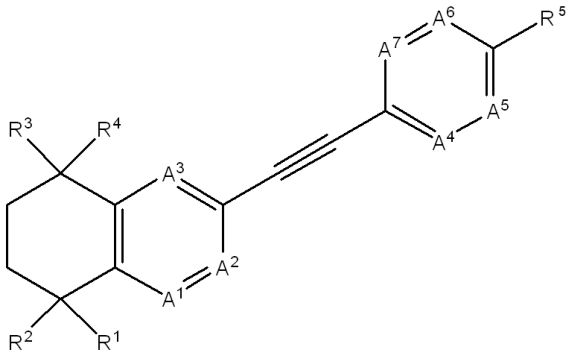
Claims:

1. A compound of formula I:



I

in which:

A^1 is N or CR^6;

A^2 is N or CR^7;

A^3 is N or CR^8;

R^6 and R^8, are each independently hydrogen, C_1-C_{10} alkyl, F, Br or Cl;

R^7 is independently hydrogen, C_1-C_{10} alkyl, F, Br, Cl or -OCR^9 in which R^9 is H or C_1-C_6 alkyl;

R^1 to R^4 are each independently ~~alkyl~~ C_1-C_{10} alkyl, or R^1 and R^2 and/or R^3 and R^4 join to form a 3-membered ring;

A^4 is N or CR^{12};

A^5 is N or CR^{13};

A^6 is N or CR^{14};

A^7 is N or CR^{15};

each R^{12} to R^{15} is independently H, halogen or haloalkyl C_1-$C_{10;}$ and

R^5 is -C(=O)R^{16} or -C(=O)OR^{16} in which R^{16} is C_1-$_{10}$ alkyl, or R^5 is -COOH;

with the proviso that at least one of A^1 to ~~A^7~~-A^3 is N ~~or at least one of R^{12} to R^{15} is F, Cl or Br~~;

and isomers thereof;

in free or in salt form.

~~2. The compound as claimed in claim 1, wherein at least one of A^1 to A^3 is N.~~

~~3~~2. The compound as claimed in claim 1, wherein A^1 and A^3 are N.

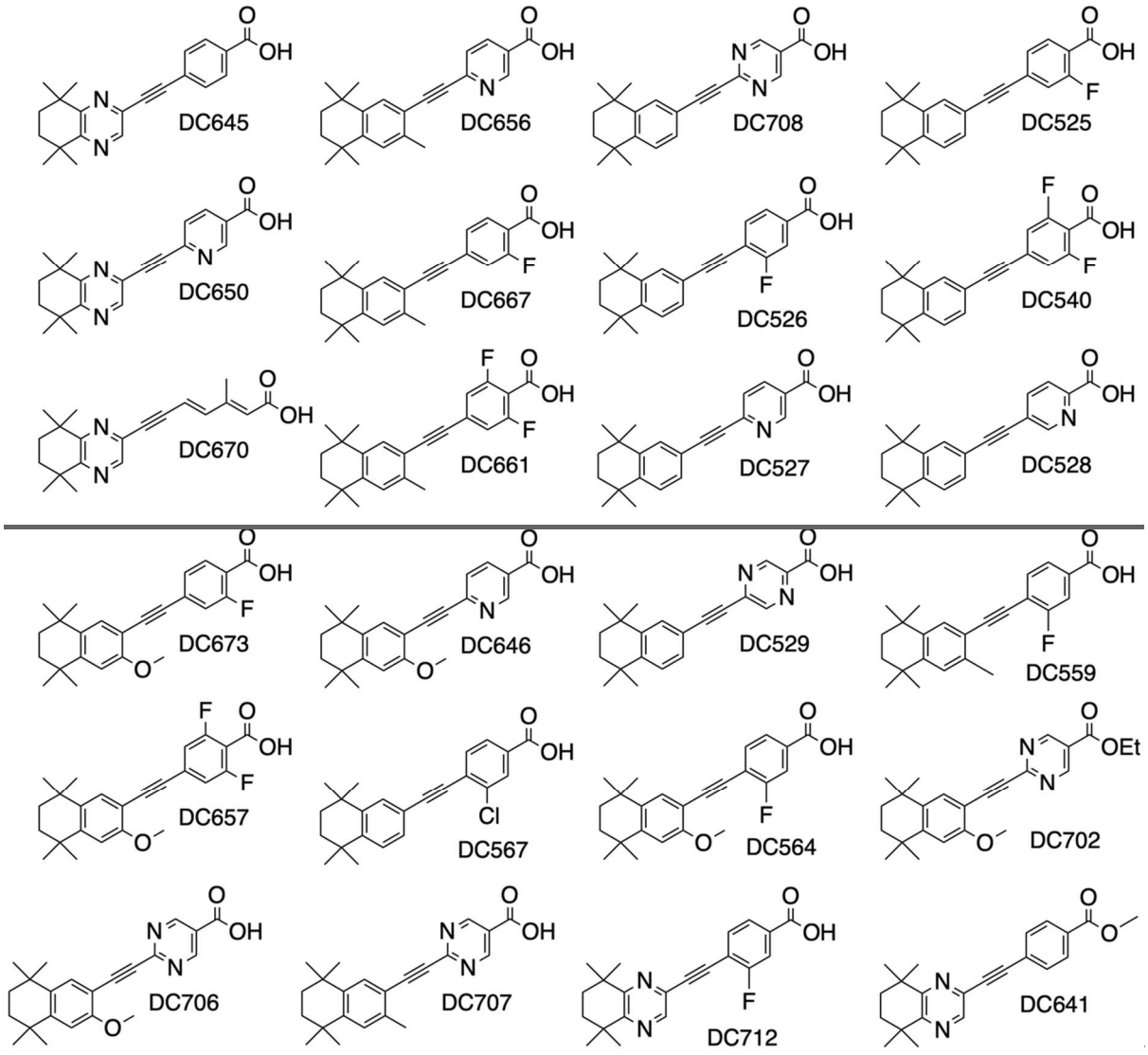
~~4~~3. The compound as claimed in any one of the preceding claims, wherein A^2 is CR^7.

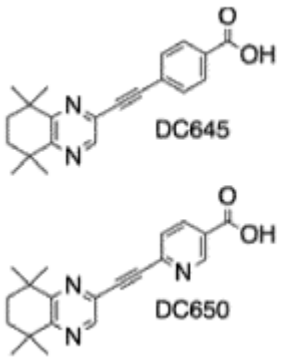
45. The compound as claimed in claim 34, where R^7 is hydrogen.

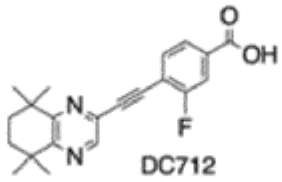
65. The compound as claimed in any one of the preceding claims, wherein R^5 is -COOH.

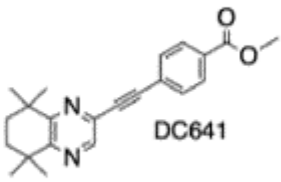
~~7. The compound as claimed in any one of the preceding claims, wherein at least one of A^4, A^5 or A^6 is CF.~~

68. The compound ~~according to~~as claimed in claim 1, which is selected from:



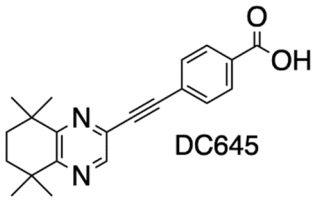




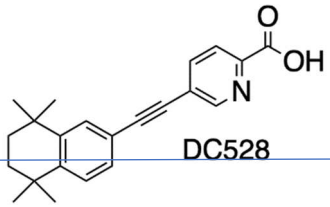


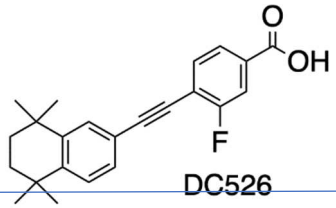
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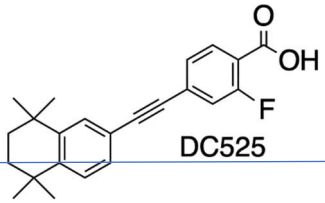
79. The compound according to claim 86, which is ~~selected from~~:



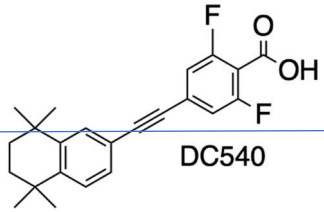
,







;



~~, and~~

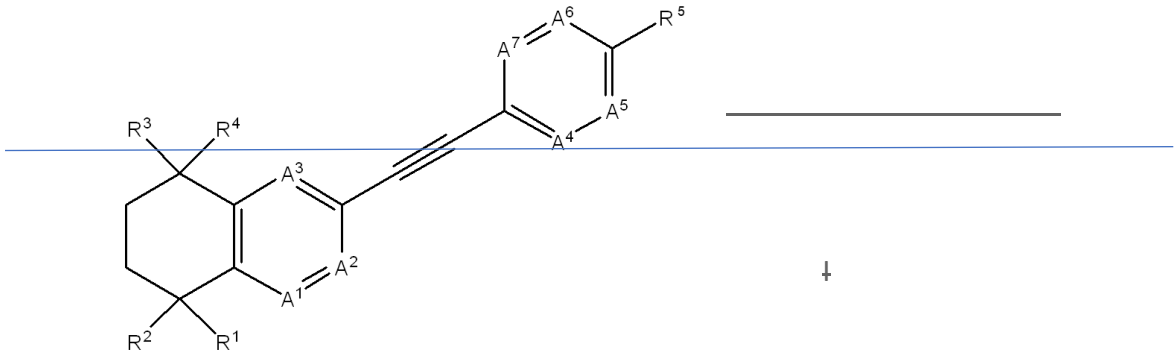
~~10~~8. Use of the compound as claimed in any one of claims 1 to ~~7~~9, in the manufacture of a medicament for the treatment of a disease or condition which is alleviated by the activation of retinoic acid receptors (RAR)~~.~~

~~11. The use of claim 10,~~ wherein the disease or condition which is alleviated by the activation of RAR is selected from Amyotrophic lateral sclerosis (ALS), Parkinson's disease, multiple sclerosis (MS), Alzheimer's disease, early-stage Alzheimer's disease, intermediate-stage Alzheimer's disease, late-stage Alzheimer's disease, cognitive disorders, memory impairment, memory deficit, senile dementia, cognitive impairment, mild cognitive impairment, stroke, traumatic brain injury, epilepsy and spinal cord injury.

~~12~~9. The use of claim ~~10~~ 8~~or claim 11~~, wherein the medicament is to be administered in conjunction with one or more pharmaceutically acceptable excipients, diluents or carriers.

~~13~~10. A compound of formula I as defined in any one of claims 1 to ~~7~~9, for use in therapy.

~~14. A compound of formula I:~~



~~in which:~~

~~A^1 is N or CR^6;~~

~~A^2 is N or CR^7;~~

~~A^3 is N or CR^8;~~

~~R^6 and R^8, are each independently hydrogen, C_1-C_{10} alkyl, F, Br or Cl;~~

~~R^7 is independently hydrogen, C_1-C_{10} alkyl, F, Br, Cl or -OCR^9 in which R^9 is H or C_1-C_6 alkyl;~~

~~R^1 to R^4 are each independently alkyl C_1-C_{10} alkyl, or R^1 and R^2 and/or R^3 and R^4 join~~

~~to form a 3-membered ring;~~

~~A^4 is N or CR^{12};~~

~~A^5 is N or CR^{13};~~

~~A^6 is N or CR^{14};~~

~~A^7 is N or CR^{15};~~

~~each R^{12} to R^{15} is independently H, halogen or haloalkyl C_1-C_{10}, and~~

~~R^5 is -C(=O)R^{16}, or -C(=O)OR^{16} in which R^{16} is C_1-$_{10}$ alkyl;~~

~~with the proviso that at least one of A^1 to A^3 is N or at least one of A^4 is CR^{12} or A^5 is CR^{13} in which R^{12}/R^{13} is halogen; and~~

~~isomers thereof;~~

~~in free or in salt form.~~

~~15. The compound as claimed in claim 14 in which at least one of A^1 to A^3 is N or at least one of A^4 is CR^{12} or A^5 is CR^{13} in which R^{12}/R^{13} is F.~~

~~16. The compound as claimed in claim 14 or claim 15 in which at least one of A^1 to A^3 is N.~~

~~17. The compound as claimed in any one of claims 14 to 16 in which A^1 and A^3 are both N.~~

~~18. A method of screening compounds for therapeutic potential in the treatment of conditions or diseases which are alleviated by the activation of RAR, the method comprising:~~

~~- performing an assay to determine the efficacy (E_{max}) of a compound in activating a RAR as an indicator of genomic activity;~~

~~- performing an assay to determine the efficacy (E_{max}) of a compound as an indicator of non-genomic activity;~~

~~for each assay, comparing the E_{max} to a baseline value; and~~

~~- selecting those compounds which have an E_{max} above the baseline value in both assays for further investigation.~~

~~19. The method as claimed in claim 18, wherein the assay to determine the efficacy (E_{max}) of a compound as an indicator of non-genomic activity is a kinase phosphorylation assay.~~

~~20. The method as claimed in claim 19, wherein the kinase phosphorylation assay is an ERK1/2 phosphorylation assay.~~