Over the last decade, the field of C–H activation has evolved from using bespoke strongly chelating functional groups to the development of much more appealing transformations which exploit the directing ability of native functionalities such as carboxylic acids, amides and amines, among others. In this regard, the group of Professor Matthew Gaunt at the University of Cambridge (UK) recently reported the first examples of a tertiary alkylamine directed C(sp³)–H activation reaction. “Tertiary alkylamines have been historically used in palladium-catalysed reactions to reduce a Pd(II) pre-catalyst into the desired active Pd(0) species to initiate, for example, a Suzuki cross-coupling reaction,” said Professor Gaunt, who continued: “A consequence of this reaction pathway is the oxidative decomposition of the tertiary alkylamine, which has precluded their use in C–H activation reactions.”

The Gaunt group discovered that a simple N-acetyl amino acid ligand was capable of preventing amine decomposition, thereby facilitating the desired C–H activation pathway and ultimately leading to a method of directly introducing functionalized aryl groups into the tertiary alkylamine scaffolds. “The tertiary alkylamine starting materials are readily available and a plentiful supply of diversely functionalized arylboronic acid coupling partners can be acquired from commercial sources; all other reaction components are available from commercial vendors,” said Professor Gaunt. He added: “We believe that the operational simplicity of this new high-yielding transformation, combined with its broad substrate scope, will be appealing to practitioners of the synthetic and medicinal communities in academic and industrial institutions. For example, starting from a common tertiary alkylamine, it is possible to incorporate many different aromatic features directly into the amine scaffold, enabling the rapid assembly of a library of compounds with potentially promising biological activity.”

“We aim to use this new platform to introduce other functionalisations into tertiary alkylamines, while continuing to improve the efficiency and sustainability of the process,” explained Professor Gaunt. He concluded: “Furthermore, we are also investigating the capacity of this transformation to effect enantioselective C–H bond functionalizations at the γ-methylene position in tertiary alkylamines, which would provide direct access to valuable non-racemic molecules of potential biological interest.”

![Figure 1 Mechanism of the reaction](image-url)
Scheme 1  Selected scope and applications of the palladium-catalysed arylation of tertiary alkylamines
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Prof. Matthew Gaunt is the 1702 Yusuf Hamied Professor of Chemistry in the Department of Chemistry at the University of Cambridge (UK). Matthew began his higher education at the University of Birmingham and graduated with first class honours in 1995. He moved to Cambridge for his PhD studies to work under the supervision of the late Dr Jonathan Spencer. He graduated in 1999 before moving to the University of Pennsylvania, Philadelphia (USA) as a GlaxoWellcome Postdoctoral Fellow. In 2000, he returned to Cambridge as a Junior Research Fellow at Magdalene College and a Ramsay Memorial Trust Fellow, where he worked with Professor Steven V. Ley. Matthew began his independent research career in 2003 and was awarded a Royal Society University Research Fellowship at the University of Cambridge in 2004. He was promoted to Lecturer in 2006, Reader in 2010, Full Professor in 2012, and was Elected to the 1702 Chair in 2019.