Simone Di Noja, 27/02/2023

Organogel delivery vehicles for the stabilization of organolithium reagents

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Nat. Chem. **2023** https://doi.org/10.1038/s41557-023-01136-x

Who are the corresponding authors and what are their research areas?

Peter O'Brien

Peter O'Brien received his PhD in 1995 at the University of Cambridge, under the supervision of Prof. Stuart Warren. After that, he moved to the University of York where he started his independent career. Since 2007 he is Professor in Organic chemistry in the same institution. His research interests include asymmetric synthesis, organolithium methodology, synthesis of saturated heterocycles, medicinal chemistry and fragment-based drug discovery.

David K. Smith

David K. Smith is a professor of chemistry at the University of York (UK). He received his Ph.D. in 1996 under the supervision of Prof. Paul Beer, and after, he was a postdoctoral researcher with Prof. François Diederich. He began his independent career at University of York in 1999 and was promoted to professor in 2006. His research focuses on nanochemistry and self-assembling nanomaterials. In particular, Smith's research group studies the properties of self-assembling molecular gels applied to molecular electronics, biomaterials and drug delivery. He is also known for his outreach in chemistry education. In addition to science, Smith also writes about the role of the impact of LGBT community in science.

What is the main claim of the article?

Main claim: In this work, the authors report an encapsulating method for the stabilization of air and water-sensitive organolithium reagents—PhLi, *n*-BuLi and *s*-BuLi—in a low-cost hexatriacontane ($C_{36}H_{74}$) organogel. The gel substantially enhances organolithium stability, allows simple storage, delivery and handling (the gel can also be cut into pieces), enabling reproducible reagent portioning. The use of this technology is demonstrated under ambient and air conditions for nucleophilic addition reactions, bromine–lithium exchange, ortho-lithiation and C–H functionalization. This approach is highly versatile, because it can be applied also to other air sensitive compounds, *e.g*. organomagnesium reagents. Remarkably, it allows these powerful reactions being safer and handier.

How is it demonstrated?

Demonstration: The morphology of the gel is demonstrated by SEM analysis.

Titration: The organolithium content in the gels was checked using (+)-menthol and 2,2'-bipyidine as indicators. The analyses are carried out for gels stored in different conditions (inert atmosphere, under air, in vial, as block, in water) and checked during the time.

The organomagnesium content in the gels was checked using propan-2-ol and 1,10-phenanthroline as indicators.

The products obtained to check the different reactivities are characterized by ^{1}H-NMR and ^{13}C-NMR.

Conditions for gel fabrications: strictly inert atmosphere, $C_{36}H_{74}$ gelator (from 2.8% wt/vol to 20% wt/vol), commercial organolithium solution (final concentration from 0.6 M to 1.9 M, depending on the vessel in which gel is made).

Which are the key related papers?

- Vidal, C., García-Álvarez, J., Hernán-Gómez, A., Kennedy, A. R. & Hevia, E. Introducing deep eutectic solvents to polar organometallic chemistry: chemoselective addition of organolithium and Grignard reagents to ketones in air. *Angew. Chem. Int. Ed.* **2014**, 53, 5969–5973.
    - First paper in which the authors demonstrate the possibility to carry out reactions with organolithium in DES solvents in the presence of air

- Dilauro, G., Quivelli, A. F., Vitale, P., Capriati, V. & Perna, F. M. Water and sodium chloride: essential ingredients for robust and fast Pd-catalysed cross-coupling reactions between organolithium reagents and (hetero)aryl halides. *Angew. Chem. Int. Ed.* **2019** 58, 1799–1802.
    - First paper in which the authors demonstrate the possibility to carry out metal-catalyzed cross-coupling reactions with organolithium in aqueous media in the presence of air

Additional comments

Despite the idea at the basis is simple, this research is groundbreaking. I believe that this kind of gels represent a turning point for reactions with air- and water-sensitive reagents.

Negative point: I could not find any information on how the titrations on the gels have been performed.