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1,3-Diazepane-2,4-diones: bench-stable, bifunctional and customisable isocyanate precursors

Jake. P. C. L. Painter[1*], **David Dailler**[1], **Neil G. Berry**[1], **Craig. M. Roberston**[1], **John F. Bower**[1]
1) Department of Chemistry, University of Liverpool, Crown Street, Liverpool, L69 7ZD, United Kingdom
e-mail: jake.painter@liverpool.ac.uk

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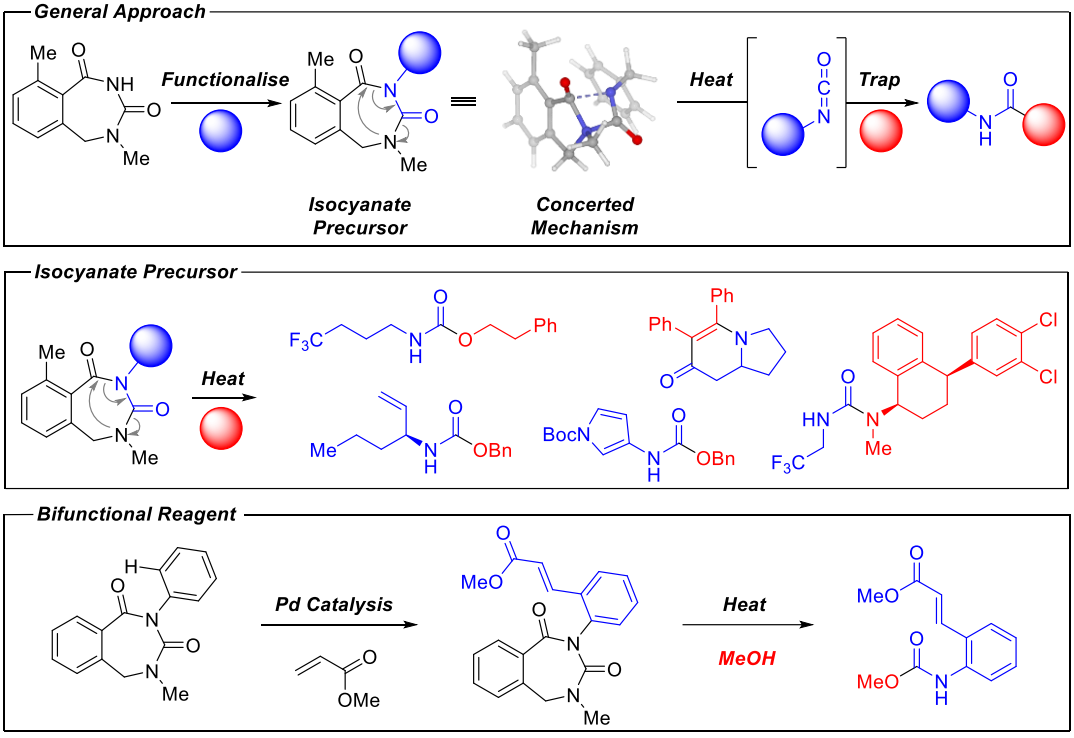
ABSTRACT

Isocyanates are extremely useful reagents in the synthesis of ureas, carbamates and *N*-heterocycles which are ubiquitous amongst bio-active molecules.[1,2] However, accessing novel isocyanates on a scale relevant to the analogue synthesis of bio-active compounds can be synthetically challenging. Furthermore, commercially available isocyanates can be expensive, limited to aliphatic carbon chains/substituted aromatics and toxic and/or volatile to handle. The work presented addresses these issues by utilising the DFT-directed design of 1,3-diazepane-2,4-diones reagents which undergo a metal-free ring contraction acting as bench-stable isocyanate precursors.[3,4] A series of mild functionalisation techniques such as Chan-Lam, Mitsunobu, S_N2-alkylation and asymmetric allylic amination were developed yielding a diverse set of isocyanate precursors which could be utilised to form unsymmetrical ureas, carbamates and thio-carbamates, as well as *N*-heterocycles *via* Rh-catalysed cycloaddition and electrocyclic ring closure. The reagents also exhibit bifunctionality by directing C-H activation before acting as an isocyanate precursor.



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REFERENCES

1. A. K. Ghosh and M. Brindisi, *J. Med. Chem.* ***2015***, *58, 2895–2940*
2. A. K. Ghosh and M. Brindisi, *J. Med. Chem.* ***2020***, *63, 2751–2788*
3. G. Bocelli, M. Catellani, F. Cugini and R. Ferraccioli, *Tetrahedron Lett.* ***1999***, *40, 2623–2624*
4. G.-W. Wang, O. O. Sokolova, Tom. A. Young, E. M. S. Christodoulou, C. P. Butts and J. F. Bower, *J. Am. Chem. Soc.* ***2020***, *142, 19006–19011*