

Reaction of 3-(1-Arylsulfonylalkyl)-indoles with Easily Enolisable Derivatives Promoted by Potassium Fluoride on Basic Alumina

Roberto Ballini,^a Alessandro Palmieri,^a Marino Petrini,^{a,*} and Rafik R. Shaikh^a

^a Dipartimento di Scienze Chimiche, Università di Camerino, via S. Agostino 1, 62032 Camerino, Italy
Fax: (+39)-0737-402-297; e-mail: marino.petrini@unicam.it

Received: August 22, 2007; Published online: December 14, 2007



Supporting information for this article is available on the WWW under <http://asc.wiley-vch.de/home/>.

Abstract: Active methylene compounds and nitro derivatives react with 3-(1-arylsulfonylalkyl)-indoles in the presence of potassium fluoride on basic alumina at room temperature leading to the corresponding adducts in good yields. Under basic conditions, sulfonylindoles suffer elimination of arenesulfinic acid leading to an intermediate vinylogous imine that

promptly adds stabilized carbanions. The obtained 3-indolyl derivatives are pivotal intermediates for the synthesis of indole-based alkaloids and amino acids.

Keywords: basic alumina; carbanions; conjugate addition; heterogeneous catalysis; indoles

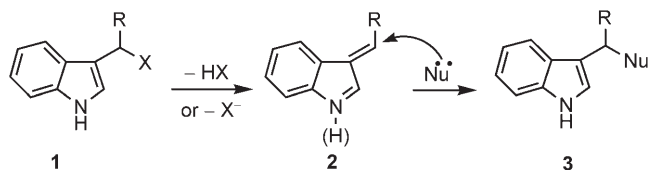
Introduction

Functional group implementation on 3-substituted indoles represents a subtle device in many synthetic plans oriented to the preparation of indole-based biologically active compounds.^[1] This strategy nicely complements direct functionalization at the 3-position of indoles using strong electrophilic reagents, a process widely known as the Friedel–Crafts reaction.^[2] The synthetic approach consists in the introduction of a leaving group at the ‘benzylic’ position of 3-substituted indoles **1** that can be subsequently eliminated under both acidic and basic conditions. The obtained intermediate **2** closely resembles a vinylogous imino derivative that upon nucleophilic addition affords the corresponding 1'-substituted indole **3** (Scheme 1).

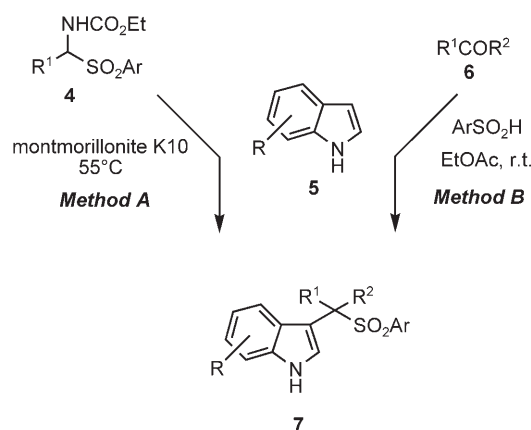
Practically, this procedure may constitute a valid option to the venerable Friedel–Crafts reaction providing that an efficient access to 3-substituted indoles **1** is possible and a rapid elimination step leading to the vinylogous intermediate **2** is achievable. For a

long time, gramine derivatives (**1**, X=NR₂) have represented the most viable substrates to prepare compounds **3** following this approach.^[3] Gramines that are usually prepared exploiting a Mannich reaction on indoles, eliminate the dialkylamino moiety under basic conditions at high temperature (reflux in toluene or xylene) leading to intermediate **2**. Alkylation of the tertiary amino group in gramines affords a quaternary ammonium salt which, being a better leaving group, can be eliminated in mild conditions.^[4] Other derivatives such as 3-(1-hydroxyalkyl)-indoles (**1**, X=OH, OR) have found only occasional utilisation for this purpose,^[5] although these compounds are certainly involved as intermediates in the synthesis of bisindoles and related compounds.^[6] The arylsulfonyl group is recognised as a good leaving group in many synthetic processes,^[7] but its utilisation in indolyl derivatives of type **1** has been somewhat hampered by the paucity of procedures to access these compounds.^[8]

Recently, we have introduced two complementary procedures to efficiently prepare 3-(1-arylsulfonylalkyl)-indoles starting from simple precursors. Reaction of α -amidosulfones **4**^[9] with indoles **5** in the presence of Montmorillonite K-10 under solventless conditions affords sulfonylindoles **7** (Scheme 2, *Method A*).^[10] Alternatively, a simplified method involving a three-component coupling of carbonyls **6**, indoles **5** and arenesulfinic acids leads to the same compounds **7** in comparable yields (Scheme 2, *Method B*).^[11] The effectiveness of sulfonylindoles **7** as precursors of vinyl-



Scheme 1. Synthetic approach to functionalized 3-substituted indoles.



Scheme 2. General syntheses of 3-(1-arylsulfonylalkyl)-indoles.

ogous imino derivatives **2** has been proved in the reaction with Grignard and Reformatsky reagents as well as in different reductive removals of the arene-sulfonyl group.^[10,11]

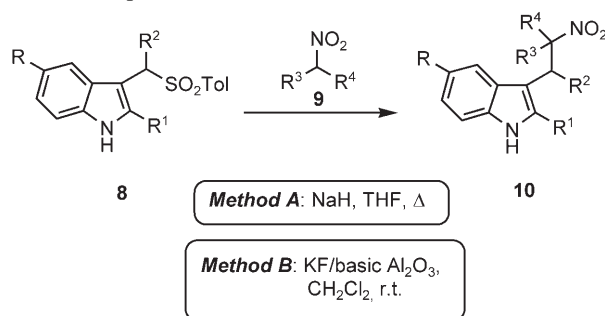
Stabilised carbanions which can be readily obtained from easily enolisable precursors represent a formidable source of functionalised nucleophiles in the reaction with various electrophilic systems. The enhanced acidity of the hydrogen atoms in these compounds allows the utilisation of basic promoters of moderate strength under mild reaction conditions. In this context, solid bases are particularly appealing reagents since their activity can be suitably tuned by the appropriate choice of the base-solid support couple. Furthermore, the heterogeneous conditions in which these bases are employed favours the development of environmentally friendly chemical processes working with a limited amount of solvent or even in solventless conditions. This paper reports on the utilisation of KF on basic alumina as solid base for the reaction of 3-(1-arylsulfonylalkyl)-indoles **7** with readily enolisable compounds leading to functionalised 3-substituted indoles **3**.

Results and Discussion

Nitroalkanes can be easily converted into the corresponding nitronate anions using a wide range of bases and then used as effective nucleophiles with carbonyls, Michael acceptors and other electrophilic substrates.^[12] Furthermore, the nitro group, once introduced in a molecular framework, is amenable to several synthetic transformations including reduction, conversion into carbonyls and reductive removal.^[13] A preliminary study on the reaction of sulfonylindoles **8** with nitroalkanes **9** was carried out using NaH in THF at reflux, a basic system that is able to promote

both elimination of arenesulfinic acid from **8** and enolisation of the nitroalkane **9** (Table 1, *Method A*).^[14] Nitroalkylindoles **10** are obtained in good yields (78–91 %) using nitromethane and nitroethane, but this procedure has proved to be quite unsatisfactory when homologous and functionalised nitroalkanes are employed for the same purpose. Other bases working under homogeneous conditions such as trialkylphosphines, potassium *tert*-butoxide, alkaline metal hydroxides, DBU and guanidines also gave disappointing results when tested on the same reaction. The activating properties of KF on basic alumina have been demonstrated in a consistent number of processes,^[15] and we were delighted to observe that this solid basic system is also able to promote the addition of different nitroalkanes **9** to sulfonylindoles **8** at room temperature (Table 1, *Method B*).^[16] The reaction is usually carried out in dichloromethane in such a minimum amount that is needed to completely dissolve the reactants before the addition of the basic promoter. A work-up procedure of the resulting heterogeneous mixture is avoided since purification of the final products **10** is easily performed by adding a small amount of silica and, after removal of the solvent, by direct application of the solid mixture to the head of a chromatographic column followed by elution with an appropriate solvent system. The results displayed in Table 1, show that a consistent number of simple and functionalised nitroalkanes **9** efficiently add to various sulfonylindoles **8** leading to the corresponding 3-(2-nitroalkyl)-indoles **10** in good yields. Substitution at the 2-position of the indole ring in compounds **8** does not provide any reduction in the reactivity even when phenyl or ester groups are present (Table 1, entries 5, 6, 9, 15). ω -Nitro esters as well as *O*-protected β -nitro alcohols are effective in the reaction with sulfonylindoles allowing the introduction of an additional functional group in the molecular framework (Table 1, entries 13–17). When nitromethane is used as reagent, dichloromethane must be replaced by THF as a solvent in order to ensure a complete consumption of the sulfonylindole. Particularly interesting is the reaction of secondary nitroalkanes such as 2-nitropropane and nitrocyclopentane that maintain a satisfactory reactivity with different substrates **8** (Table 1, entries 8, 9, 12).

The obtained 3-(2-nitroalkyl) indoles **10h, i** and **l** belong to a rather unknown class of tertiary nitro compounds that are not accessible through the very popular Friedel–Crafts reaction of indoles with nitroalkenes.^[17] The interest in 3-(2-nitroalkyl)-indoles **10** mainly stems from the subsequent reduction of the nitro group that generates the corresponding tryptamines **11**, a class of biologically active compounds that also provide a prompt access to β -carboline alkaloids **12** by means of a Pictet–Spengler reaction (Scheme 3).^[18]

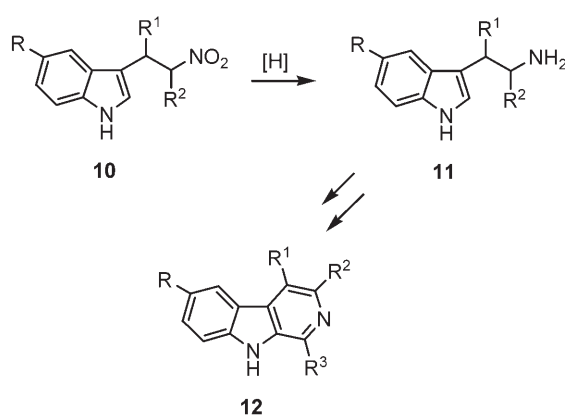
Table 1. Potassium fluoride on basic alumina-promoted additions of nitroalkanes **9** to sulfonylindoles **8**.

Entry	Product 10	R	R ¹	R ²	R ³	R ⁴	Time [h]	Yield ^[a] [%]
1	10a	H	H	<i>n</i> -C ₅ H ₁₁	H	H	4	75 ^[b] (81)
2	10b	H	Me	<i>n</i> -C ₅ H ₁₁	H	H	4	76 ^[b] (85)
3	10c	H	Me	<i>c</i> -C ₆ H ₁₁	H	H	4	85 ^[b,c] (88)
4	10d	MeO	H	Et	H	H	4	75 ^[b]
5	10e	H	CO ₂ Et	Et	H	Me	3	87
6	10f	H	CO ₂ Et	<i>n</i> -C ₅ H ₁₁	H	Me	6	88
7	10g	H	Me	<i>n</i> -C ₅ H ₁₁	H	Et	3	89
8	10h	H	Me	<i>n</i> -C ₅ H ₁₁	Me	Me	5	77
9	10i	H	Ph	<i>n</i> -C ₅ H ₁₁	Me	Me	15	73
10	10j	H	Me	<i>n</i> -C ₅ H ₁₁	H	Ph(CH ₂) ₂	3	85
11	10k	H	Me	<i>c</i> -C ₆ H ₁₁	H	Ph(CH ₂) ₂	15	77 ^[c]
12	10l	H	H	<i>n</i> -C ₅ H ₁₁		-(CH ₂) ₄ -	3	71
13	10m	H	Me	<i>n</i> -C ₅ H ₁₁	H	THPOCH ₂	3	77
14	10n	H	Me	<i>c</i> -C ₆ H ₁₁	H	THPOCH ₂	15	70 ^[c]
15	10o	H	Ph	<i>n</i> -C ₅ H ₁₁	H	EtO ₂ C(CH ₂) ₄	4	81
16	10p	H	H	<i>n</i> -C ₅ H ₁₁	H	EtO ₂ C(CH ₂) ₄	2	86
17	10q	H	Me	<i>n</i> -C ₅ H ₁₁	H	MeO ₂ C(CH ₂) ₄	4	83

^[a] Isolated yields after column chromatography using method B (KF/basic alumina, dichloromethane at room temperature). Yields in parentheses were obtained using *Method A* (NaH in THF at reflux, see ref.^[14]).

^[b] Reaction was carried out in THF at room temperature.

^[c] Phenylsulfonylindole was used.

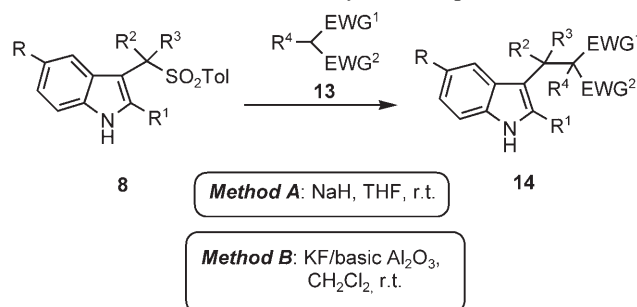
**Scheme 3.** Synthetic elaboration of 3-(2-nitroalkyl)-indoles **10**.

The effectiveness of KF on basic alumina as promoter in nucleophilic additions on sulfonylindoles **8** has been subsequently tested using active methylene reagents **13** bearing electron-withdrawing groups

other than the nitro one (Table 2). The results obtained using the heterogeneous basic promoter (KF/basic alumina, dichloromethane at room temperature, *Method B*) when compared with those achieved using NaH in THF at room temperature (*Method A*), show the superior activity of the former system in producing adducts **14** (Table 2).

Diethyl malonate and malononitrile are particularly reactive toward a large number of sulfonylindoles **8** including that prepared from 2-methylindole and acetone which presents a certain steric crowding at the electrophilic tertiary centre (Table 2, entries 9 and 23). Similarly, malonate derivatives bearing methyl or amido groups at the 2-position, provide adducts **14l–n** in good yields (Table 2, entries 12–14). Mixed malonic acid esters are particularly interesting reagents since the presence of a *tert*-butyl group in the obtained indoles **14j** and **k** would allow an easy chemoselective cleavage of a single ester group (Table 2, entries 10 and 11). The resulting mono esters **15** undergo a Curtius rearrangement *via* acyl azide leading to tryptophan analogues **16** (Scheme 4).^[19] Hydrolysis and de-

Table 2. KF on basic alumina-promoted additions of active methylene compounds **13** to indoles **8**.



Entry	Product 14	R	R ¹	R ²	R ³	R ⁴	EWG ¹	EWG ²	Yield ^[a,b] [%]
1	14a	H	H	<i>n</i> -C ₅ H ₁₁	H	H	CO ₂ Et	CO ₂ Et	86 (70)
2	14b	H	Me	<i>n</i> -C ₅ H ₁₁	H	H	CO ₂ Et	CO ₂ Et	95 (65)
3	14c	H	Me	<i>c</i> -C ₆ H ₁₁	H	H	CO ₂ Et	CO ₂ Et	90 (86) ^[c]
4	14d	MeO	H	Et	H	H	CO ₂ Et	CO ₂ Et	88 (–)
5	14e	H	CO ₂ Et	Et	H	H	CO ₂ Et	CO ₂ Et	67 (66)
6	14f	H	Ph	<i>n</i> -C ₅ H ₁₁	H	H	CO ₂ Et	CO ₂ Et	83 (72)
7	14g	H	Me	Ph(CH ₂) ₂	H	H	CO ₂ Et	CO ₂ Et	84
8	14h	H	Me		H	H	CO ₂ Et	CO ₂ Et	84
9	14i	H	Me	Me	Me	H	CO ₂ Et	CO ₂ Et	68 (65)
10	14j	H	H	<i>n</i> -C ₅ H ₁₁	H	H	CO ₂ Et	CO ₂ - <i>t</i> -Bu	82
11	14k	H	Me	<i>n</i> -C ₅ H ₁₁	H	H	CO ₂ Et	CO ₂ - <i>t</i> -Bu	84 (70)
12	14l	H	H	<i>n</i> -C ₅ H ₁₁	H	Me	CO ₂ Et	CO ₂ Et	83 ^[d] (63)
13	14m	H	H	<i>n</i> -C ₅ H ₁₁	H	NHCHO	CO ₂ Et	CO ₂ Et	78 ^[d]
14	14n	H	H	<i>n</i> -C ₅ H ₁₁	H	NHCOMe	CO ₂ Et	CO ₂ Et	84
15	14o	H	H	<i>n</i> -C ₅ H ₁₁	H	H	COMe	COMe	86 ^[e]
16	14p	H	H	<i>n</i> -C ₅ H ₁₁	H	H	CO ₂ Et	COMe	87 ^[e]
17	14q	H	H	<i>n</i> -C ₅ H ₁₁	H	H	CO ₂ Et	CN	88
18	14r	H	H	<i>n</i> -C ₅ H ₁₁	H	H	CN	CN	87 ^[e] (76)
19	14s	H	Me	<i>n</i> -C ₅ H ₁₁	H	H	CN	CN	83 ^[e] (70)
20	14t	H	Me	<i>c</i> -C ₆ H ₁₁	H	H	CN	CN	87 ^[c]
21	14u	H	CO ₂ Et	Et	H	H	CN	CN	71 ^[d]
22	14v	H	Ph	<i>n</i> -C ₅ H ₁₁	H	H	CN	CN	85 (74)
23	14w	H	Me	Me	Me	H	CN	CN	73
24	14x	H	Me	<i>n</i> -C ₅ H ₁₁	H	H	TolSO ₂	NC	63

^[a] Isolated yields after column chromatography using method B (KF/basic alumina, dichloromethane at room temperature).

Unless otherwise stated reaction time was 2 h at room temperature

^[b] Yields in parentheses were obtained using method A (NaH in THF 2 h at room temperature).

[c] Phenylsulfonylindole was used.

[d] Reaction time was 15 h at room temperature.

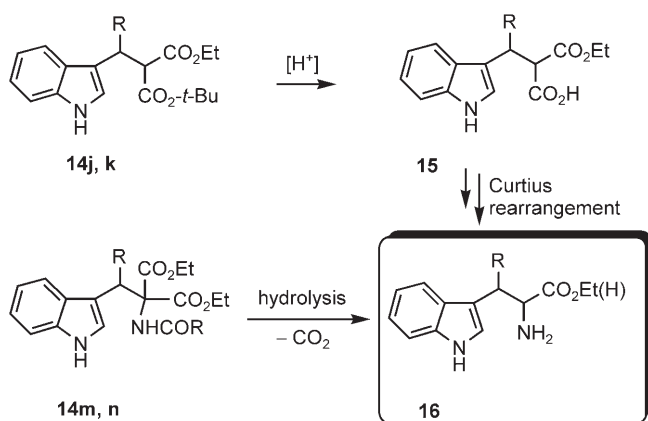
[e] Reaction time was 4 h at room temperature.

carboxylation on compounds **14m** and **n** also provides a straightforward entry to the same amino acid derivatives.^[20] Other active methylene derivatives tested such as 2,4-pentanedione, ethyl 3-oxobutanoate and ethyl 2-cyanoacetate also give satisfactory results including *p*-toluenesulfonyl isocyanide which affords adduct **14x**, although only in moderate yield (Table 2, entries 15–17 and 24).

Conclusions

Potassium fluoride supported on basic alumina has been demonstrated as a superior promoter in the re-

action of easily enolisable reagents such as nitro compounds, malonic acid derivatives, diketones and keto esters with 3-(1-arylsulfonylalkyl)-indoles. The reactivity of these sulfonylindoles toward nucleophiles is due to the formation of an intermediate vinylogous imine caused by a base-assisted elimination of arene-sulfinic acid. The obtained adducts are interesting building blocks that allow a rapid entry to biologically active indole derivatives endowed of practical interest. This process is operationally simple since it occurs at room temperature under heterogeneous conditions and requires enough solvent needed to dissolve the reactants before addition of the solid base. Removal of the solvent and application of the solid



Scheme 4. Tryptophan analogues from malonyl adducts **14**.

mixture to the head of a chromatographic column represents the only work-up procedure required. The whole procedure represents a valid option to the Friedel–Crafts reaction of indoles with nitroalkenes and other electron-poor olefins.

Experimental Section

General Remarks

All chemicals, unless otherwise stated, were purchased and used without further purifications. Tetrahydrofuran used for the reaction with sodium hydride was dried by refluxing it over sodium wire and then distilled. Sulfonylindoles **8** were prepared according to previous procedures.^[10,11] 2-Phenylnitroethane and alkyl 6-nitrohexanoates were prepared using known procedures.^[21,22] Potassium fluoride on basic alumina was prepared using commercial basic alumina (Baker) following Bergbreiter's procedure.^[23]

Typical Procedures for the Reaction of Sulfonylindoles with Nucleophiles

Method A: To a stirred suspension of NaH (3.0 mmol) in dry THF (10 mL) the active methylene compound **13** (2.0 mmol) was added at room temperature. After stirring for 20 min at room temperature, sulfonylindole **8** (1 mmol) dissolved in dry THF (5 mL) was added dropwise and the suspension stirred for 2 h at room temperature. The reaction mixture was quenched with saturated ammonium chloride (4 mL) and extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layer was dried over MgSO₄ and after removal of the solvent at reduced pressure, the crude product obtained was purified by column chromatography (hexane-ethyl acetate, 8:2).

Method B: To a stirred solution of sulfonylindole **8** (1.0 mmol) and nitroalkane **9** or active methylene compound **13** (1.5 mmol) in dichloromethane (5 mL) [THF (5 mL) for nitromethane], potassium fluoride on basic alumina (1.5 g) was added at room temperature. After stirring for the appropriate time (reaction was monitored by TLC analysis, see Tables) silica (0.8 g) was added and solvent was removed at

reduced pressure. The resulting solid mixture was directly charged on a chromatography column and eluted (hexane-ethyl acetate, 8:2) to afford pure products **10** and **14**.

Acknowledgements

Financial support from University of Camerino and MIUR (National Project "Sintesi organiche ecosostenibili mediate da nuovi sistemi catalitici") is gratefully acknowledged.

References

- [1] a) D. J. Faulkner, *Nat. Prod. Rep.* **2002**, 1–48; b) J. E. Saxton, in: *The Alkaloids*, (Ed.: G. A. Cordell), Academic Press, New York, **1998**; c) R. J. Sundberg, *Indoles*, Academic Press, New York, **1997**; d) J. E. Saxton, *Nat. Prod. Rep.* **1997**, 559–590.
- [2] M. Bandini, A. Melloni, S. Tommasi, A. Umani-Ronchi, *Synlett* **2005**, 1199–1222.
- [3] a) B. B. Semenov, V. G. Granik, *Pharm. Chem. J.* **2004**, 38, 287–310; for some recent applications of gramine in synthesis: b) G. de La Herrán, A. Segura, A. G. Csáky, *Org. Lett.* **2007**, 9, 961–964; c) B. B. Semenov, K. A. Novikov, K. A. Lysenko, V. V. Kachala, *Tetrahedron Lett.* **2006**, 47, 3479–3483; d) K. H. Low, N. A. Magomedov, *Org. Lett.* **2005**, 7, 2003–2005.
- [4] a) M. Iwao, O. Motoi, *Tetrahedron Lett.* **1995**, 36, 5929–5932; b) G. D. H. Dijkstra, M. T. M. Tulp, P. H. H. Hermkens, J. H. van Maarseveen, H. W. Scheeren, C. G. Kruse, *Rec. Trav. Chim. Pays-Bas* **1993**, 112, 131–136; c) P. H. H. Hermkens, J. H. van Maarseveen, H. C. J. Ottenheijm, C. G. Kruse, H. W. Scheeren, *J. Org. Chem.* **1990**, 55, 3998–4006; d) P. H. H. Hermkens, van J. H. Maarseveen, P. L. H. M. Cobben, H. C. J. Ottenheijm, C. G. Kruse, H. W. Scheeren, *Tetrahedron* **1990**, 46, 833–846.
- [5] a) Y. Gong, K. Kato, H. Kimoto, *Tetrahedron Lett.* **1999**, 40, 5743–5744; b) D. R. Witty, G. Walker, J. H. Bateson, P. J. O'Hanlon, R. Cassels, *Bioorg. Med. Chem. Lett.* **1996**, 6, 1375–1380.
- [6] a) H.-M. Dong, H.-H. Lu, L.-Q. Lu, C.-B. Chen, W.-J. Xiao, *Adv. Synth. Cat.* **2007**, 349, 1597–1603; b) H. Hagiwara, M. Sekifuji, T. Hoshi, K. Qiao, C. Yokoyama, *Synlett* **2007**, 1320–1322; c) H. M. Kaiser, W. F. Lo, A. M. Riahi, A. Spannenberg, M. Beller, M. K. Tse, *Org. Lett.* **2006**, 8, 5761–5764; d) G. Cravotto, G. B. Giovenzana, A. Maspero, T. Pilati, A. Penoni, G. Palmisano, *Tetrahedron Lett.* **2006**, 47, 6439–6443; e) P. K. Pradham, D. Dey, V. S. Giri, P. Jaisankar, *Synthesis* **2005**, 1779–1782; f) S. Kumar, V. Kumar, S. S. Chimmi, *Tetrahedron Lett.* **2003**, 44, 2101–2104.
- [7] a) C. Nájera, M. Yus, *Tetrahedron* **1999**, 55, 10547–10658; b) N. S. Simpkins, *Sulphones in Organic Synthesis*, Pergamon Press, Oxford, **1993**.
- [8] a) J. J. Licari, G. Dougherty, *J. Am. Chem. Soc.* **1954**, 76, 4039–4040; for the synthesis of a particular 3-(1,2-bisarylsulfonyl-2-trifluorocarbonyl)-indole see: b) A. L. Krasovsky, S. V. Druzhinin, V. G. Nenajdenko, E. S. Balenkova, *Tetrahedron Lett.* **2004**, 45, 1129–1132.

- [9] M. Petrini, *Chem. Rev.* **2005**, *105*, 3949–3977.
- [10] a) R. Ballini, A. Palmieri, M. Petrini, E. Torregiani, *Org. Lett.* **2006**, *8*, 4093–4096; for a Yb(OTf)₃-catalysed reaction of α -amido sulfones with electron-rich aromatics see: b) C. Kuhakarn, K. Tangdenpaisal, P. Kongsaree, S. Prabpai, P. Tuchinda, M. Pohmakotr, V. Reutrakul, *Tetrahedron Lett.* **2007**, *48*, 2467–2470.
- [11] A. Palmieri, M. Petrini, *J. Org. Chem.* **2007**, *72*, 1863–1866.
- [12] a) N. Ono, *The Nitro Group in Organic Synthesis*, Wiley-VCH, New York, **2001**; b) R. Ballini, G. Bosica, D. Fiorini, A. Palmieri, M. Petrini, *Chem. Rev.* **2005**, *105*, 933–971; c) F. A. Luzzio, *Tetrahedron* **2001**, *57*, 915–945.
- [13] a) R. Ballini, M. Petrini *Tetrahedron* **2004**, *60*, 1017–1047; b) N. Ono, H. Miyake, R. Tamura, A. Kaji, *Tetrahedron Lett.* **1981**, *22*, 1705–1708; c) T. C. Fessard, H. Motoyoshi, E. M. Carreira, *Angew. Chem.* **2007**, *119*, 2124–2127; *Angew. Chem. Int. Ed.* **2007**, *46*, 2078–2081.
- [14] A. Palmieri, M. Petrini, E. Torregiani, *Tetrahedron Lett.* **2007**, *48*, 5653–5656.
- [15] a) G. W. Kabalka, R. M. Pagni, *Tetrahedron* **1997**, *53*, 7999–8065; for some recent applications of KF-basic alumina see: b) Y. Ge, L. Hu, *Tetrahedron Lett.* **2007**, *48*, 4585–4588; c) M. Boruah, D. Konwar, S. D. Sharma, *Tetrahedron Lett.* **2007**, *48*, 4535–4537; d) R. Ballini, A. Palmieri, *Adv. Synth. Cat.* **2006**, *348*, 1154–1156; e) R. Ballini, R. R. Clemente, A. Palmieri, M. Petrini, *Adv. Synth. Cat.* **2006**, *348*, 191–196.
- [16] Reaction of nitroalkanes with gramines occurs at reflux under various conditions: a) K. Miyashita, K. Kondoh, K. Tsuchiya, H. Miyabe, T. Imanishi, *Chem. Pharm. Bull.* **1997**, *45*, 932–935; b) M. W. Maichrzak, J. N. Zobel, D. J. Obradovich, *Synth. Commun.* **1997**, *27*, 3201–3211; c) Y. Endo, T. Imada, K. Yamaguchi, K. Shudo, *Heterocycles* **1994**, *39*, 571–579; d) A. M. Thompson, D. W. Fry, A. J. Kraker, W. A. Denny, *J. Med. Chem.* **1994**, *37*, 598–609; e) J. Quick, B. Saha, P. E. Driedger, *Tetrahedron Lett.* **1994**, *35*, 8549–8552; f) M. Li, M. E. Johnson, *Tetrahedron Lett.* **1994**, *35*, 6255–6258.
- [17] W. E. Kreighbaum, W. L. Matier, R. D. Dennis, J. L. Minielli, D. Deitchman, J. L. Perlach, W. T. Comer, *J. Med. Chem.* **1980**, *23*, 285–289.
- [18] a) R. Cao, W. Peng, Z. Wang, A. Xu, *Curr. Med. Chem.* **2007**, *14*, 479–500; b) Z. Czarnocki, A. Siwicki, J. Szawkało, *Curr. Org. Synth.* **2005**, *2*, 301–331; c) L. Jeannin, M. Boisbrun, C. Nemes, F. Cochard, M. Laronze, E. Dardennes, Á. Kovács-Kulyassa, J. Sapi, J.-Y. Laronze, *C. R. Chimie* **2003**, *6*, 517–528.
- [19] a) L. Jeannin, T. Nagy, E. Vassileva, J. Sapi, J.-Y. Laronze, *Tetrahedron Lett.* **1995**, *36*, 2057–2058; b) C. Nemes, L. Jeannin, J. Sapi, M. Laronze, H. Seghir, F. Augé, J.-Y. Laronze, *Tetrahedron* **2000**, *56*, 5479–5492.
- [20] a) D. T. Jones, G. T. Hartman III, R. M. Williams, *Tetrahedron Lett.* **2007**, *48*, 1291–1294; b) X. Teng, A. Degterev, P. Jagtap, X. Xing, S. Choi, R. Denu, J. Yuan, G. D. Cuny, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5039–5044; c) R. M. Williams, J. Cao, H. Tsujishima, R. J. Cox, *J. Am. Chem. Soc.* **2003**, *125*, 12172–12178; d) V. Marcq, C. Mirand, M. Decarme, H. Emonard, W. Hornebeck, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2843–2846; e) B. Meseguer, D. Alonso-Díaz, N. Griebenov, T. Herget, H. Waldmann, *Chem. Eur. J.* **2000**, *6*, 3943–3957.
- [21] A. K. Sinhababu, R. T. Borchardt, *Tetrahedron Lett.* **1983**, *24*, 227–230.
- [22] R. Ballini, M. Petrini, *Synth. Commun.* **1986**, *16*, 1781–1788.
- [23] D. E. Bergbreiter, J. J. Lalonde, *J. Org. Chem.* **1987**, *52*, 1601–1603.