New access to bicyclic heterocyclic structures bearing a fused nitropyrazole

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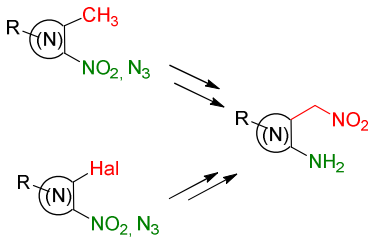
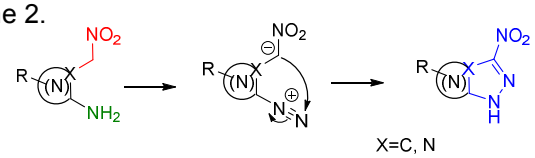
The strategy described in this work provides new access to bicyclic structures, with a 3-nitropyrazole fused with a six or a five-membered ring. The point is that cyclization occurs during the last sequence of the synthesis, so that reactivity relies mostly on the main ring.

The key point of the strategy was the introduction of the nitromethylene moiety, as few techniques exist to synthesize this kind of fragments, as well as its handling. Indeed this fragment makes compounds hard to purify and very sensitive to many reaction conditions(acidic protons, ease of oxidation and reduction…). This work also describes a new, practical and scalable method for isolation and purification of nitromethyl(het)arenes (scheme 1).



Scheme 1 – The route to 1-amino-2-(nitromethyl)arenes

The last reaction implies a condensation of a nitromethylene fragment on a diazonium placed in the ortho position on the main cycle. After re-aromatization, the newly formed heterocyclic compound presents a higher nitrogen content with a 3-nitropyrazole moiety. The reaction is summarized in scheme 2.



Scheme 2 – Intramolecular cyclization to fused 3-nitropyrazoles