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PII: S0040-4039(14)01601-3
DOI: http://dx.doi.org/10.1016/j.tetlet.2014.09.086
Reference: TETL 45180

To appear in: *Tetrahedron Letters*

Received Date: 5 August 2014
Revised Date: 17 September 2014
Accepted Date: 18 September 2014

Please cite this article as: Muthusamy, S., Ramkumar, R., Solvent- and transition metal-free synthesis of spiro[cyclopropane-1,3-oxindoles] from cyclic diazoamides, *Tetrahedron Letters* (2014), doi: http://dx.doi.org/10.1016/j.tetlet.2014.09.086

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TETRAHEDRON LETTERS

Solvent- and transition metal-free synthesis of spiro[cyclopropane-1,3-oxindoles] from cyclic diazoamides

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Metal-free
Diazoamides
Oxindoles
Spirocyclopropanes

ABSTRACT

A highly efficient method to synthesize spiro[cyclopropane-1,3-oxindoles] from cyclic diazoamides and mono-substituted or 1,2-disubstituted alkenes under solvent- and transition metal-free conditions is reported. The reaction offers proficient access to synthetically useful and biologically important spiro[cyclopropane-1,3-oxindoles]. The advantageous features of this sustainable method are metal-free, shorter reaction time, cost-effective, eco-friendly and excellent yields. The selectivity and yield are comparable with transition metal-catalyzed reactions.

Spirooxindole unit present in a large number of bioactive natural alkaloids and its derivatives find wide spread applications in medicinal chemistry.[1–3] Synthesis of spirocyclopropanes is having a great interest due to their presence in naturally occurring molecules,[4] applications in pharmaceuticals[5] and synthetic intermediates.[6] Spiro[cyclopropan-1,3-oxindoles] are known to have inotropic[7] and herbicidal[8] properties. Their novel ring-expansion reactions[9] are well-known in providing indole-based natural product such as spiro[pyrrolidin-3,3′-oxindoles].[10] Spirocyclopropane-1,3-oxindole **1** act as a kinase inhibitor and **2a,b** are potent HIV-1 non-nucleoside reverse transcriptase inhibitor (Figure 1).[11] The cyclopropanation formation from diazo compounds and alkenes has been usually performed[12] in the presence of transition metal catalysts. Further, spirocyclopropanes have also been reported from diazo compounds and alkenes in the presence of expensive and toxic transition metals such as $Rh_2(OAc)_4$, CuOTf, $Hg(OTf)_2$ or Au(I)-complexes.[13] Another disadvantage of the metal-catalyzed process is that heteroatom containing alkenes could bind tightly to a transition metal present in the catalyst, resulting in loss of their catalytic activity.[14] Thus, there is a need for straightforward and highly sustainable approach to synthesize spirocyclopropanes. There is a recent report that demonstrates the metal-free thermal decomposition of ethyl diazoacetate or 2,2,2-trifluorodiazoethane with 1,2-diactivated alkenes in solvents led[15] to spirocyclopropanation products. In continuation of our interest[16] on the chemistry of cyclic diazoamides, we herein demonstrate the solvent- as well as transition metal-free synthesis of spiro[cyclopropane-1,3-oxindoles] from diazoamides and mono-substituted or 1,2-disubstituted alkenes.

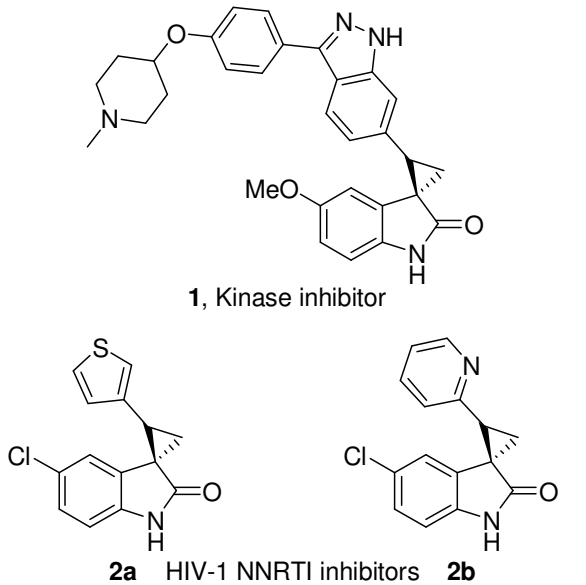

Figure 1. Biological important oxindole containing spiro[cyclopropane-1,3-oxindoles]

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