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Lingyu Kong, Bohdan Biletskyi, Didier Nuel, Hervé Clavier. Cobalt(III)-catalysed C–H allylation with vinylaziridines. *Organic Chemistry Frontiers*, 2018, 5 (10), pp.1600 - 1603. 10.1039/c8qo00173a . hal-01816352

**HAL Id: hal-01816352**

**<https://hal.science/hal-01816352>**

Submitted on 15 Jun 2018

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## Cobalt(III)-Catalysed C-H Alkylation with Vinylaziridines

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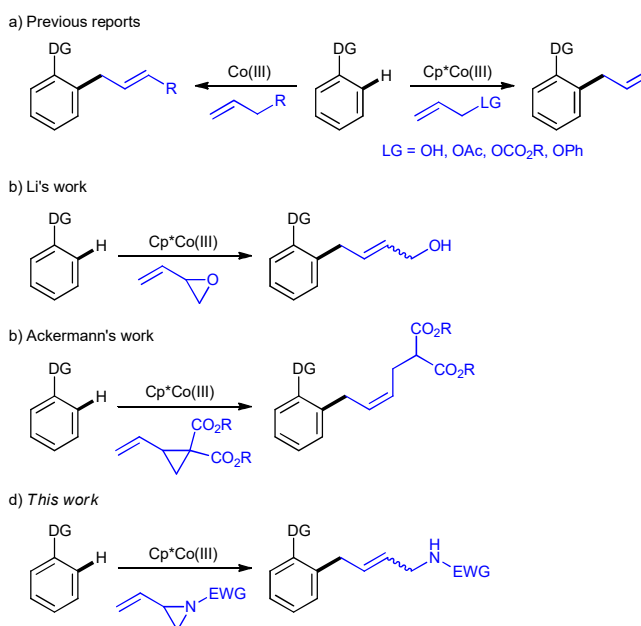
Received 00th January 20xx,

Accepted 00th January 20xx

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**A cobalt-catalysed C-H alkylation of aromatic and heteroaromatic compounds with vinylaziridines is described. This transformation occurring under mild reaction conditions proceeds through C-H activation, carbon-carbon double insertion and  $\beta$ -nitrogen elimination. Its scope and limitations have been investigated and a synthetic application of products has been achieved.**

The development of direct functionalization of aromatic C-H bonds catalysed by transition metal complexes has increased tremendously over the past decade<sup>1</sup> to reach now a status of powerful synthetic methodology for the preparation of natural compounds, pharmaceuticals, agrochemical products, polymers and commodity and specialty chemicals.<sup>2</sup> Among the various functionalizations, C-H alkylation is of interest since allyl moieties can be straightforwardly manipulated to afford a wide range of useful functionalities.<sup>3</sup> Various transition metal-based catalytic systems enable direct C-H alkylation such as 3d (iron, cobalt, nickel), 4d (ruthenium, palladium, rhodium) or 5d (iridium) metals. For quite some time Rh was considered to be superior to other metals regarding its reactivity. Recently, research has demonstrated cobalt complexes, in particular high-valent species,<sup>4,5</sup> represent efficient catalysts for C-H functionalization<sup>6</sup> including C-H alkylation. For example, a Co-catalysed C-H alkylation using unactivated olefin partners was recently developed (Scheme 1a).<sup>7</sup> A major catalytic breakthrough was accomplished in this field with the development of Cp\*Co(III)-type complexes.<sup>8,9</sup> With this catalyst, Glorius and Matsunaga and Kanai reported independently C-H alkylation processes with allylic derivatives involving carbon-carbon double bond insertion and subsequent  $\beta$ -oxygen elimination.<sup>10</sup> From an atom economy point of view, the release of a leaving group is not desirable. Therefore, Li and coworkers



Scheme 1 Co-catalysed C-H alkylation.

explored successfully the possibility to perform C-H alkylation with vinylloxirane (Scheme 2b).<sup>11</sup> Importantly, allylated products were obtained as mixture of *E*- and *Z*-isomers with ratios spanning from 3.2 to 1.7 to 1. Prior to this work, Ackermann had described that activated vinylcyclopropanes could be used as allylating partners.<sup>12</sup> The  $\beta$ -carbon elimination being highly selective, mainly *Z*-isomers were isolated. Of note, these two reactions were successfully performed with enamides substrates.<sup>13</sup> As a part of our interest for the metal-catalysed activation of small rings,<sup>14,15</sup> we report now herein the use of vinylaziridines to carry out the Cp\*Co(III)-cobalt catalysed direct C-H alkylation involving a  $\beta$ -nitrogen elimination step.<sup>16</sup> We have optimized the cobalt-catalysed C-H alkylation using the benchmark substrates 2-phenylpyridine **1a** and tosyl-containing vinylaziridine **2a** and determined that, through the appropriate choice of conditions, the reaction can be achieved with good

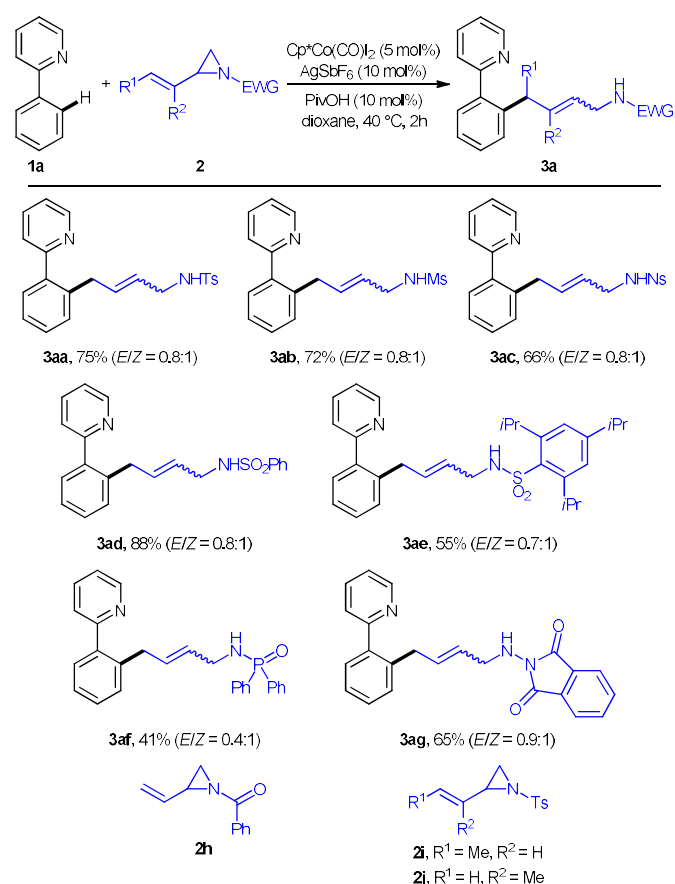
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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x



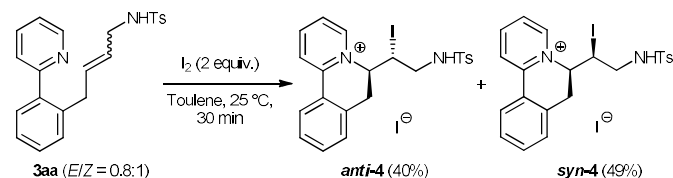
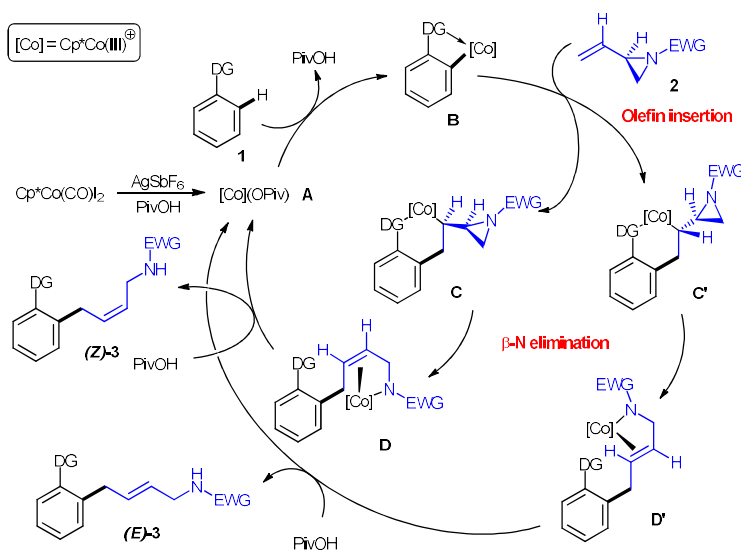
**Table 3** Substrate scope and limitations of various vinylaziridines<sup>a</sup>

<sup>a</sup> Reaction conditions: **1a** (36  $\mu\text{L}$ , 0.25 mmol), vinylaziridine **2** (0.25 mmol, 1 equiv.),  $\text{Cp}^*\text{Co(CO)}_2\text{I}_2$  (6.0 mg, 5 mol%),  $\text{AgSbF}_6$  (8.6 mg, 10 mol%), PivOH (2.4 mg, 10 mol%), 1,4-dioxane (0.5 mL). E/Z ratio determined by  $^1\text{H NMR}$ . Ns = 4-nitrobenzenesulfonyl.

occurred with vinylaziridine **2h**; since under the reaction conditions used, **2h** was converted into the more stable vinyloxazoline. Unfortunately and despite harsher reaction

conditions, when the carbon-carbon double bond of the vinylaziridine was substituted by a methyl, either in terminal or internal position, **2i** and **2j** respectively, no formation of the expected allylation products was observed. In the case of allylating reagents bearing a leaving group, this type of substitution did not shut down the reaction;<sup>10b-d</sup> but this point was not discussed for vinylcyclopropane and vinyloxirane.<sup>11,12</sup> Considering recent related mechanistic studies,<sup>10b,12,18</sup> a plausible mechanism is shown in Scheme 2. Formation of catalytically active species **A** is followed by C-H activation process giving rise to cobaltacycle **B**. Olefin insertion leads to intermediates **C** and **C'** (only one enantiomer depicted) and subsequent *syn*  $\beta$ -N eliminations afford **D** and **D'** respectively. Of note,  $\beta$ -H elimination process seems to be disfavoured since the formation of alkylideneaziridine was never detected. A protonolysis step releases products **3** and regenerates active species **A**. The low or no selectivity in the formation of *E*- and *Z*-isomers seems to indicate that the selective-determining step, olefin insertion, cannot be selectively achieved. Thus, intermediates **C** and **C'** are formed in almost equal amounts.

To illustrate the synthetic usefulness of allylated compounds **3**, **3aa** was treated with iodine in toluene at 25  $^\circ\text{C}$  (Scheme 3). After only 30 min, the starting material was completely consumed and pyridinium salt **4** was obtained as a separable mixture of diastereomers with a ratio *anti*/*syn* (0.8:1) corresponding to the *E*/*Z* ratio of **3aa**.<sup>19</sup> This of note that the 6,7-dihydro-benzo[*a*]quinolizinium moiety of compounds **4** is present in the skeleton of various natural products such as Berberine and related alkaloids.<sup>20</sup>

**Scheme 3** Iodocyclisation of C-H allylation product **3aa**.**Scheme 2** Proposed mechanism.

## Conclusions

In summary, we have developed a Co-catalysed direct C-H allylation of arenes using vinylaziridines to prepare various allylated aromatic and heteroaromatic compounds overall in good yields. Despite a low *E/Z* selectivity, this reaction occurring under mild reactions conditions was found relatively broad in scope for both arenes and vinylaziridines. The reaction pathway probably involves a C-H activation step carried out by the versatile cationic cobalt(III) complex, olefin insertion that determines the formation of either *E*- or *Z*-isomer, and subsequent  $\beta$ -nitrogen elimination that triggers the aziridine ring-opening. A synthetic application of the allylation products has been achieved. Further developments are currently underway in our laboratory and will be reported in due course.

## Acknowledgements

L.K. thanks the China Scholarship Council for a Ph.D. grant. This work was supported by the Ministère de l'Enseignement Supérieur et de la Recherche (B. B. Ph.D. grant), the CNRS, AMU, and Centrale Marseille. We thank Christophe Chendo and Dr. Valérie Monnier for mass spectrometry analyses (Spectropole, Fédération des Sciences Chimiques de Marseille). Dr A. Tenaglia is gratefully acknowledged for helpful discussions.

## Conflicts of interest

There are no conflicts to declare.

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