Enhancing the Hydroalkylation of CF_3 Alkenes with Gaseous Alkanes Through Flow Photochemistry

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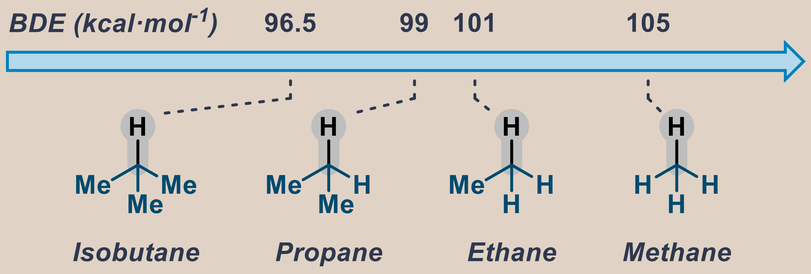
Introduction

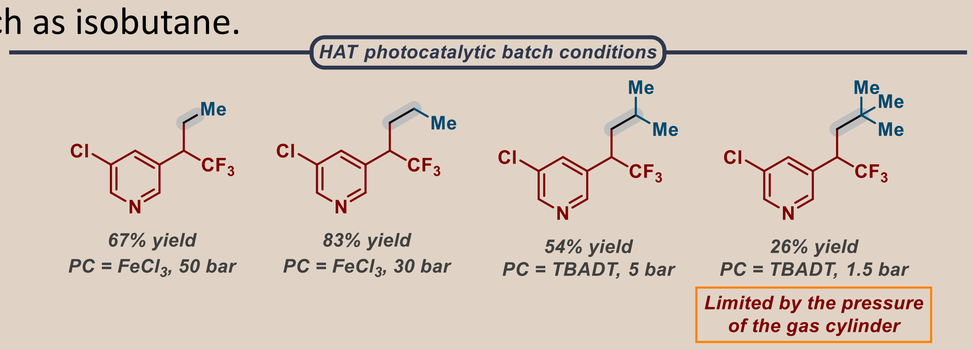
Gaseous alkanes are among the most abundant carbon-based chemical feedstocks. Nonetheless, their high bond-dissociation energies and their low solubility in most organic solvents hinder their use as alkylating agents.[1]



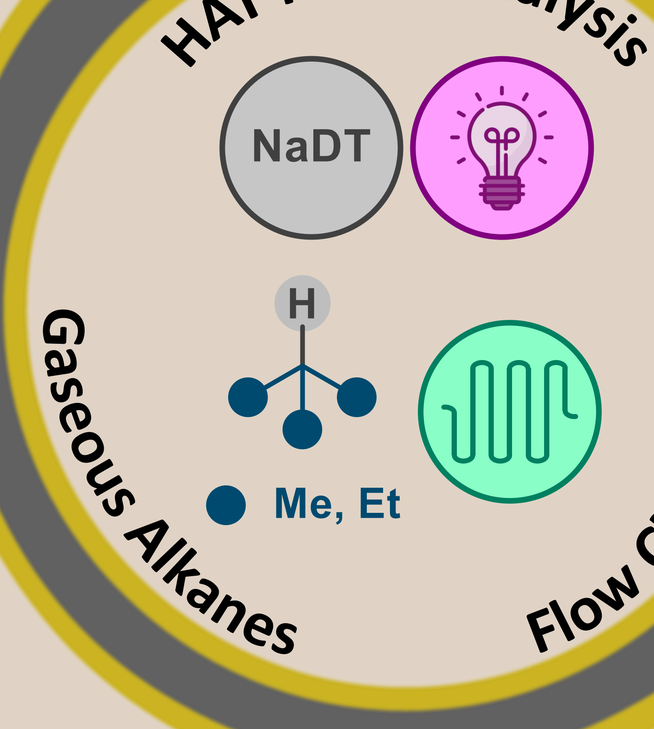
In this context, the use of **hydrogen atom transfer (HAT) catalysis** has allowed the direct and efficient activation of the inert C(sp^3)-H bonds present in gaseous alkanes.[2] In addition to this, **flow chemistry** has emerged as a valuable option for the enhancement of multiphasic reactions, mainly due to improved mass and heat transfer, fast mixing and larger interfacial areas, making it a perfect choice for the use of gaseous alkanes in organic transformations.[3]

Previous work and challenges

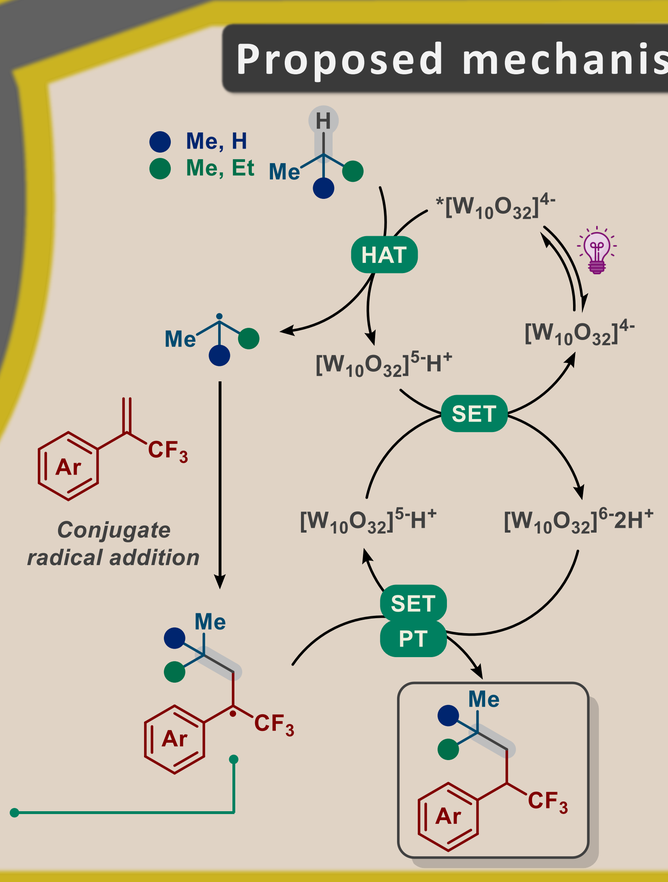
We have reported a new methodology for the **hydroalkylation of trifluoromethyl alkenes with gaseous alkanes** under batch conditions, achieving the functionalization of methane, ethane and propane.[4] Nonetheless, the system faced huge limitations regarding the pressure of the gas cylinder, preventing the use of other gases such as isobutane.



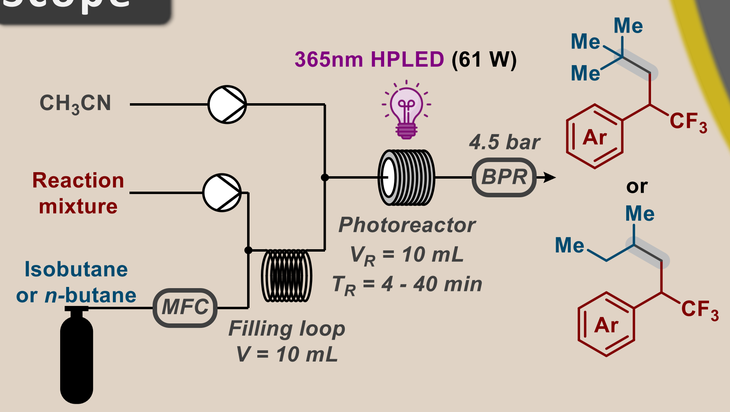
The use of a **novel flow chemistry system** for the hydroalkylation of trifluoromethyl alkenes with gaseous alkanes is presented, overcoming previous pressure limitations using **back-pressure regulators**.



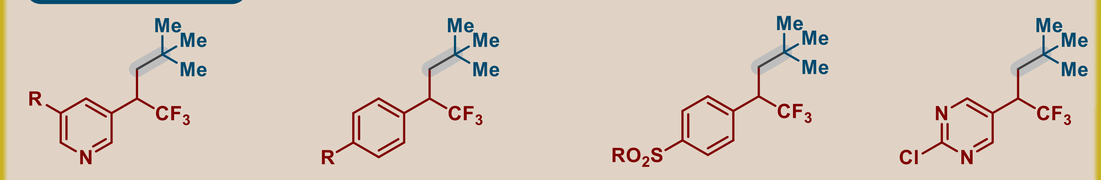
Proposed mechanism



Scope[a]



Isobutane (30:1 g:l)



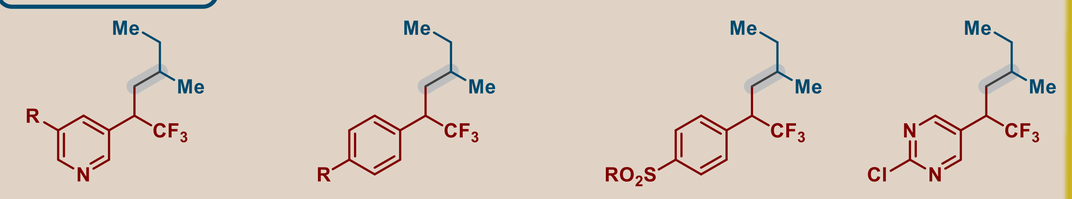
R = Cl, 60% (>20:1)
R = CN, 62% (>20:1)

R = CO_2Me, 62% (>20:1)[b]
R = CN, 69% (12:1)[b]

R = Me, 63% (>20:1)[b]
R = NMe_2, 25% (>20:1)[b]

64% (>20:1)[b]

***n*-Butane (50:1 g:l)**



R = Cl, 63% (11[dr 1:1]:1)
R = CN, 66% (7[dr 1:1]:1)

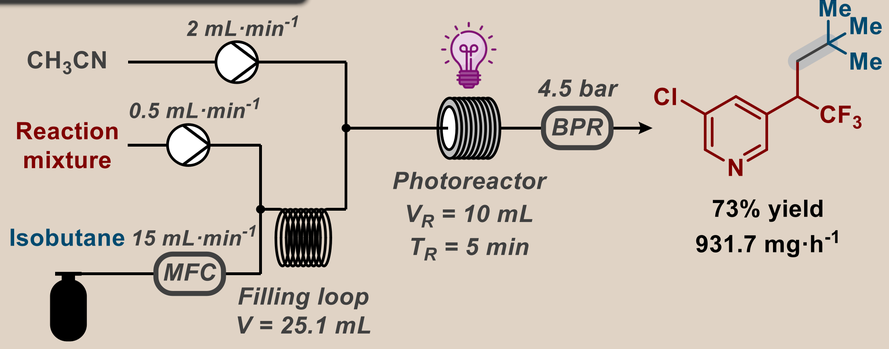
R = CO_2Me, 64% (9[dr 1:1]:1)[b]
R = CN, 36% (7[dr 1:1]:1)[b]

R = Me, 50% (9[dr 1:1]:1)[b]
R = NMe_2, 22% (8[dr 1:1]:1)[b]

49% (11[dr 1:1]:1)[b]

[a] Reaction mixture: trifluoromethyl alkene (0.2 mmol) and NaDT (5 mol%) in CH_3CN (0.1 M).
[b] HFIP (1 equiv) was added to the reaction mixture.

1 mmol scale-up



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