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# Insertion of Benzene Rings into the Amide Bond: One-Step Synthesis of Acridines and Acridones from Aryl Amides

ORGANIC LETTERS
2010
Vol. 12, No. 1
168−171

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StéRéO

# Autor presentation

**Research Interests: synthetic organic chemistry, natural product synthesis, dynamic combinatorial chemistry**

Michael Greaney was born in Liverpool in 1973. He took his undergraduate degree at Oxford, completing his part II research project in the group of **Sir Jack Baldwin** in 1996. He then moved to London to carry out PhD work with **William Motherwell** at UCL, completing his thesis entitled "fluorinating studies using difluoroiodotoluene" in 1999. Michael then left the UK on a GlaxoWellcome scholarship to take up a postdoctoral position with **Jeffrey Winkler** at the University of Pennsylvania, where he worked on the total synthesis of the tumour-promoting diterpene ingenol. He returned to the UK in early 2002, where he is now a Senior Lecturer in chemistry and EPSRC Leadership Fellow at the University of Edinburgh.

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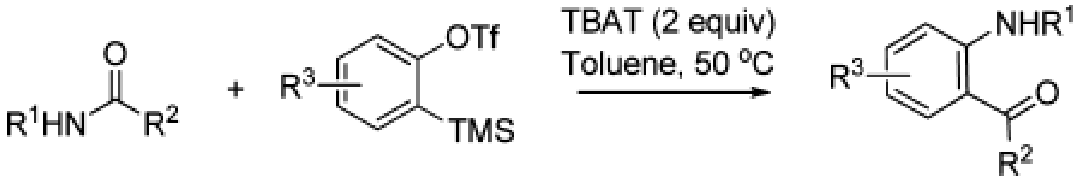
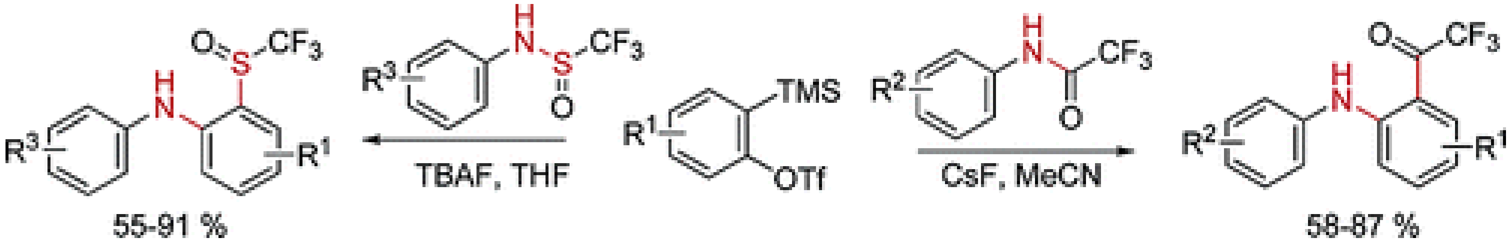


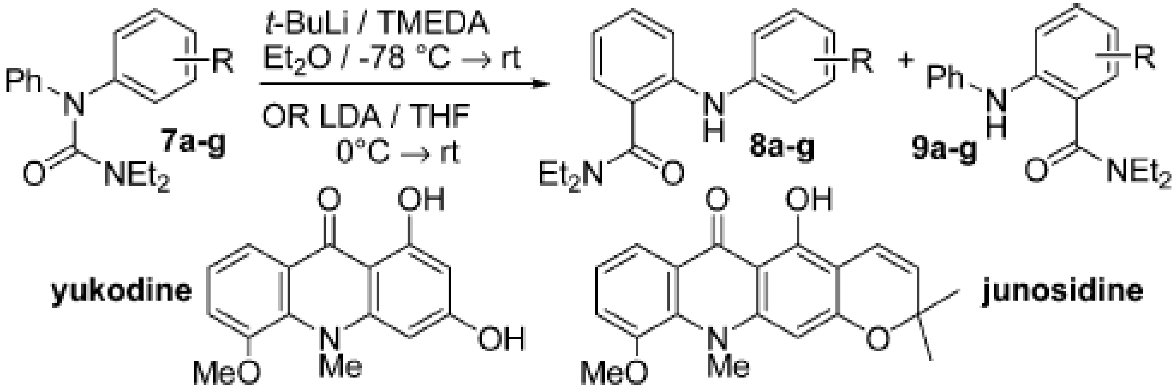
The amide bond is split to form one new aryl **C-N** and one aryl **C-C** bond, forming aminobenzophenone products of fundamental importance in the synthesis of biologically active heterocycles such as **benzodiazepines**, **quinolines**, and **acridones**.



Zhijian Liu and Richard C. Larock, *J. Am. Chem. Soc.*, **2005**, *127* (38), pp 13112–13113

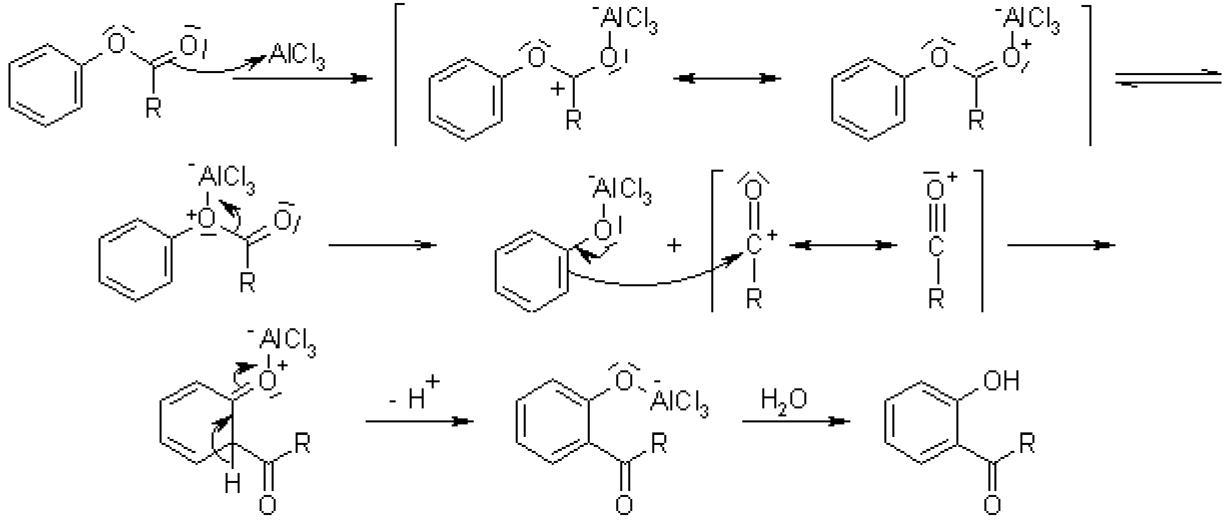
# Anionic N-Fries Rearrangement of N-Carbamoyl Diarylamines to Anthranilamides

Stephen L. MacNeil, Brian J. Wilson, and Victor Snieckus**.** *Org. Lett.*, **2006,** Vol. 8, No. 6, 1133-1136.



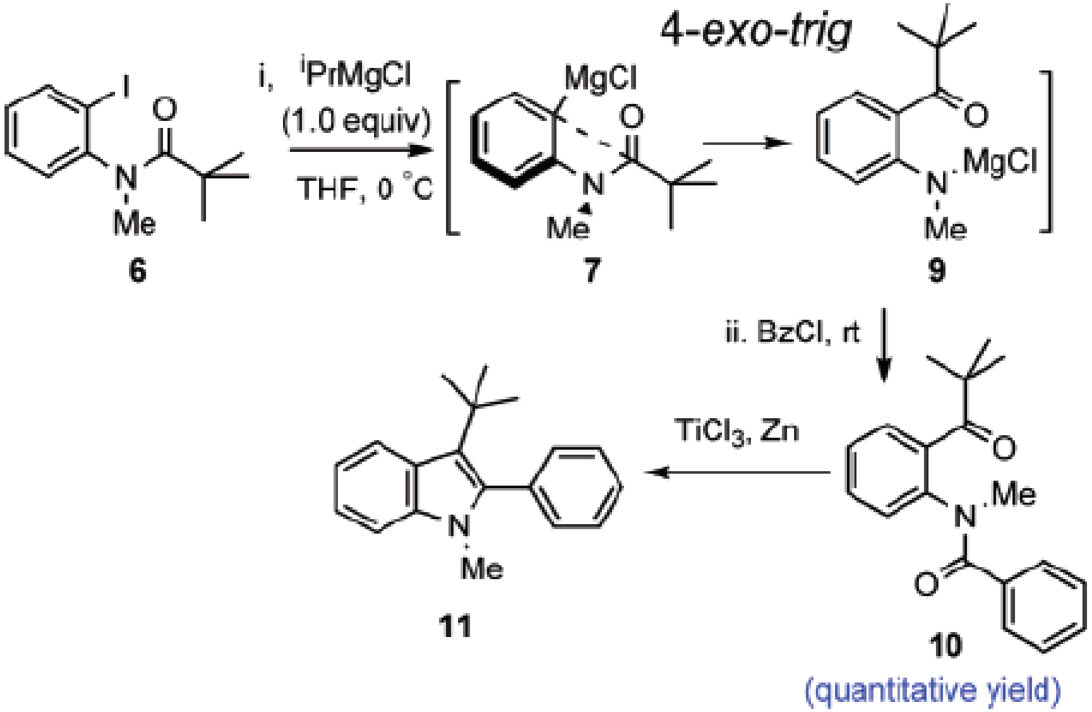
He reports on the scope and regioselectivity of this new version of the anionic ***N-ortho-Fries* rearrangement**, show its link to further D*oM* (combined directed *ortho metalation) chemistry, and* demonstrate its application to the synthesis of acridone and pyranoacridone alkaloids

**Fries rearrangement**:



# Anionic N-Fries Rearrangement of N-Alkyl-2-iodo Anilides Induced by Iodine-Magnesium Exchange.

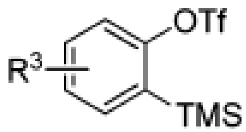
Fei Ding, Yongda Zhang, Bo Qu, Guisheng Li, Vittorio Farina,† Bruce Z. Lu,* and Chris H. Senanayake, *Org. Lett.*, **2008,**Vol. 10, No. 6, 1067-1070

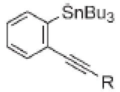
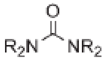
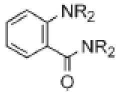
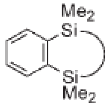
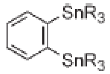
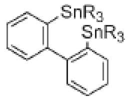
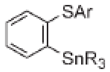
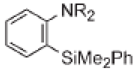
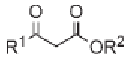
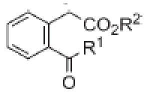
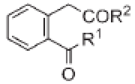
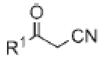
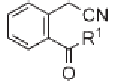
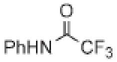
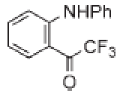
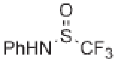
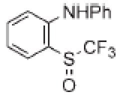
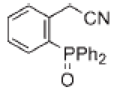


A superior, mild, high-yielding one-pot process for rapid access to oxo anilides has been developed that involves three cascade reactions: iodine-magnesium exchange, regiospecific ortho N-Fries rearrangement, and in situ trapping of the formed aniline anion. Coupled with McMurry cyclization, the two-step process allows ready synthesis of strained 1,2,3-trisubstituted indoles regioselectively.

# Insertion of Arynes into s Bonds

Diego Pea, Dolores Prez, and Enrique Guitin, *Angew. Chem. Int. Ed*. **2006**, *45*, 3579 – 3581



| Entry | Substrate | X–Y | Cat. | Product |
|---|---|---|---|---|
| 1 | $Bu_3Sn{-}{\equiv}{-}R$ | Sn–C | Pd |  |
| 2 |  $R_2NC(O)NR_2$ | N–C | – |  |
| 3 |  | Si–Si | Pd |  |
| 4[a] | $R_3Sn{-}SnR_3$ | Sn–Sn | Pd |  |
| 5[b] | $R_3Sn{-}SnR_3$ | Sn–Sn | Pd |  |
| 6 | $ArS{-}SnR_3$ | S–Sn | – |  |
| 7 | $R_2N{-}SiMe_2Ph$ | N–Si | – |  |
| 8 |  $R^1C(O)CH_2C(O)OR^2$ | C–C | – |  |
| 9 |  $R^1C(O)CH_2C(O)R^2$ | C–C | – |  |
| 10 |  $R^1C(O)CH_2CN$ | C–C | – |  |
| 11 |  $PhHNC(O)CF_3$ | N–C | – |  |
| 12 |  $PhHNS(O)CF_3$ | N–S | – |  |
| 13 |  $Ph_2P(O)CH_2CN$ | C–P | – |  |

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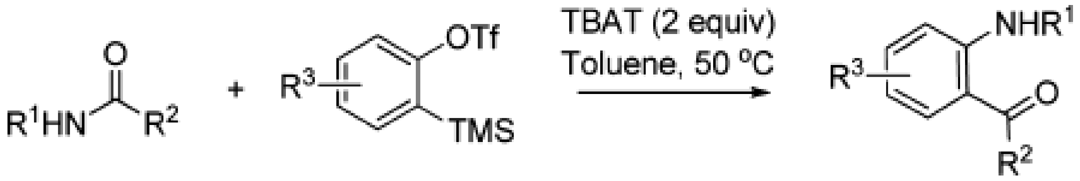
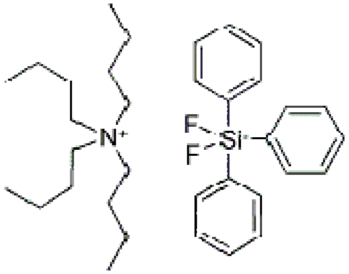
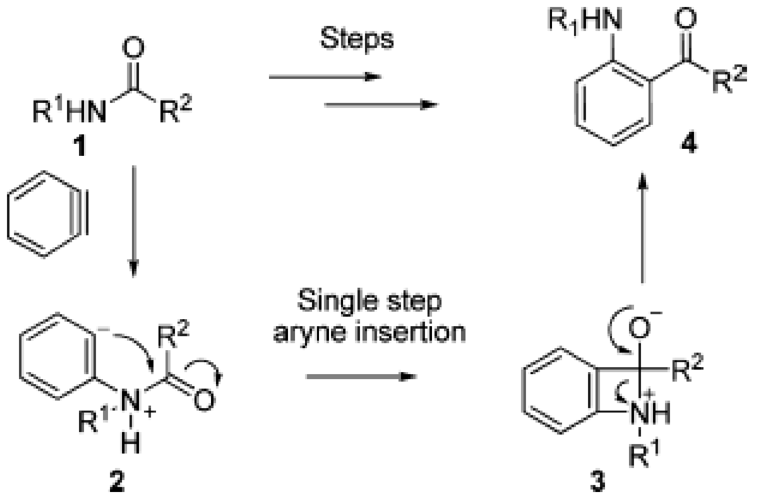


(TBAT): tetrabutylammonium triphenyldifluorosilicate





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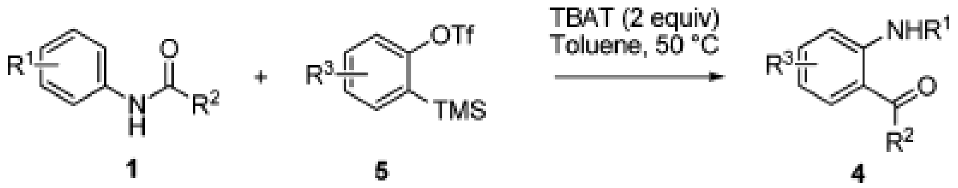
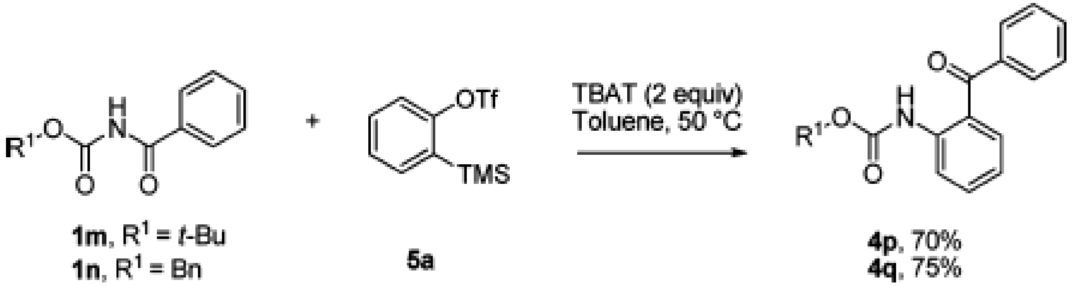
## Amide Insertion:



$R^1$ = H, EWG, EDG, X,
$R^2$ = Ar, *t*-Bu, $CF_3$
$R^3$ = H, OMe, Acetal, Ar

Yields = 61 to 90 %

## Imide Insertion:



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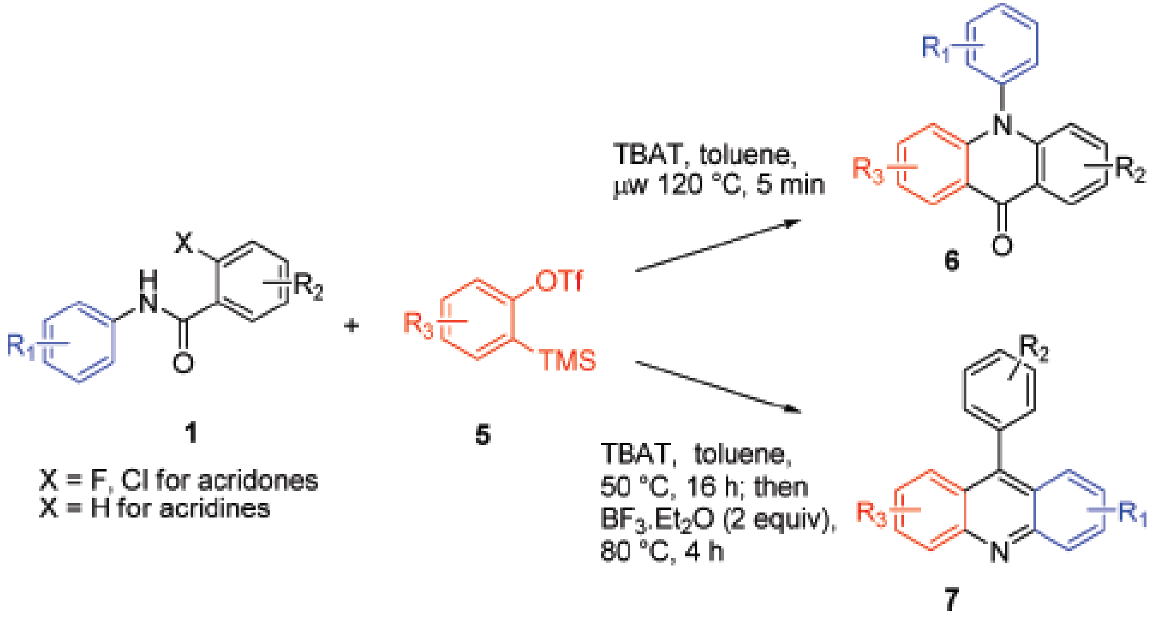
## Divergent synthesis of acridones and acridines:



Acridones (5 examples)

$R^1$ = H, EWG,

$R^2$ = H, Cl

$R^3$ = H, OMe, Acetal, Me

Yields = 62 to 92%

Acridines (5 examples)

$R^1$ = Cl, EWG, OMe

$R^2$ = H

$R^3$ = H, Me

Yields = 62 to 78%

Conclusion:

They have developed an aryne *σ-insertion* reaction for the ubiquitous aryl amide and imide functional groups. The process is high-yielding and operationally simple and uses no metal reagents. The process has been applied to the one-pot synthesis of acridones and acridines.