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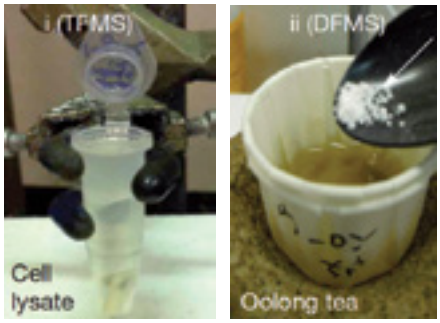
Frequently Asked Questions: Baran Reagents

General Information



(Photo credit: Baran Group)

Functional even in unconventional media!

For more information on the Baran group and the reagents available from Aldrich® Chemistry, visit **Aldrich.com/baranreagents**

What do the Baran reagents do?

Allow the placement of alkyl groups onto molecules in drug discovery by replacing a C-H bond with the corresponding C-C bond (trifluoromethyl, difluoromethyl, isopropyl, etc.). Alternative technologies require a catalyst in conjunction with the reagent to perform the same application.

What is the benefit of using a Baran reagent compared to other products that do similar applications?

These reagents are air and water stable, and chemistry can be implemented in the presence of air and/or water. The reaction also works in a wide variety of solvents and regioselectivity can sometimes be tuned by choice of solvent on pH.

Which Baran reagents provide the more unique alkylation patterns?

The DFMS reagent (767840) and DFES-Na reagent provide difluoromethyl and difluoroethyl groups, which are highly unique.

Who would be interested in using Baran reagents?

Drug discovery researchers and medicinal chemists in industry and academia. Some academic customers doing chemical methodology in fluorination may be interested, but this is more of a niche market at this level.

What are similar products to the corresponding Baran reagents?

Baran Reagent	Application	Alternative Product(s)
DFMS (767840)	Difluoromethylation	None
TFMS (771406)	Trifluoromethylation	777692, 771147, 754218, 743232, L511315, 488712, 483869
IPS (745480)	Isopropylation	230111, 648787, 667153, 680966
TFES (745499)	Trifluoroethylation	64297, 177814, 177822, 752924
DFES-Na (745405)	Difluoroethylation	None

What other products are generally required to use the Baran reagents?

Typically a 70% aqueous solution of *t*-butyl hydroperoxide (Sigma-Aldrich 458139, Luperox®) and solvent (i.e. water, chlorinated solvent and/or DMSO).

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To find out more about the zinc sulphinate toolkit available from Aldrich® Chemistry, visit **Aldrich.com/baranreagents**

What technical problems do the Baran reagents solve?

Heterocycles containing basic heteroatoms (especially nitrogen) are often difficult to functionalize because reagents and catalysts can be deactivated by the heteroatom. Also solubility often becomes an issue with nitrogen-containing heterocycles, so the solvents used (DMSO or chloroform:water) allow proper solubility. The Baran reagents have high functional group tolerance and have been shown to be applicable to a range of more complex molecules.

What mode of reactivity do these reagents undergo?

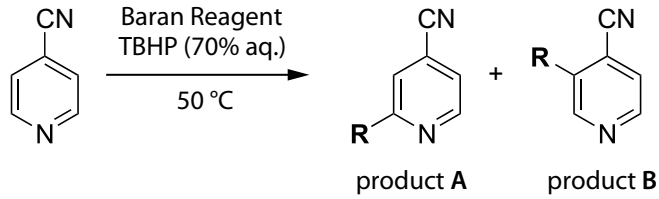
These products undergo radical functionalization of C-H bonds. Other products with similar applications undergo electrophilic or nucleophilic alkylation.

What are the standard conditions for alkylation of a heterocycle using a Baran reagent?

For every 0.125 mmol of substrate, 2.0–3.0 equiv of Baran reagent, 3.0–5.0 equiv of TBHP and either 0.7 mL of DMSO (with or without 0.010 mL of sulfuric acid or TFA), or 0.7 mL/0.2 mL $CHCl_3$/water (other chlorinated solvents can be used as well). These conditions can be performed at RT or 50 °C, and work well for a wide variety of heterocycles and small drugs/agrochemicals, and are easy to monitor by LCMS or NMR.

Which solvent is best to use for my reaction?

Two solvent systems are generally used, either DMSO or a 2.5:1 ratio of chloroform:water. The desired regioselectivity can sometimes be tuned by choice of solvent. Using acid in the system (lowering the pH) can also influence the regioselectivity. DMSO or DMSO/acid are useful solvent systems for ensuring good solubility with larger or more complex heteroarenes. For example:



Solvent	Acid	Result
DMSO	**Sulfuric acid**	Best to obtain **A**
DMSO	**None**	Best to obtain **B**

For more detailed information on the effects solvents have on regioselectivity: O'Hara, F.; Blackmond, D. G.; Baran, P. S. *J. Am. Chem. Soc.* **2013**, ASAP (DOI: 10.1021/ja406223k).

What if my reaction does not go to completion?

If the reaction does not go to completion upon the first addition of Baran reagent and TBHP, it is not uncommon to add a second dose of both to drive the reaction. The reaction temperature can also be increased or an addition of 1-2 eq. of acid can be made to promote reactivity.

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