Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 48 (2007) 4047–4050
Tetrahedron Letters

Triflic acid controlled successive annelation of aromatic sulfonamides: an efficient one-pot synthesis of *N*-sulfonyl pyrroles, indoles and carbazoles

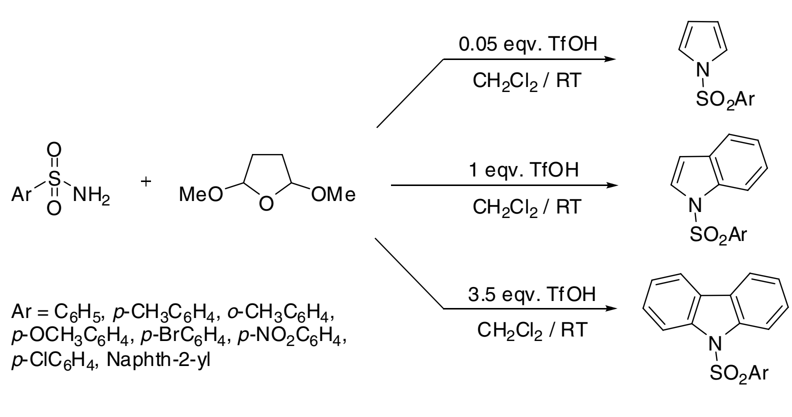
Mohammed Abid, Liliana Teixeira and Béla Török*

Department of Chemistry, University of Massachusetts Boston, 100 Morrissey Blvd., Boston, MA 02125-3393, USA

Received 12 January 2007; revised 3 April 2007; accepted 4 April 2007
Available online 11 April 2007

Abstract—A novel one-pot synthesis of N-substituted heterocycles via successive cyclization/annelation starting from primary sulfonamides is described. This process directly leads to *N*-sulfonyl pyrroles, indoles and carbazoles. The selection of an appropriate reactant/triflic acid ratio successfully controls the formation of the desired product.

Nitrogen containing heterocycles, such as pyrroles, indoles and carbazoles have attracted considerable attention due to their numerous applications in pharmaceutical and synthetic chemistry.[1] These heterocyclic moieties are also found in a variety of biologically active synthetic and natural products.[2] Many efficient processes had already been reported, however, the development of new methods is still in demand.[3] Most methods involve two or more steps to synthesize these heterocycles resulting in 2,3-di- or polysubstituted products.[4] Ideally the synthesis of these heterocycles would involve only one step, directly from simple, readily available substrates. Although, a similar idea had been proposed earlier, it suffered serious drawbacks such as low yields (up to 50%) and low selectivities.[4] In the present study, we report a convenient one-pot synthesis of *N*-sulfonyl-pyrroles, indoles and carbazoles from commercially available sulfonamides using trifluomethanesulfonic acid (TfOH) as an effective catalyst. This methodology provides the desired N-substituted products only, preserving other positions open for further functionalization (Scheme 1).



Scheme 1.

Keywords: Triflic acid; Annelation; Sulfonamides; N-Heterocycles.
* Corresponding author. Tel.: +1 617 287 6159; fax: +1 617 287 6030; e-mail: bela.torok@umb.edu

0040-4039/$ - see front matter
doi:10.1016/j.tetlet.2007.04.021

Introduction of electron-withdrawing groups such as phenylsulfonyl group on the pyrrole nitrogen directs subsequent Friedel–Crafts electrophilic substitution predominantly to the 3-position. Similarly, it makes the 2-position of indole more facile for electrophilic substitution.[5] This indicates that depending on the substituent on the nitrogen we can achieve unusual regioselective synthesis of pyrrole and indole derivatives. Traditional methods for synthesis of *N*-sulfonyl pyrroles involve strong base catalyzed nucleophilic substitution of pyrroles with sulfonyl chlorides.[4,5]

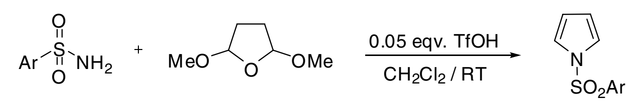
Paal–Knorr type cyclization reactions are often facilitated by strong acids.[6] TfOH is a commonly used superacid ($H_o = -14.1$) and effective catalyst for many transformations. Its use is preferable to other acids with similar acid strength (e.g., H_2SO_4, $ClSO_3H$, FSO_3H) since it does not promote oxidative side reactions.[7] We explored the effectiveness of triflic acid in cyclialkylations of sulfonamides to form *N*-sulfonyl pyrroles, which underwent successive annelation to form corresponding indoles and carbazoles depending upon the amount of triflic acid used. We have carried out several reactions using benzenesulfonamide as a probe and 2,5-dimethoxytetrahydrofuran as an alkylating agent to assess suitable reaction parameters. The results are summarized in Table 1.

We optimized reaction conditions first by varying the amount of triflic acid from catalytic to quantitative. We have observed that the amount of triflic acid had a significant effect on the chemoselectivity of the reaction. The maximum yield of pyrrole was observed with 5 mol % TfOH, however, indole and carbazole syntheses required 1.0 and 3.5 equiv, respectively. To learn about the effects of time and temperature, the reaction was stirred for a longer time at elevated temperatures, but no improvement was observed in yields. After proper optimization of reaction conditions, we were able to obtain the corresponding products in nearly quantitative yields and selectivities.

With the optimized one-pot annelation reaction conditions, we explored the scope of the methodology using several commercially available substituted sulfonamides. We initially synthesized the sequence of various N-substituted pyrroles using 5 mol % TfOH and obtained excellent yields (90–95%) and almost exclusive selectivities. Representative examples are shown in Table 2.

As the data show, the corresponding substituted pyrroles are formed in good to excellent yields. The reaction can be carried out effectively with a wide variety of sulfonamides. In all cases the reaction occurred smoothly without showing any substituent effect. Also, the formation

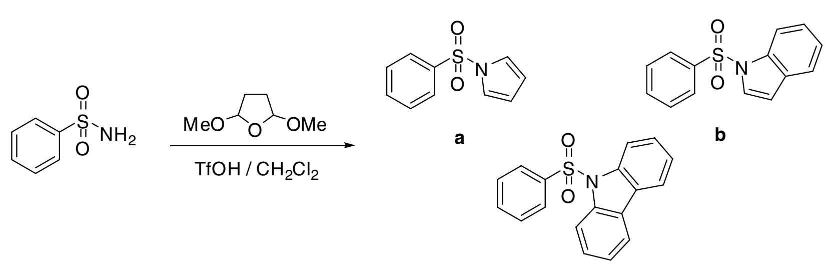
Table 2. Triflic acid catalyzed synthesis of *N*-sulfonyl pyrroles from aryl sulfonamides and 2,5-dimethoxytetrahydrofuran[a]



Entry	Ar	Time (h)	Selectivity[b] (%)	Yield[c] (%)
1	C_6H_5	2	98	92
2	*p*-$CH_3C_6H_4$	2	95	90
3	*p*-$OCH_3C_6H_4$	2	98	89
4	*p*-BrC_6H_4	2	92	86
5	*o*-$CH_3C_6H_4$	2	90	88
6	*p*-ClC_6H_4	2	92	90
7	*p*-$NO_2C_6H_4$	2	88	80
8	Naphth-2-yl	2	90	85

[a] Reaction conditions: sulfonamide (0.636 mmol), 2,5-dimethoxytetrahydrofuran (5 equiv), TfOH (5 mol %), rt, 2 h.
[b] Determined by GC–MS.
[c] Isolated yields after flash chromatography.

Table 1. Triflic acid catalyzed synthesis of *N*-phenylsulfonyl pyrrole, indole and carbazole[a]



Entry	TfOH (mol %)	Yield[b] (%)		
		a	b	c
1	3	85	0	0
2	5	98	0	0
3	50	40	60	0
4	100	5	95	0
5	200	0	30	70
6	300	0	15	85
7	325	0	11	89
8	350	0	8	92

[a] Reaction conditions: sulfonamide (0.636 mmol), 2,5-dimethoxytetrahydrofuran (5 equiv), rt, 2 h.
[b] Based on sulfonamide, determined by GC–MS.