

Arylation of Hydrocarbons Enabled by Organosilicon Reagents and Weakly Coordinating Anions

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Aryl carbocations are not frequently used for intermolecular arylation and alkylation reactions, owing to their high energy, challenging controlled generation and difficulties in taming their reactivity. However, if these problems could be overcome, the use of phenyl carbocations and related intermediates could represent a very efficient and straightforward way to synthesize biaryls and alkyl arenes. Recently, the group of Professor Hosea Nelson from the University of California, Los Angeles (USA) reported in *Science* a breakthrough method for generating and reacting β -silicon-stabilized aryl cation equivalents having very weakly coordinating anions, that can be generated via silylium-mediated fluoride activation.

“The chemistry is built on a mountain of foundational work by Siegel, Reed, Ozerov and others,” explained Professor Nelson, “while we added a bit of an organic methodology twist. Specifically, we looked at ways to make phenyl cation equivalents that were more competent intermolecular reaction partners.” Through β -silicon substitution, Professor Nelson and co-workers were able to achieve this and enable a cationic chain reaction that required substoichiometric amounts of silane. “We were quite surprised to observe the halogen selectivity inherent in the system,” said Professor Nelson. “We were even more surprised to see that we could arylate methane, and that n -alkyl nucleophiles react at the terminal CH_3 group! Arylation of alkanes is very rare, and we feel that our chemistry forms a nice conceptual foundation for moving this area forward.”

Interestingly, Professor Nelson revealed that this project was fuelled by a team of ‘rookies’. In fact, Professor Nelson was a brand-new faculty member, who had been trained in organic methodology and total synthesis, while the two co-first-authors, Brian Shao and Alex Bagdasarian, were 1st year graduate students and the third author, Stasik Popov, was a summer rotation student who hadn’t even officially started graduate school at UCLA. Professor Nelson said: “We found ourselves making advances in a field that was completely new to us...quite exciting and unexpected.”

The new methodology can be used to achieve intermolecular arylation (Scheme 1) as well as alkylation reactions (Scheme 2), affording respectively biaryls and alkyl arenes.

In terms of future potential, the group is trying to expand the chemistry in two areas. “Firstly, we are looking to develop new initiators and phenyl cation precursors that allow for greater substrate compatibility. Our roots are in organic methodology and total synthesis, so we would love to be able to do reactions with more complex substrates,” explained Professor Nelson. He continued: “Secondly, we are also pursuing a better mechanistic understanding. We feel that will also allow us to improve the chemistry with respect to efficiency and cost in the area of simple hydrocarbon functionalization.”

Professor Nelson concluded: “Finally, the hunt for unambiguous evidence (crystallographic evidence) of a phenyl cation intermediate is an ongoing project in the group.”

Mattes female

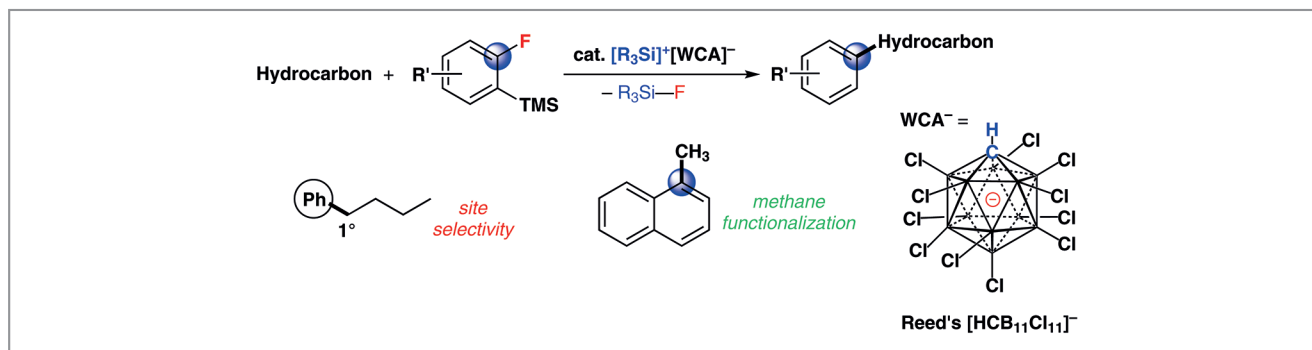


Figure 1 The novel synthetic methodology

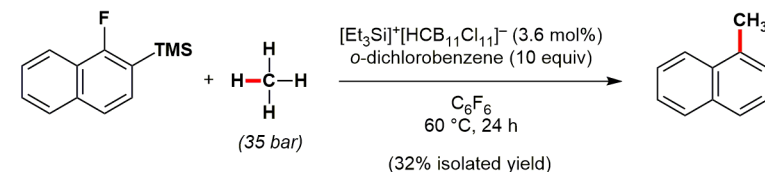
Entry	Substrate	Temp. (°C)	Time (h)	Product	Yield (%)
1		60	1		47–71
2		30	1		45–99
3		60	48		29

Scheme 1 Arylation reactions

A. Alkanes

Entry	Alkane	Temp. (°C)	Time (h)	Product	Yield (%)
1		60–100	1		40–54
2		60	8		42

B. Methane



Scheme 2 Alkylation reactions

About the authors



From left: S. Popov, Prof. H. Nelson, B. Shao, A. Bagdasarian
(Photo credit: Penny Jennings)

Brian Shao was born and raised in Alhambra, California (USA). He obtained his B.Sc. degree at the University of California, Davis (USA) in 2015 and continued his studies at the University of California, Los Angeles (USA) as a Ph.D. candidate that same year. Joining Professor Hosea Nelson's group, his research focuses on silylium-mediated catalysis.

Alex Bagdasarian was born in Cupertino, California (USA) in 1993. He completed his B.S. in Pharmaceutical Chemistry at the University of California, Davis (USA) in 2015. During his time there, he worked under the supervision of Professor Mark J. Kurth focusing on the synthesis of biologically active heterocyclic scaffolds through novel methodologies. During the summer of 2015, he joined the lab of Professor Hosea Nelson where he has been working on developing new reactions using main-group catalysts.

Stasik Popov was born in Kazakhstan in 1994. He obtained his B.S. degree in Chemistry and Mathematics from Brandeis University (USA) in 2016. In the same year, he joined Professor Nelson's group at University of California, Los Angeles (USA) as a graduate researcher. His research focuses on the development of new synthetic reactions utilizing silylium catalysis.

Hosea Nelson earned a B.S. in Chemistry from the University of California at Berkeley (USA) in 2004 and a Ph.D. from the California Institute of Technology (USA) in 2012 (advisor Professor Brian Stoltz). After postdoctoral training at the University of California at Berkeley (advisor Professor Dean Toste), Professor Nelson joined the UCLA faculty in 2015. His research focuses on the discovery of new chemical reactions.