2-ethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(m-tolyl)octahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(5-methylthiophen-3-yl)octahydrobenzo[c]isoxazole; 1-ethyl-3,3,7-trimethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(2-ethylphenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(2,6-dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(benzo[d][1,3]dioxol-5-yl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-5-(6-methoxypyridin-2-yl)-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(5-chloro-2-methylphenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; 5-butyl-1,3,3-trimethyloctahydrobenzo[c]isoxazole; 5-(2,4-dimethoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,7-trimethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 1-isopropyl-3,3,7-trimethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(5-fluoro-2-methylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(3,5-dimethylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 1,3,3-trimethyl-6-(4-methylcyclohex-3-en-1-yl)octahydrobenzo[c]isoxazole; 5-(3-fluoro-5-(trifluoromethyl)phenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3-dimethyl-5-propyloctahydrobenzo[c]isoxazole; 1,3,3-trimethyl-5-pentyloctahydrobenzo[c]isoxazole; 1-ethyl-3,3,5,7-tetramethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 5-(3,5-dimethylphenyl)-1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(2,5-dimethylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5,7-diethyl-1-isopropyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(2-methyl-5-(trifluoromethyl)phenyl)octahydrobenzo[c]isoxazole; 1-ethyl-3,3-dimethyl-5-

propyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-propyloctahydrobenzo[c]isoxazole; 1,3,3-trimethyl-5-propyloctahydrobenzo[c]isoxazole; 2-methyl-3-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1,3,3,7-tetramethyl-5-(o-tolyl)octahydrobenzo[c]isoxazole; 5-butyl-1-ethyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 5-(4-fluorophenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(furan-3-yl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazol-1-ium chloride; 1,3,3,5,7-pentamethyl-5-(naphthalen-1-yl)octahydrobenzo[c]isoxazole; 5-(2-ethoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(3-chloro-2-methylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(6-methoxypyridin-2-yl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(5-methylthiophen-2-yl)octahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(4-methylpyridin-3-yl)octahydrobenzo[c]isoxazole; 1-ethyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(2-ethylphenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-butyl-1-isopropyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 1-ethyl-3,3,5,7-tetramethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-(4-fluoro-2-methylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1-isopropyl-5,7-dimethylhexahydro-1H-spiro[benzo[c]isoxazole-3,1'-cyclopentane]; 1,5,7-triethyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 1-isopropyl-3,3,5,7-tetramethyl-5-propyloctahydrobenzo[c]isoxazole; 6-isopentyl-1,4,4,8-tetramethyloctahydro-2H-benzo[d][1,3]oxazine; 5-(3,5-dimethoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5,7-diethyl-1,3,3-trimethyloctahydrobenzo[c]isoxazole; 1-isopropyl-5-(4-methoxyphenyl)-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(3-isopropylphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3-trimethyl-6-phenyloctahydrobenzo[c]isoxazole; 5-ethyl-1-isopropyl-3,3-dimethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(2-(methylthio)phenyl)octahydrobenzo[c]isoxazole; 1,5,7-trimethylhexahydro-1H-spiro[benzo[c]isoxazole-3,1'-cyclopentane]; 5-ethyl-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(4-methoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-

pentamethyloctahydrobenzo[c]isoxazole; 1,3,3,4,5,7-hexamethyloctahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyl-5-(pyridin-3-yl)octahydrobenzo[c]isoxazole; 1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole hydrochloride; 5-(4-fluoro-2-methoxyphenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(4-fluorophenyl)-1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 4-methyl-2-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 1,3,3,5-tetramethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 6-isopentyl-1,4,4,8-tetramethyloctahydro-2H-benzo[d][1,3]oxazin-2-one; 1-isopropyl-3,3,5,7-tetramethyl-5-(3-methylbut-2-en-1-yl)octahydrobenzo[c]isoxazole; 5-isopentyl-1-isopropyl-3,3,5,7-tetramethyloctahydrobenzo[c]isoxazole; 2-chloro-5-(1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazol-5-yl)benzonitrile; 5-(4-(tert-butyl)phenyl)-1,3,3,5,7-pentamethyloctahydrobenzo[c]isoxazole; 5-(4-(tert-butyl)phenyl)-1,3,3,7-tetramethyloctahydrobenzo[c]isoxazole; 5-(4-(tert-butyl)phenyl)-1-isopropyl-3,3,7-trimethyloctahydrobenzo[c]isoxazole; and 1,3,3,6-tetramethyloctahydrobenzo[c]isoxazole, or a salt or solvate thereof.