heteroaromatics like nitro derivatives or pyridazines require metalations below -50 °C, which is not convenient for the reaction upscaling ((a) Wunderlich, S. H.; Knochel, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 7685. (b) Mosrin, M.; Knochel P. *Chem. Eur. J.* **2009**, DOI: 10.1002/chem.200801831; Wunderlich, S. H.; Knochel, P. *Chem. Comm.* **2008**, *47*, 6387).

Summary

In one aspect, the present invention refers to a reagent of the general formula: R^1R^2N-ZnYLiY (I) wherein R^1, R^2 are independently selected from H, substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or silyl derivatives thereof; wherein R^1 and R^2 together can be part of a cyclic or polymeric structure, where at least one of groups R^1 and R^2 is not H; Y is selected from F; Cl; Br; I; CN; SCN; NCO; $HalO_n$ (wherein n = 3 or 4 and Hal is selected from Cl, Br and I); NO_3; BF_4; PF_6; H; a carboxylate of the general formula R^xCO_2; an alcoholate of the general formula OR^x; a thiolate of the general formula SR^x; $R^xP(O)O_2$; or $SCOR^x$; or $SCSR^x$; O_nSR^x (wherein n = 2 or 3); or NO_n (wherein n = 2 or 3) and a derivative thereof; wherein R^x is a substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or derivatives thereof, or H or as adduct with a solvent. In another aspect, the present invention is directed to a solution of the reagent according to the present invention in a solvent. In still another aspect, the present invention refers to a process for the preparation of a reagent of the general formula: R^1R^2N-ZnYLiY (I) wherein R^1, R^2 are independently selected from H, substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or silyl derivatives thereof; and R^1 and R^2 together can be part of a cyclic or polymeric structure; and wherein at least one of the R^1 and R^2 groups is not H; Y is selected from F; Cl; Br; I; CN; SCN; NCO; $HalO_n$ (wherein n = 3 or 4 and Hal is selected from Cl, Br and I); NO_3; BF_4; PF_6; H; a carboxylate of the general formula R^xCO_2; an alcoholate of the general formula OR^x; a thiolate of the general formula SR^x; $R^xP(O)O_2$; or $SCOR^x$; or $SCSR^x$; O_nSR^x (wherein n = 2 or 3); or NO_n (wherein n = 2 or 3); and a derivative thereof; wherein R^x is a substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or derivatives thereof, or H, comprising a reaction in a solvent of R^1R^2N-H with R^xLi in the presence of ZnY_2, wherein X is defined as Y above. In one other aspect, the present invention refers to the use of the reagent according to the present invention in a reaction with an electrophile. In another aspect, the present invention refers to the use of the reagent according to the present invention for the deprotonation of any substrate which can form stabilized or

unstabilized carbanions. In still another aspect, the present invention refers to the use of the reagent according to the present invention for the preparation of: 3,6-dichloro-4-iodopyridazine, (3,6-dichloropyradizin-4-yl)(4-fluorophenyl)methanone, 3,6-dichloro-4-(3-(trifluoromethyl)phenyl)pyridazine, 4,6-dichloro-5-iodo-pyrimidine, (4,6-dichloropyrimidin-5-yl)(furan-2-yl)methanone, 5-allyl-4,6-dichloropyrimidine, 3,5-dichloro-2-iodopyrazine, ethyl-4-(3,5-dichloropyrazin-2-yl)benzoate, ethyl-2-((3,5-dichloropyrazin-2-yl)methyl)acrylate, 8-(4-chlorophenyl)-1,3,7-trimethyl-1H-purine-2,6(3H,7H)-dione, ethyl-2-((1,3,7-trimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1H-purin-8-yl)methyl)acrylate, ethyl-2',6'-difluoro-3'-nitrobiphenyl-4-carboxylate, (2,6-difluoro-3-nitrophenyl)(phenyl)methanone, 1,3-difluoro-2-iodo-4-nitrobenzene, 2-chloro-4-cyclohex-2-enyl-3-nitropyridine, ethyl-2-(6-fluoro-3-methoxy-2-nitrobenzyl)acrylate, methyl-3-(cyclohex-2-enyl)-5-nitrofuran-2-carboxylate, 2-(3-(trifluoromethyl)phenyl)benzo[b]thiophene-3-carbaldehyde, 2-(4-chlorophenyl)benzo[b]thiophene-3-carbaldehyde, or 2-(phenylethynyl)benzo[b]thiophene-3-carbaldehyde.

Detailed Description

A reagent of the general formula

$$R^1R^2N\text{-}ZnY\ LiY\ (I)$$

wherein

R^1, R^2 are, independently, selected from H, substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or silyl derivatives thereof; and R^1 and R^2 together can be part of a cyclic or polymeric structure; and wherein at least one of R^1 and R^2 is other than H;

Y is selected from the group consisting of F; Cl; Br; I; CN; SCN; NCO; $HalO_n$, wherein n = 3 or 4 and Hal is selected from Cl, Br and I; NO_3; BF_4; PF_6; H; a carboxylate of the general formula R^XCO_2; an alcoholate of the general formula OR^X; a thiolate of the general formula SR^X; $R^XP(O)O_2$; or $SCOR^X$; or $SCSR^X$; O_nSR^x, wherein n = 2 or 3; or NO_n, wherein n = 2 or 3; and a derivative thereof; wherein R^x is a substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or derivatives thereof, or H;

or as adduct with a solvent.

R^1, R^2 are cyclic and substituted by R^3, and R^4 that are, independently, selected from H, substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or silyl derivatives thereof; and R^1 and R^2 together, or R^3 and R^4 together can be part of a cyclic or polymeric structure; and wherein at least one of R^1 and R^2 and at least one of R^3 and R^4 is other than H.

Preferable the reagent R^1R^2N-ZnY LiY (I) is 2,2,6,6-Tetramethylpiperide Zinc Chloride Lithium Chloride or the solution of the reagent in a solvent. The solvent is polar and aprotic. Preferable is the solvent selected from cyclic, linear or branched mono or polyethers, thioethers, amines, phosphines, and derivatives thereof containing one or more additional heteroatoms selected from O, N, S and P, preferably tetrahydrofuran (THF), 2-methyltetrahydrofuran, dibutyl ether, diethyl ether, tert- butylmethyl ether, dimethoxyethane, dioxanes, preferably 1,4-dioxane, triethylamine, ethyldiisopropyl amine, dimethylsulfide, dibutylsulfide; cyclic amides, preferably N- methyl-2-pyrrolidone (NMP), N-ethyl-2-pyrrolidone (NEP), N-butyl-2-pyrrolidone (NBP); cyclic, linear or branched alkanes and/or alkenes wherein one or more hydrogens are replaced by a halogen, preferably dichloromethane, 1,2-

Claims

1. Reagent of the general formula:

R^1R^2N-ZnYLiY (I)

wherein R^1, R^2 are independently selected from H, substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or silyl derivatives thereof; wherein R^1 and R^2 together can be part of a cyclic or polymeric structure, where at least one of groups R^1 and R^2 is not H;

Y is selected from F; Cl; Br; I; CN; SCN; NCO; $HalO_n$ (wherein n = 3 or 4 and Hal is selected from Cl, Br and I); NO_3; BF_4; PF_6; H; a carboxylate of the general formula R^XCO_2; an alcoholate of the general formula OR^X; a thiolate of the general formula SR^X; $R^XP(O)O_2$; or $SCOR^X$; or $SCSR^X$; O_nSR^X (wherein n = 2 or 3); or NO_n (wherein n = 2 or 3) and a derivative thereof; wherein R^X is a substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or derivatives thereof, or H or as adduct with a solvent.

2. Reagent according to Claim 1 wherein R^1, R^2 are cyclic groups and substituted by R^3 and R^4, which are independently selected from H, substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or silyl derivatives thereof; and R^1 and R^2 together, or R^3 and R^4 together can form a part of a cyclic or polymeric structure; wherein at least one of groups R^1 and R^2 and at least one of groups R^3 and R^4 are not H.

3. Reagent according to any one of Claims 1 and 2 wherein R^1R^2N-ZnYLiY of formula (I) is 2,2,6,6-tetramethylpiperide - zinc chloride - lithium chloride.

4. Solution of the reagent according to any one of Claims 1 to 3 in a solvent.

5. Solution of the reagent according to any one of Claims 1 to 4 wherein the solvent is polar and aprotic.

6. Solution according to Claim 5, wherein the solvent is selected from cyclic, linear or branched mono- or polyethers, thioethers, amines, phosphines, and derivatives thereof containing one or more heteroatoms selected from O, N, S and P; cyclic

amides; cyclic, linear or branched alkanes and/or alkenes (wherein one or more hydrogen atoms are substituted by a halogen atom); urea derivatives; aromatic, heteroaromatic or aliphatic hydrocarbons; hexamethyl phosphorus triamide (HMPA), CS_2; or combinations thereof.

7. Process for the preparation of a reagent of the general formula:

$R^1R^2N\text{-}ZnYLiY$ (I)

wherein R^1, R^2 are independently selected from H, substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or silyl derivatives thereof; and R^1 and R^2 together can be part of a cyclic or polymeric structure; and wherein at least one of the R^1 and R^2 groups is not H;

Y is selected from F; Cl; Br; I; CN; SCN; NCO; $HalO_n$ (wherein n = 3 or 4 and Hal is selected from Cl, Br and I); NO_3; BF_4; PF_6; H; a carboxylate of the general formula R^xCO_2; an alcoholate of the general formula OR^x; a thiolate of the general formula SR^x; $R^xP(O)O_2$; or $SCOR^x$; or $SCSR^x$; O_nSR^x (wherein n = 2 or 3); or NO_n (wherein n = 2 or 3); and a derivative thereof; wherein R^x is a substituted or unsubstituted aryl or heteroaryl containing one or more heteroatoms, linear, branched or cyclic, substituted or unsubstituted alkyl, alkenyl, alkynyl, or derivatives thereof, or H,

comprising a reaction in a solvent of $R^1R^2N\text{-}H$ with R^xLi in the presence of ZnY_2, wherein X is defined as Y above.

8. Process according to Claim 7, wherein X and Y are independently or both Cl, Br or I.

9. Process according to Claim 7 or 8, wherein R^xLi is sec-butyl-Li.

10. Process according to any one of Claims 7 to 9, wherein the solvent is selected from cyclic, linear or branched mono- or polyethers, thioethers, amines, phosphines, and derivatives thereof containing one or more heteroatoms selected from O, N, S and P; cyclic amides; cyclic, linear or branched alkanes and/or alkenes (wherein one or more hydrogen atoms are substituted by a halogen atom); urea derivatives; aromatic, heteroaromatic or aliphatic hydrocarbons; hexamethyl phosphorus triamide (HMPA), CS_2; or combinations thereof.

11. Use of the reagent according to any one of Claims 1 to 6 in a reaction with an electrophile.

12. Use of the reagent according to any one of Claims 1 to 6 for the deprotonation of any substrate which can form stabilized or unstabilized carbanions.

13. Use of the reagent according to any one of Claims 1 to 6 for the preparation of:

- 3,6-dichloro-4-iodopyridazine,
- (3,6-dichloropyradizin-4-yl)(4-fluorophenyl)methanone,
- 3,6-dichloro-4-(3-(trifluoromethyl)phenyl)pyridazine,
- 4,6-dichloro-5-iodo-pyrimidine,
- (4,6-dichloropyrimidin-5-yl)(furan-2-yl)methanone,
- 5-allyl-4,6-dichloropyrimidine,
- 3,5-dichloro-2-iodopyrazine,
- ethyl-4-(3,5-dichloropyrazin-2-yl)benzoate,
- ethyl-2-((3,5-dichloropyrazin-2-yl)methyl)acrylate,
- 8-(4-chlorophenyl)-1,3,7-trimethyl-1H-purine-2,6(3H,7H)-dione,
- ethyl-2-((1,3,7-trimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1H-purin-8-yl)methyl)acrylate,
- ethyl-2',6'-difluoro-3'-nitrobiphenyl-4-carboxylate,
- (2,6-difluoro-3-nitrophenyl)(phenyl)methanone,
- 1,3-difluoro-2-iodo-4-nitrobenzene,
- 2-chloro-4-cyclohex-2-enyl-3-nitropyridine,
- ethyl-2-(6-fluoro-3-methoxy-2-nitrobenzyl)acrylate,
- methyl-3-(cyclohex-2-enyl)-5-nitrofuran-2-carboxylate,
- 2-(3-(trifluoromethyl)phenyl)benzo[b]thiophene-3-carbaldehyde,
- 2-(4-chlorophenyl)benzo[b]thiophene-3-carbaldehyde, or
- 2-(phenylethynyl)benzo[b]thiophene-3-carbaldehyde.