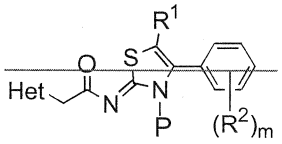
~~Claims:~~

~~1. A compound of formula (I):~~

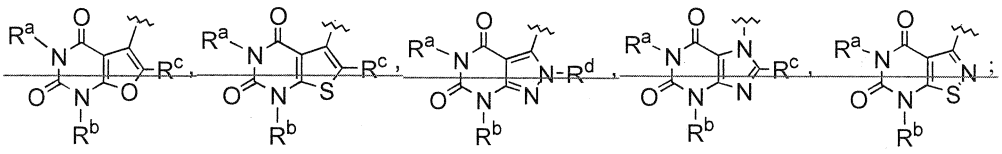


~~(I)~~

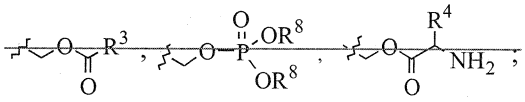
~~or a pharmaceutically acceptable salt thereof,~~

~~wherein,~~

~~Het is selected from the group consisting of~~



~~P is selected from the group consisting of~~



~~R^1 is hydrogen;~~

~~at each occurrence, R^2, which may be the same or different, is independently selected from halogen, haloC_1-C_8alkyl, and haloC_1-C_8alkoxy;~~

~~R^3 is selected from C_1-C_8alkyl and 3 to 15 membered heterocyclic ring;~~

~~R^4 is selected from hydrogen, C_1-C_8alkyl and C_6-C_{14}aryl C_1-C_6alkyl;~~

~~R^8 is selected from hydrogen, C_1-C_4alkyl, C_6-C_{14}aryl C_1-C_6alkyl and pharmaceutically acceptable cation (M^{+} or M^{2+});~~

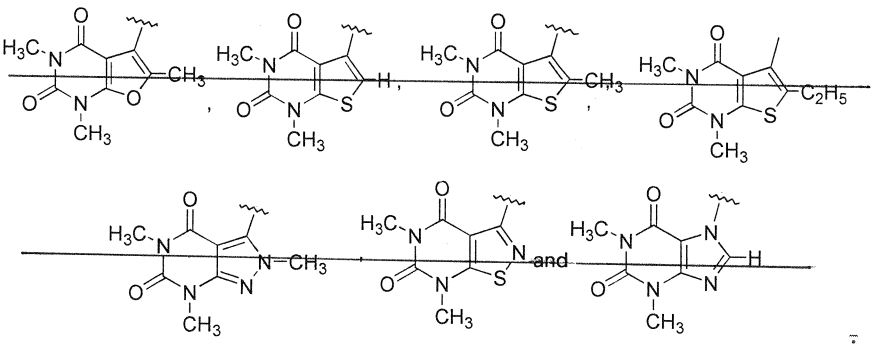
~~R^a, R^b and R^d, which may be the same or different, are each independently selected from hydrogen and C_1-C_4alkyl;~~

~~R^e is selected from hydrogen and C_1-C_4alkyl; and~~

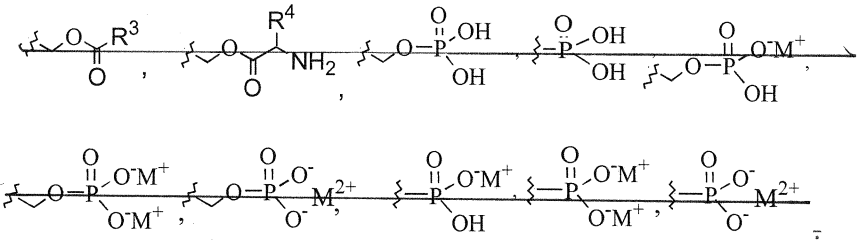
~~'m' is an integer ranging from 0 to 5, both inclusive.~~

~~2. The compound according to claim 1, wherein R^2 is fluorine, chlorine, trifluoromethyl or trifluoromethoxy and 'm' is 2 or 3.~~

~~3. The compound according to claim 1 or 2, wherein 'Het' is selected from~~



~~4. The compound according to any of the preceding claims, wherein 'P' is selected from~~



~~5. The compound according to claim 4, wherein M^+ is pharmaceutically acceptable cation comprising sodium, potassium, and ammonium; M^{2+} is pharmaceutically acceptable cation comprising calcium, and magnesium.~~

Claims:

~~6~~1. ~~The~~ A compound ~~according to claim 1~~ selected from:

~~[2-{[(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl) acetyl]imino}-4-[3-fluoro-4-(trifluoromethyl)phenyl]-1,3-thiazol-3(2*H*)-yl]methyl dihydrogen phosphate;~~

~~Disodium[2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-4-[3-fluoro-4-(trifluoromethyl)phenyl]-1,3-thiazol-3(2*H*)-yl]methyl phosphate;~~

[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl dihydrogen phosphate;

Disodium[4-[2,4-difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl phosphate;

~~4-(2,4-Difluoro-3-(trifluoromethyl)phenyl)-2-((2-(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidin-5-yl)acetyl)imino)thiazol-3(2H)-yl)methyl dihydrogen phosphate;~~

~~Disodium (4-(2,4-difluoro-3-(trifluoromethyl)phenyl)-2-((2-(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidin-5-yl)acetyl)imino)thiazol-3(2H)-yl)methyl phosphate;~~

~~[2-{[(6-ethyl-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-4-[3-fluoro-4-(trifluoromethyl)phenyl]-1,3-thiazol-3(2*H*)-yl]methyl dihydrogen phosphate;~~

~~Disodium [2-{[(6-ethyl-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-4-[3-fluoro-4-(trifluoromethyl)phenyl]-1,3-thiazol-3(2*H*)-yl]methyl phosphate;~~

[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl dihydrogen phosphate;

Disodium [4-[3-chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro [2,3-*d*] pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl phosphate~~:~~;

~~4-[2,3-Difluoro-4-(trifluoromethyl)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-d]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2H)-yl]methyl dihydrogen phosphate;~~

4-(2,4-Difluoro-3-(trifluoromethyl)phenyl)-2-((2-(2,5,7-trimethyl-4,6-dioxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl)acetyl)imino)thiazol-3(2H)-yl)methyl dihydrogen phosphate;

Disodium-(4-(2,4-difluoro-3-(trifluoromethyl)phenyl)-2-((2-(2,5,7-trimethyl-4,6-dioxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl)acetyl)imino)thiazol-3(2H)-yl)methyl phosphate;

~~(4-(3,4-Dichlorophenyl)-2-((2-(1,3-dimethyl-2,6-dioxo-2,3-dihydro-1H-purin-7(6H)-yl)acetyl)imino)thiazol-3(2H)-yl)methyl dihydrogen phosphate;~~

[4-[2,3-Difluoro-4-(trifluoromethyl)phenyl]-2-{[(5,7-dimethyl-4,6-dioxo-4,5,6,7-tetrahydro[1,2]thiazolo[5,4-*d*]pyrimidin-3-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl dihydrogen phosphate; and

Disodium -(4-(2,3-difluoro-4-(trifluoromethyl)phenyl)-2-((2-(5,7-dimethyl-4,6-dioxo-4,5,6,7-tetrahydroisothiazolo[5,4-d]pyrimidin-3-yl)acetyl)imino)thiazol-3(2H)-yl)methyl phosphate.

~~7~~2. ~~The~~ A compound ~~according to claim 1~~ selected from:

~~[2-{[(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-4-[3-fluoro-4-(trifluoromethyl)phenyl]-1,3-thiazol-3(2*H*)-yl]methyl-2-methylpropanoate;~~

~~[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl-2-methylpropanoate;~~

~~[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl 2,2-dimethylpropanoate;~~

~~[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-prolinate;~~

~~[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-prolinate hydrochloride;~~

~~[2-{[(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-4-[3-fluoro-4-(trifluoromethyl)phenyl]-1,3-thiazol-3(2*H*)-yl]methylpiperidine-4-carboxylate;~~

~~[2-{[(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-4-[3-fluoro-4-(trifluoromethyl)phenyl]-1,3-thiazol-3(2*H*)-yl]methylpiperidine-4-carboxylate hydrochloride;~~

[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl piperidine-4-carboxylate;

[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl piperidine-4-carboxylate hydrochloride;

[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl piperidine-4-carboxylate;

[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl piperidine-4-carboxylate hydrochloride;

~~[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl glycinate;~~

~~[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl glycinate hydrochloride;~~

~~[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-alaninate;~~

~~[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-alaninate hydrochloride;~~

[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-valinate;

[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-valinate hydrochloride;

~~[2-{[(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-4-[3-fluoro-4-(trifluoromethyl)phenyl]-1,3-thiazol-3(2*H*)-yl]methyl L-isoleucinate;~~

~~[2-{[(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-4-[3-fluoro-4-(trifluoromethyl)phenyl]-1,3-thiazol-3(2*H*)-yl]methyl L-isoleucinate hydrochloride;~~

[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-isoleucinate;

[4-[2,4-Difluoro-3-(trifluoromethyl)phenyl]-2-{[(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-isoleucinate hydrochloride;

[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl glycinate;

[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl glycinate hydrochloride;

[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-valinate; and

[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-valinate hydrochloride;.

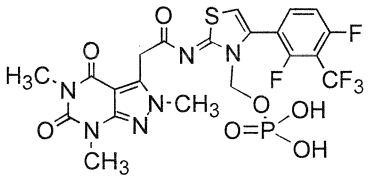
~~[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-isoleucinate;~~

~~[4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-*d*]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2*H*)-yl]methyl L-isoleucinate hydrochloride;~~

~~4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-d]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2H)-yl]methyl L-phenylalaninate; and~~

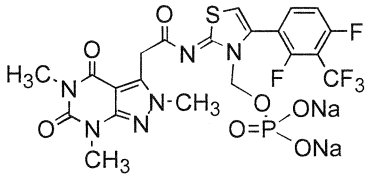
~~4-[3-Chloro-4-(trifluoromethoxy)phenyl]-2-{[(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydrofuro[2,3-d]pyrimidin-5-yl)acetyl]imino}-1,3-thiazol-3(2H)-yl]methyl L-phenylalaninate hydrochloride.~~

~~8~~3. ~~The~~ A compound ~~according to claim 1~~of formula



or a pharmaceutically acceptable salt thereof.

~~9~~4. ~~The~~ A compound ~~according to claim 1~~of formula



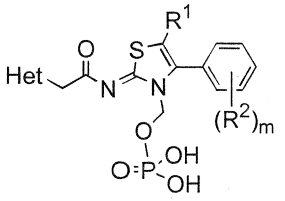
~~10~~5. A pharmaceutical composition comprising one or more compounds selected from the compounds of any one of claims 1 to ~~9~~4, and one or more pharmaceutically acceptable excipients, carriers, diluents or mixture thereof.

~~11. Use of the compound according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of disease or condition associated with TRPA1 function in a subject.~~

~~12~~6. Use of the compound according to any one of claims 1 to ~~9~~4 in the manufacture of a medicament for the treatment of the symptoms of a disease or condition associated with TRPA1 function which is selected from pain, chronic pain, complex regional pain syndrome, neuropathic pain, postoperative pain, rheumatoid arthritic pain, osteoarthritic pain, back pain, visceral pain, cancer pain, algesia, neuralgia, migraine, neuropathies, diabetic neuropathy, sciatica, HIV-related neuropathy, post-herpetic neuralgia, fibromyalgia, nerve injury, ischaemia, neurodegeneration, stroke, post stroke pain, multiple sclerosis, ~~respiratory diseases,~~ asthma, cough, COPD, ~~inflammatory disorders,~~ oesophagitis, gastroeosophagal reflux disorder (GERD), irritable bowel syndrome, inflammatory bowel disease, pelvic hypersensitivity, urinary incontinence, cystitis, burns, psoriasis, eczema, emesis, stomach duodenal ulcer and pruritus.

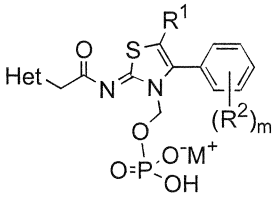
~~13~~7. Use of the compound according to any one of claims 1 to ~~9~~4 in the manufacture of a medicament for the treatment of chronic pain, neuropathic pain, rheumatoid arthritic pain or osteoarthritic pain.

~~14~~8. A process for preparing a compound of formula Ic-1



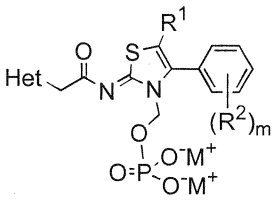
(Ic-1)

or a pharmaceutically acceptable salt thereof (Id-1 or Id),



(Id-1)

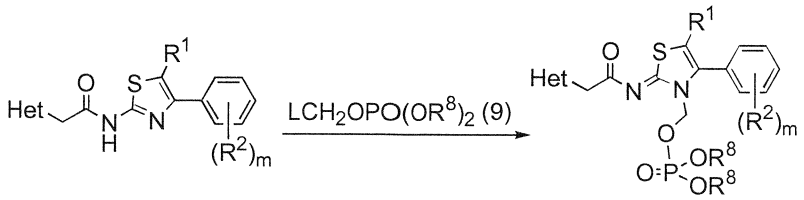
or



(Id)

comprising,

a. reacting a compound of formula (1) or its salt with a compound of formula (9) to form a compound of formula Ic;



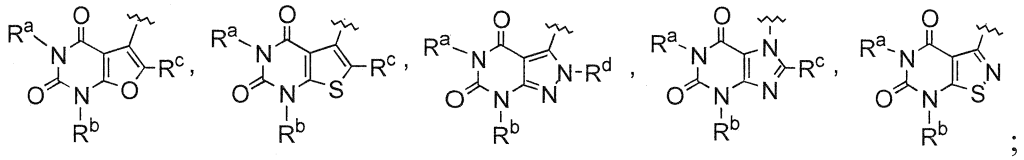
(1) (Ic)

b. converting compound of formula Ic to corresponding compound of formula Ic-1; and

c. optionally converting compound of formula Ic-1 to a pharmaceutically acceptable salt of formula Id-1 or Id,

wherein,

Het is selected from the group consisting of



;

R^1 is hydrogen;

at each occurrence, R^2, which may be the same or different, is independently selected from halogen, haloC_1-C_8alkyl and haloC_1-C_8alkoxy;

R^8 is selected from hydrogen, C_1-C_4alkyl, C_6-C_{14}arylC_1-C_6alkyl and pharmaceutically acceptable cation (M$^+$ or M^{2+});

R^a, R^b and R^d, which may be the same or different, are each independently selected from hydrogen and C_1-C_4alkyl;

R^c is selected from hydrogen and C_1-C_4alkyl;

'm' is an integer ranging from 0 to 5, both inclusive;

L is Cl, Br, OTs or I and

M^+ is a pharmaceutically acceptable cation.

~~159~~. The process of claim ~~148~~, wherein the step 'a' is performed in presence of a base selected from sodium hydride or sodium *tert*-butoxide or potassium *tert*-butoxide in a solvent and compound of formula (9) is di-*tert*-butyl iodomethyl phosphate.