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Asymmetric Allylation/Pauson–Khand Reaction: A Simple Entry to Polycyclic Amines. Application to the Synthesis of Aminosteroid Analogues

Santos Fustero,*[,†,‡] Rubén Lázaro,[†] Nuria Aiguabella,[§] Antoni Riera,[§,∥] Antonio Simón-Fuentes,[†] and Pablo Barrio*[,†]

[†]Departamento de Química Orgánica, Universidad de Valencia, E-46100 Burjassot, Spain

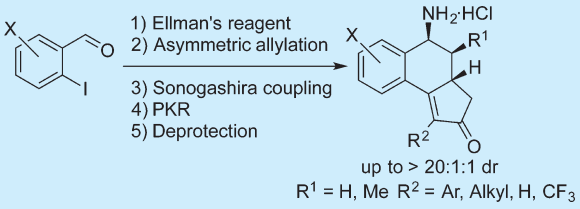
[‡]Laboratorio de Moléculas Orgánicas, Centro de Investigación Príncipe Felipe, E-46012 Valencia, Spain

[§]Institute for Research in Biomedicine (IRB Barcelona), c/Baldiri Reixac, 10, 08028 Barcelona, Spain

[∥]Departament de Química Orgànica, Universitat de Barcelona, c/Martí i Franques, 1, 08028 Barcelona, Spain

Supporting Information

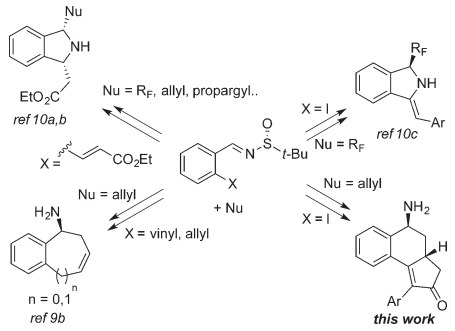
ABSTRACT: Asymmetric allylation of *o*-iodoarylsulfinylimines has been achieved in high diastereoselectivities. The thus-obtained *o*-iodoarylhomoallylic sulfinamides participate in a subsequent Sonogashira coupling followed by a diastereoselective intramolecular Pauson–Khand reaction. In this way, tricyclic amines showing a unique benzo-fused indenyl backbone were obtained. The methodology has been applied to the synthesis of amino steroid analogues.



Chiral homoallylic amines are versatile building blocks in organic synthesis. The presence of a pendant double bond enables further synthetic transformations for the assembly of more complex backbones.[1] Undoubtedly, the asymmetric allylation of imines[2,3] is the most widely used methodology for their synthesis, and among the existing methods, the addition of allylmetal reagents to Ellman's *tert*-butylsulfinimines[4] shows some salient features: high degree of stereocontrol and chemical yields, reliability, and functional group compatibility, among others. On the other hand, the Pauson–Khand reaction (PKR) is arguably the method of choice for the construction of the cyclopentenone ring from acyclic precursors.[5,6] Astonishingly, despite the impressive development undergone by these two powerful transformations they have never been combined for the construction of complex polyclyclic amines.[7] To the best of our knowledge, there is only one example of PKR of a homoallylic amine bearing a pendant triple bond in its carbon backbone reported in the literature in a racemic form.[8]

On the other hand, our group has been interested in the use of 2-halobenzaldehyde-derived Ellman's sulfinimines for the asymmetric synthesis of a variety of benzo-fused carbo-[9] and heterocycles[10] in the context of diversity-oriented synthesis (DOS).[11] Hence, we have found that the introduction of a suitable functional group at the *ortho*-position of substrates of this kind enables a series of reaction sequences initiated by a nucleophilic addition (A_N) of a suitable nucleophile to the imine, namely: A_N/intramolecular aza-Michael reaction,[10a,b] A_N/RCM,[9b] and A_N/intramolecular hydroamination (Scheme 1).[10c] Continuing with our interest in expanding the structural diversity from these readily available starting materials, we

Scheme 1. Synthetic Versatility of 2-substituted Aromatic Ellman's Sulfinimines



disclose here our results in the allylation/PKR sequence giving rise to polycyclic amines in very high diastereoselectivities (Scheme 1). Building on the principles of diversity-oriented synthesis, we selected *o*-iodobenzylidene *tert*-butanesulfinamides, previously described by our research group, as starting materials for our study.

First, we tested the allylzinc addition to a model substrate in order to rule out any possible interaction between the organometallic reagent and the labile C–I bond[12] and check the diastereoselectivity, which is known to be sensitive to steric hindrance.[13] Based on our recent findings,[10b] the allylation reaction was performed on the crude imine giving rise to

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