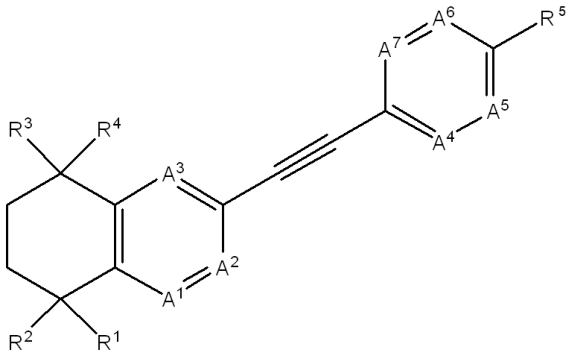
Claims:

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;

with the proviso that at least one of A^1 to A^7 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. The compound as claimed in claim 1, wherein A^1 and A^3 are N.

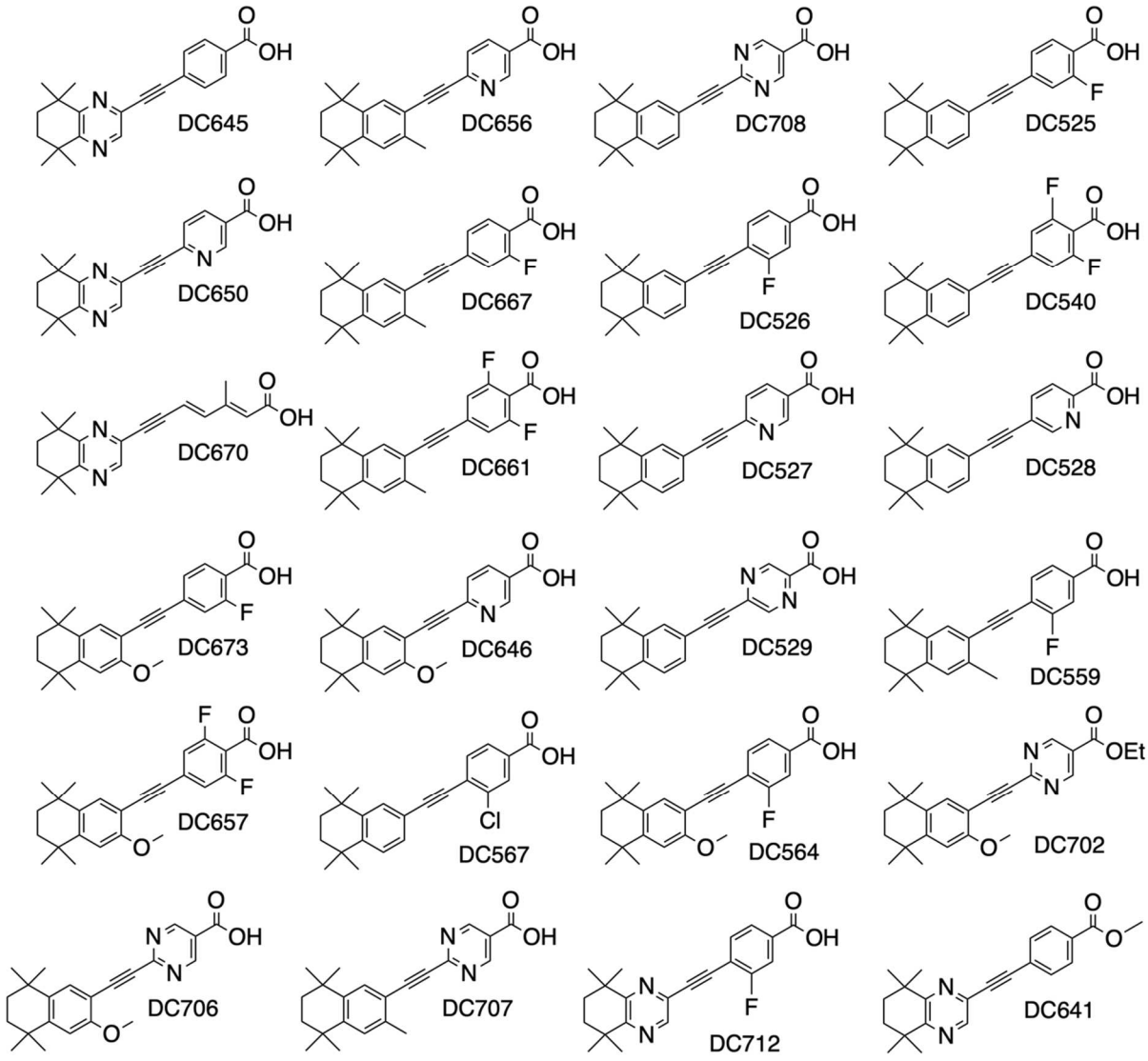
4. The compound as claimed in any one of the preceding claims, wherein A^2 is $CR^{7.}$

5. The compound as claimed in claim 4, where R^7 is hydrogen.

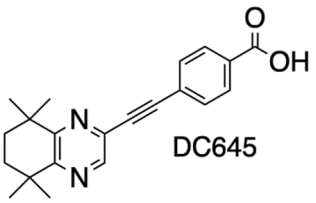
6. The compound as claimed in any one of the preceding claims, wherein R^5 is -COOH.

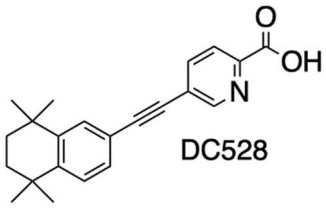
7. The compound as claimed in any one of the preceding claims, wherein at least one of A^4, A^5 or A^6 is CF.

8. The compound according to claim 1, which is selected from:

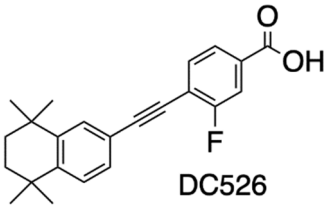


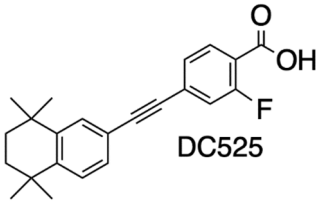
9. The compound according to claim 8, which is selected from:



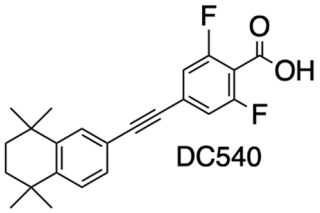
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, and



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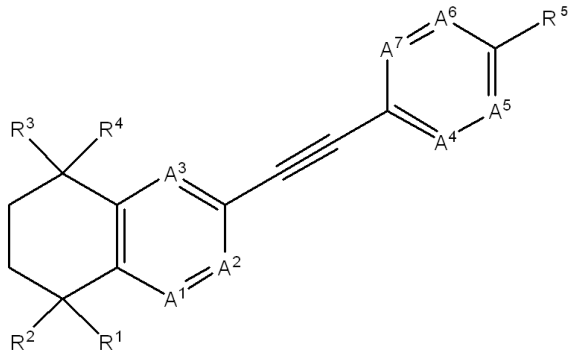
10. Use of the compound as claimed in any one of claims 1 to 9, in the manufacture of a medicament for the treatment of a disease or condition which is alleviated by the activation of retinoic acid receptors (RAR).

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

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

14. 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;

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.