O-Substituted N-oxy arylsulfinamides and sulfonamides in Michael reactions

Vasco D. B. Bonifácio,* Rakesh P. Kumar, Sundaresan Prabhakar, and Ana M. Lobo

REQUIMTE, Chemistry Department, and SINTOR-UNINOVA, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, 2829-516 Caparica, Portugal
E-mail: vasco.bonifacio@dq.fct.unl.pt

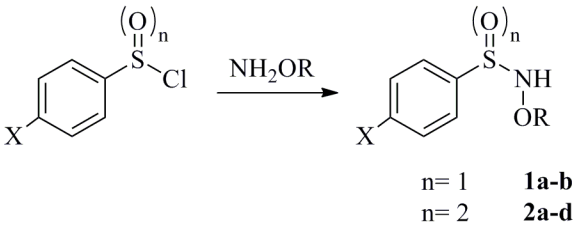
DOI: http://dx.doi.org/10.3998/ark.5550190.0012.a21

Abstract
O-Substituted N-oxy arylsulfinamides and sulfonamides undergo fast aza-Michael reaction in the presence of base and electron-deficient α,β-unsaturated olefins under mild conditions. With N-silyloxy benzenesulfinamides, no aza-Michael product is observed and a hetero aza-Brook type rearrangement takes place induced by the base. Room temperature N-desulfinylation of *N*-benzyloxybenzenesulfinamide is achieved using $BF_3.Et_2O$. N-Alkoxy arylsulfonamides aza-Michael adducts are found to be generally highly stable under strongly acidic and basic conditions.

Keywords: Michael addition, rearrangement, arylsulfinamides, arylsulfonamides, desulfurization

Introduction

N-Alkoxy arylsulfinamides were first described by Maricich and co-workers in 1973.[1] In this work N-unsubstituted alkoxysulfinamides were presented as a novel class of alkylating agents. The alkylation mechanism was postulated to involve a sulfonimidate intermediate via migration of the alkoxy group from nitrogen to the adjacent sulfur. However, the potential of this class of compounds has not yet been fully explored. We conducted the synthesis of O-substituted N-oxy benzenesulfinamides **1a-b** and also of the parent O-substituted N-oxy arylsulfonamides **2a-d** starting from benzenesulfinyl[2] and *p*-toluenesulfonyl chlorides, respectively, and from readily available O-substituted hydroxylamines (Scheme 1 and Table 1).



Scheme 1. Synthesis of O-substituted N-oxy benzenesulfinamides **1a-b** and O-substituted N-oxy arylsulfonamides **2a-d**.

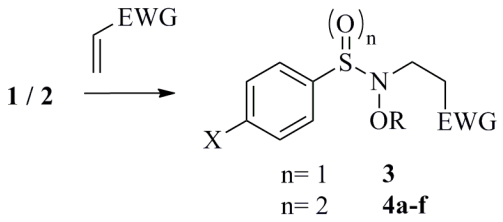
Table 1. Synthesis of O-substituted N-oxy arylsulfinamides **1a-b** and O-substituted N-oxy arylsulfonamides **2a-d** via Scheme 1

Compound	n	X	R	Yield (%)[a]	Mp (ºC)
1a	1	H	Bn	50	90-91
1b	1	H	TBDMS	82	114-115
2a	2	H	Bn	99	102-105
2b	2	Me	Bn	92	93-95
2c	2	Me	Ph	54	113-115
2d	2	Me	4-NO_2Ph	85	176-179

[a]The arylsulfinyl chloride (1.0 equiv.) was added to the free hydroxylamine (1.0 equiv.) in THF at 0 ºC.

Results and Discussion

The reactivity of compounds **1** and **2** was evaluated under basic conditions (NaH, 0 ºC) in the presence of different Michael acceptors. The aza-Michael adducts of *N*-alkoxy arylsulfonamides were the major isolated products (Scheme 2 and Table 2). The adducts **3** and **4** were the major isolated products in yields that ranged from 52 to 96% (Scheme 2 and Table 2). The preparation of β-amino sulfones **4f** is of special interest since they readily undergo electrophilic substitution in the α position and have been used as intermediates in the synthesis of α-amino acids, amino alcohols, substituted uridines and adenosines, alkaloids, β-lactams and nitrogen heterocycles.[3]



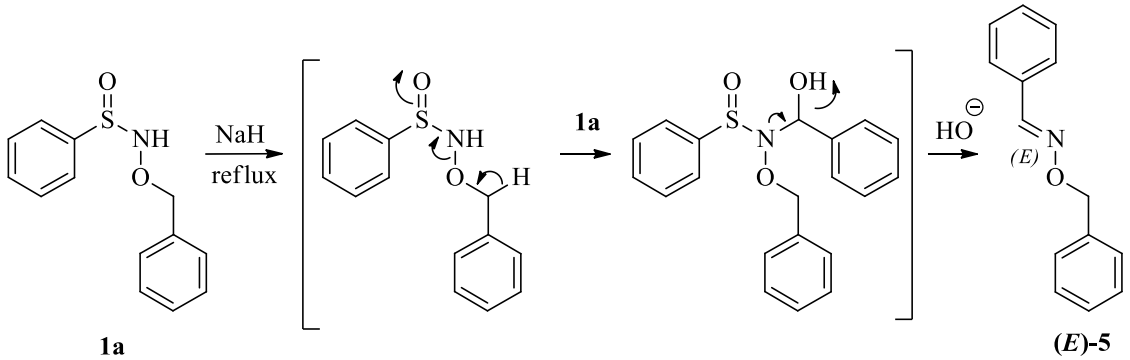
Scheme 2. Synthesis of *N*-alkoxy benzenesulfinamide **3** and N-alkoxy arylsulfonamides **4a-f** aza-Michael adducts.

Table 2. *N*-Alkoxy benzenesulfinamide **3** and N-alkoxy arylsulfonamides **4a-f** aza-Michael adducts synthesized via Scheme 2

Compound	n	X	R	EWG	Yield (%)[a]	Mp (ºC)
3	1	H	Bn	COPh	92	88-90
4a	2	H	Bn	CO_2Me	74	82-83
4b	2	H	Bn	COMe	52	95-97
4c	2	H	Bn	COPh	87	108-109
4d	2	Me	Bn	COMe	80	oil
4e	2	Me	Bn	SOPh	96	oil
4f	2	Me	Ph	SO_2Ph	93	91-93

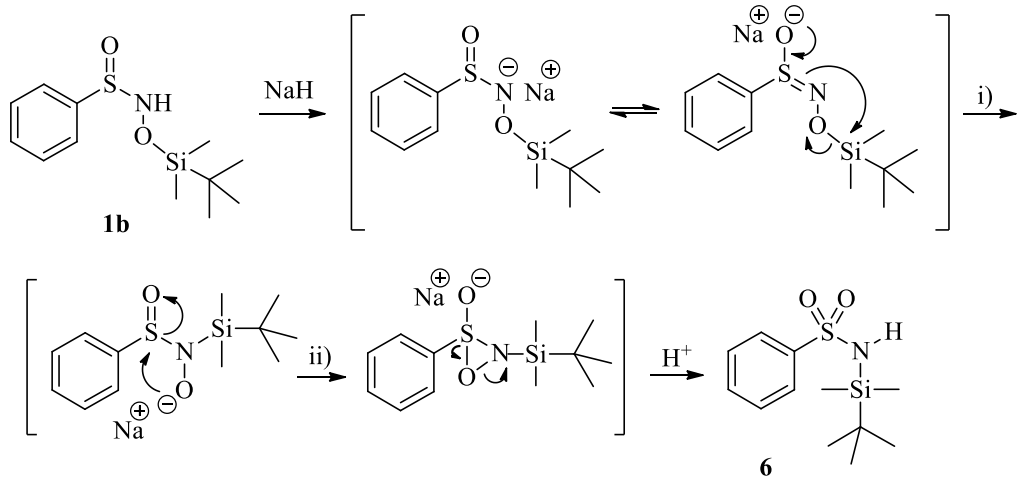
[a]Reaction conditions: NaH (1.0 equiv.), 18-crown-6 (0.1 equiv.), 0 °C, THF, 15 m.

No aza-Michael adduct was obtained from the reaction of **1a** with the less electron-deficient *N*,*N*-dimethylacrylamide. When reflux conditions were used benzaldoxime ***(E)*-5** was isolated. Investigation of this reaction in the absence of the Michael acceptor led us to conclude that ***(E)*-5** is formed from decomposition of **1a**. Under basic conditions deprotonation occurs with formation of benzaldehyde and benzenesulfinamide. Further reaction of **1a** with benzaldehyde, gives benzenesulfinic acid and ***(E)*-5** and a possible mechanism is shown in Scheme 3 for this transformation.[4]



Scheme 3. Reactivity of *N*-benzyloxy benzenesulfinamide **1a** under basic conditions.

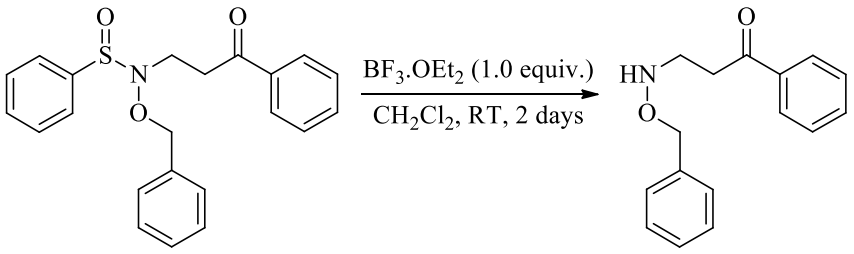
The electronic nature of the oxygen substitutent of the N-oxy group was also found to influence the reactivity of the studied arylsulfinamides. No aza-Michael adducts were detected using sulfinamide **1b**, instead a hetero aza-Brook type rearrangement appears to have taken place, leading to compound **6** (Scheme 4).[5]



Scheme 4. Aza-Brook rearrangement of *N*-silyloxybenzenesulfinamide **1b**.

Higher yields were obtained using up to 1.0 equiv. of base and short reaction times. The formation of **6** can be explained by: (i) O→N anionic 1,2-migration of *tert*-butyl-dimethylsilyl (TBDMS),[6] and (ii) formation of a sulfur imine oxide intermediate.[7] A few examples of aza-Brook rearrangements have been described,[8] however this hetero aza-Brook rearrangement is unprecedented.

In our ongoing interest in the development of novel aziridination synthetic methods,[9] we envisaged that the intramolecular cyclisation of the obtained aza-Michael adducts could potentially lead to the corresponding aziridines. Therefore we attempted its cyclisation under a variety of basic (NaH, KH, NaO^tBu, $Zr(O^tBu)_4$, LDA, DBU, $^iPr_2EtN$/TMSOTf) and acidic conditions (*p*-toluenesulfonic acid, reflux). However, under the tested conditions the starting aza-Michael adducts were found to be highly stable and were quantitatively recovered from the reaction mixture. It should be stressed that intramolecular nucleophilic displacement at the sulfoxide and sulfone nitrogen has never been observed. This is attributed to the electron-withdrawing nature of these groups where the nitrogen assumes a trigonal configuration.[10] The intramolecular cyclisation of aryl(sulfonyl)amine derivatives has been achieved but exclusively at the sp^3 carbon adjacent to the nitrogen.[11] Gratifyingly, in the presence of Lewis acid $BF_3.Et_2O$ it was found that *N*-benzyloxybenzenesulfinamide **3** undergoes N-desulfinylation to **8** at room temperature (Scheme 5).



Scheme 5. Desulfinylation of N-benzyloxybenzenesulfinamide **3** under mild conditions.

Examples of desulfinylation can be found in literature using trifluoroacetic acid as catalyst,[12] and very recently the photodesulfinylation of chiral sulfinamides in Et_2O-MeOH was also reported.[13] Therefore, to the best of our knowledge, this is the first example of a $BF_3.Et_2O$ assisted *N*-desulfinylation.

Conclusions

In summary we have synthesised and unveiled some of the reactivity of N-alkoxy arylsulfinamides, N-alkoxy arylsulfonamides and their aza-Michael adducts. N-Alkoxy arylsulfinamides were found to be unreactive towards less electron-deficient Michael acceptors leading to benzaldoximes upon heating or N-silylsulfonamides via an hetero aza-Brook type rearrangement. N-Desulfinylation of a N-benzyloxybenzenesulfinamide aza-Michael adduct was also observed using a Lewis acid under mild conditions.

Experimental Section

General. Solvents were purified by standard methods. All commercial reagents were used as received unless otherwise mentioned. Benzenesulfinyl chloride,[14] and phenylvinylketone,[15] were prepared according to literature procedures. For analytical and preparative thin-layer chromatography, Merck, 0.5 mm and 1.0 mm Kieselgel GF 254 percoated were used, respectively. Melting points were recorded on a Köfler apparatus, Reichert Thermovar model, and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 683 FT-IR spectrometer. Nuclear magnetic resonance spectra (^1H and ^{13}C NMR) were recorded on a Bruker ARX 400 spectrometer. ^1H shifts are reported relative to internal TMS. Carbon shifts are given relative to the. ^{13}C signal of $CDCl_3$ (δ 77.0 ppm) as reference. High resolution mass spectra were recorded on a Micromass autoSpecQ in the Unidade de Espectrometria de Masas from the University of Santiago de Compostela, Spain.

Preparation of O-substituted N-oxy benzenesulfinamides. The arylsulfinyl chloride (1.0 equiv.) was added to the free hydroxylamine (1.0 equiv.) in THF at 0 ºC, under inert atmosphere and magnetic stirring. Upon completion (TLC control) the reaction mixture was allowed to reach room temperature, and then diluted with diethyl ether, filtered and sucessively washed with water and a 15% $NaHCO_3$ aqueous solution. The organic phase was dried over anhydrous $MgSO_4$ and the solvent removed to dryness. The obtained product was purified by chromatography and/or by recrystallisation.

(±)-*N*-(Benzyloxy)-benzenesulfinamide (1a). To a solution of *O*-benzyl-hydroxylamine hydrochloride (1.8 g, 11.3 mmol) in toluene (10 mL) under inert atmosphere and magnetic stirring was added triethylamine (1.0 equiv., 1.57 mL, 11.3 mmol). The reaction was stirred over one hour. The presence of free *O*-benzyl-hydroxylamine was checked by TLC (silica, AcOEt/*n*-hexane 7:3; spray reagent: $PhCOCl/FeCl_3$, red spot; R_f 0.34). The mixture was filtered and the solid washed with diethyl ether. The solvent was removed under vacuum and the *O*-benzyl-hydroxylamine obtained as light yellow oil (832 mg, 6.76 mmol). To the hydroxylamine at 0 ºC was added a THF solution of benzenesulfinyl chloride (2.5 mL, 3.28 mmol). After 15 min. (TLC control: silica, AcOEt/*n*-hexane 7:3; spray reagent: $PdCl_2$, orange spot) the reaction is complete. The mixture was filtered and **1a** was obtained as a white solid (400 mg) in 50% yield. R_f 0.53 (AcOEt/*n*-hexane 7:3); mp 90-91 ºC (CCl_4/*n*-hexane) (mp lit.[1] 90-91 ºC); IR (film) ν_{max}: 3100 (s, NH) 1092 (s, S=O). ^{1}H NMR (CD_3CN) δ: 7.91 (1H, bs, exchanges with D_2O, NH), 7.28-7.57 (5H, m, SOArH), 7.39-7.27 (5H, m, ArH), 4.65 (2H, dd, J_1 = 11.3, J_2 = 11.3, OCH_2).

(±)-*N*-(*tert*-Butyldimethylsilyloxy)-benzenesulfinamide (1b).[16] Yield 82%. White solid. Mp 114-115 ºC (petroleum ether). R_f 0.31 (Et_2O/*n*-hexane 1:1, eluted twice); IR (film) ν_{max}: 3043 (s, NH), 1444 (s, S=O), 1100 (s, S=O). ^{1}H-RMN (CD_3CN) δ: 7.72-7.70 (2H, m, ArH), 7.58-7.55 (3H, m, ArH), 7.46 (1H, bs, exchanges with D_2O, NH), 0.90 [9H, s, $SiC(CH_3)_3$], 0.11 (3H, s, $SiCH_3$), 0.01 (3H, s, $SiCH_3$); Anal. calcd for $C_{15}H_{27}SiNO_2S$: C, 53.10; H, 7.80; N, 5.16; S, 11.81. Found: C, 52.10; H, 7.80; N, 5.06; S, 11.52.

Preparation of O-substituted N-oxy arylsulfonamides

The protocol described for the synthesis *O*-substituted *N*-oxy benzenesulfinamides was followed using the corresponding arylsulfonyl chlorides. In the case of aromatic hydroxylamine hydrochlorides pyridine was used as a base since the use of triethylamine led to the formation of the corresponding phenol, and only the sulfonic ester was isolated.

***N*-(Benzyloxy)-benzenesulfonamide (2a).** Yield 99%. White solid. Mp 102-105 ºC (Et_2O) (mp lit.[17] 103-105 ºC); R_f 0.27 (Et_2O/*n*-hexane 1:1); IR (KBr) ν_{max}: 3234 (s, NH), 1308 (s, SO_2), 1172 (s, SO_2). ^{1}H NMR (CD_3CN) δ: 8.39 (1H, bs, exchanges with D_2O, NH), 7.93 (2H, d, J = 7.5, SO_2ArH_o), 7.72 (1H, t, J = 7.6, SO_2ArH_p), 7.62 (2H, t, J = 7.8, SO_2ArH_m), 7.40-7.36 (5H, m, ArH), 4.95 (2H, s, OCH_2). ^{1}H NMR ($CDCl_3$) δ: 7.94 (2H, d, J=7.9, SO_2ArH_o), 7.64 (1H, t, J = 7.3, SO_2ArH_p), 7.53 (2H, t, J = 7.88, SO_2ArH_m), 7.34 (5H, m, ArH), 7.08 (1H, sl, exchanges with D_2O, NH), 4.98 (2H, s, OCH_2).

***N*-(Benzyloxy)-4-methylbenzenesulfonamide (2b).** Yield 92%. White solid. Mp 93-95 ºC (Et_2O) (mp lit.[18] 94-95 ºC); R_f 0.21 (AcOEt/*n*-hexane 3:7); IR (KBr) ν_{max}: 3220 (s, NH), 1333 (s, SO_2), 1166 (s, SO_2). ^{1}H NMR (CD_3CN) δ: 8.30 (1H, bs, exchanges with D_2O, NH), 7.8 (2H, d, *J* = 8.2, ArH), 7.42-7.36 (7H, m, ArH), 4.93 (2H, s, OCH_2), 2.43 (3H, s, $ArCH_3$). ^{1}H NMR ($CDCl_3$) δ: 8.37 (2H, d, *J* = 8.7, ArH_o), 8.11 (7H, d, *J* = 8.7, ArH_m), 7.36 (6H, m, ArH + NH), 5.01 (2H, s, OCH_2).

***N*-(Phenoxy)-4-methylbenzenesulfonamide (2c).** Yield 54%. Light yellow needles. Mp 113-115 ºC (Et_2O) [mp lit.[19] 113-114 ºC ($CHCl_3$/*n*-hexane)]; R_f 0.33 (Et_2O/*n*-hexane 6 :4); IR (KBr) ν_{max}: 3208 (s, NH), 1334 (s, SO_2), 1169 (s, SO_2). ^{1}H NMR (CD_3CN) δ: 8.83 (1H, bs, exchanges with D_2O, NH), 7.86 (2H, d, *J* = 8.2, ArH), 7.49 (2H, *J* = 8.0, ArH), 7.34 (2H, t, *J* = 8.4, ArH), 7.15 (2H, d, *J* = 8.0, ArH), 7.08 (1H, t, *J* = 7.4, ArH), 2.48 (3H, s, $ArCH_3$).

***N*-(4'-nitrophenoxy)-4-methylbenzenesulfonamide (2d).** Yield 85%. Light yellow solid. Mp 176-179 ºC (benzene) [Mp lit.[19] 178-180 ºC (benzene)]; IR (KBr) ν_{max}: 3232 (s, NH), 1590 (s, NO_2), 1518 (s, NO_2), 1342 (s, SO_2), 1169 (s, SO_2). ^{1}H NMR ($CDCl_3$) δ: 8.20 (2H, d, *J* = 9.2, ArH), 7.85 (2H, t, *J* = 8.0, ArH), 7.48 (1H, bs, exchanges with D_2O, NH), 7.40 (2H, d, *J* = 8.0, ArH), 7.28 (2H, m, ArH), 2.48 (3H, s, $ArCH_3$). When triethylamine was used as a base 4'-nitrophenyl-4-methylbenzenesulfonate was isolated in 24% yield. Light yellow solid. Mp 86-90 ºC (Et_2O/*n*-hexane) (mp lit.[20] 98 ºC); R_f 0.40 (Et_2O/*n*-hexane 1:1); IR (KBr) ν_{max}: 1530 (s, NO_2), 1378 (s, NO_2), 1352 (s, SO_2), 1170 (s, SO_2). ^{1}H NMR (CD_3CN) δ: 8.19 (2H, d, *J* = 9.2, ArH), 7.75 (2H, t, *J* = 8.3, ArH), 7.44 (2H, d, *J* = 8.1, ArH), 7.25 (2H, d, *J* = 9.2, ArH), 2.45 (3H, s, $ArCH_3$).

Reaction of O-substituted N-oxy arylsulfinamides and sulfonamides with Michael acceptors

To a THF solution (7.5 mL/mmol) of the *N*-oxy arylsulfinamide or sulfonamide (1.0 equiv.) at 0 ºC, under inert atmosphere and magnetic stirring, sodium hydride (1.0 equiv.) and 18-crown-6 (0.1 equiv.) were added. After the complete solubilization of the sodium salt the Michael acceptor (1.1 equiv.) was added. Upon completion (TLC control) the reaction mixture was neutral with a 1M CH_3CO_2H THF solution (1.0 equiv.). The solvents were removed in vacuum and the products purified by chromatography.

(±)-3-[*N*-(Benzyloxy)-*N*-benzenesulfinamide]-1-phenylpropan-1-one (3). Yield 92%. White solid. Mp 88-90 ºC (*n*-hexane). R_f 0.19 (Et_2O/*n*-hexane 8:2; spray reagent: $KMnO_4$, negative); IR (KBr) ν_{max}: 1674 (s, C=O), 1443 (s, S=O), 1106 (s, S=O). ^{1}H NMR (CD_3CN) δ: 7.79-7.44 (15H, m, ArH), 4.79 (2H, dd, J_1 = 10.8, J_2 = 10.8, OCH_2), 3.36-3.29 (1H, m, H-1), 3.21-3.10 (2H, m, H-2), 3.05-2.97 (1H, m, H-1). HRMS (FAB): Found 379.12149, calcd. for $C_{22}H_{21}NO_3S$ 379.12421.

Methyl 3-[*N*-(benzyloxy)-*N*-benzenesulfonyl]propanoate (4a). Yield 74%. White solid. M.p. 82-83 ºC (*n*-hexane); R_f 0.50 (Et_2O/*n*-hexane); IR (KBr) ν_{max}: 1736 (s, C=O), 1356 (s, SO_2), 1171 (s, SO_2). ^{1}H NMR ($CDCl_3$) δ: 7.89 (2H, d, *J* = 7.6, SO_2ArH_o), 7.65 (1H, t, *J* = 7.4, ArH_p), 7.54 (2H, t, *J* = 7.8, ArH_m), 7.39-7.37 (5H, m, ArH), 5.09 (2H, s, OCH_2), 3.64 (3H, s, OCH_3), 3.21 (2H, m, H-1), 2.9 (2H, t, *J* = 7.2, H-2). ^{1}H NMR (CD_3CN) δ: 7.90 (2H, d, *J* = 7.6,

SO_2ArH_o), 7.75 (1H, t, *J* = 7.3, ArH_p), 7.63 (2H, t, *J* = 7.6, ArH_m), 7.40-7.31 (5H, m, ArH), 5.05 (2H, s, OCH_2), 3.61 (3H, s, OCH_3), 3.19 (2H, m, H-1), 2.54 (2H, t, *J* = 6.6, H-2). ^{13}C NMR ($CDCl_3$) δ: 171.3 (C-3), 134.9, 133.9, 132.9, 132.9, 129.7, 129.6, 128.9, 128.8, 128.6 (ArC), 79.9 (OCH_2), 51.9 (CH_3), 49.1 (C-1), 32.0 (C-2); Anal. calcd for $C_{17}H_{19}NO_5S$: C, 58.44; H, 5.48; N, 4.01; S, 9.18. Found: C, 58.21; H, 5.49; N, 3.89; S, 8.96.

4-[*N*-(Benzyloxy)-*N*-benzenesulfonamide]butan-2-one (4b). Yield 52%. White solid. M.p. 95-97 ºC (Et_2O/petroleum ether); R_f 0.44 (AcOEt/*n*-hexane 3:7); IR (KBr) ν_{max}: 1721 (s, C=O), 1344 (s, SO_2), 1167 (s, SO_2). ^{1}H NMR ($CDCl_3$) δ: 7.90 (2H, d, *J* = 7.6, ArH_o), 7.65 (1H, t, *J* = 6.8, ArH_p), 7.54 (2H, t, *J* = 7.6, ArH_m), 7.42-7.35 (5H, m, ArH), 5.06 (2H, s, OCH_2), 3.26-3.1 (2H, m, H-1), 2.49 (2H, t, *J* = 6.8, H-2), 2.03 (3H, s, CH_3). ^{13}C NMR ($CDCl_3$) δ: 206.8 (C-3), 133.9, 129.9, 129.6, 128.9, 128.5 (ArC), 79.6 (OCH_2), 48.2 (C-1), 40.8 (C-2), 29.8 (CH_3). HRMS (FAB): Found 334.111502, calcd. for $C_{17}H_{19}NO_4S$ 334.111305.

3-[*N*-(Benzyloxy)-*N*-benzenesulfonamide]-1-phenylpropan-1-one (4c). Yield 87%. White solid. M.p. 108-109 ºC (Et_2O/petroleum ether); R_f 0.56 (Et_2O); IR (KBr) ν_{max}: 1677 (s, C=O), 1348 (s, SO_2), 1171 (s, SO_2). ^{1}H NMR ($CDCl_3$) δ: 7.95 (2H, d, *J* = 7.6, ArH), 7.71-7.7.65 (3H, m, ArH), 7.58-7.53 (3H, m, ArH), 7.44-7.39 (7H, m, ArH), 5.12 (2H, s, OCH_2), 3.32 (2H, m, H-1), 2.9 (2H, t, *J* = 7.2, H-2). ^{13}C NMR ($CDCl_3$) δ: 197.2 (C-3), 136.3, 135.5, 133.9, 133.3, 133.1, 130.2, 129.7, 128.9, 128.8, 128.6, 128.5, 127.9 (ArC), 79.5 (OCH_2), 48.7 (C-1), 36.1 (C-2); MS (EI) *m/z* (rel. int., %): 254 $[M\text{-}SO_2Ph]^+$ (1); 141 $[SO_2Ph]^+$ (1); 105 $[C_7H_5O]^+$ (17); 91 $[C_7H_7]^+$ (100); 77 $[C_6H_5]^+$ (30); HRMS (FAB): Found 396.126848, calcd. for $C_{22}H_{21}NO_4$ 396.126955.

4-[*N*-(Benzyloxy)-*N*-4-methylbenzenesulfonamide]butan-2-one (4d). Yield 80%. Colorless oil. R_f 0.31 (AcOEt/*n*-hexane 3:7); IR (film) ν_{max}: 1715 (s, C=O), 1354 (s, SO_2), 1167 (s, SO_2); ^{1}H NMR ($CDCl_3$) δ: 7.77 (2H, d, *J*=8.2, ArH_o), 7.39-7.36 (5H, m, ArH), 7.32 (2H, d, *J* = 8.2, ArH_m), 5.05 (2H, s, OCH_2), 3.35-3.30 (2H, m, H-1), 2.49 (2H, t, *J* = 7.2, H-2), 2.41 (3H, s, $ArCH_3$), 2.03 (3H, s, CH_3). ^{13}C NMR ($CDCl_3$) δ: 205.9 (C-3), 144.9, 135.2, 129.8, 129.6, 129.5, 128.8, 128.5 (ArC), 79.5 (OCH_2), 48.2 (C-1), 40.8 (C-2), 29.8 (CH_3), 21.6 ($ArCH_3$); MS (EI) *m/z* (rel. int., %): 192 $[M\text{-}Ts]^+$ (1.7); 91 $[C_7H_7]^+$ (100); 77 $[C_6H_5]^+$ (33); HRMS (FAB): Found 334.111502, calcd. for $C_{17}H_{19}NO_4S$ 334.111305.

(±)-*N*-Benzyloxy-*N*-(2-benzenesulfinylethyl)-4'-methylbenzenesulfonamide (4e). Yield 96%. Colorless oil. R_f 0.16 (AcOEt/*n*-hexane 3:7, eluted twice); IR (film) ν_{max}: 1364 (s, SO_2), 1167 (s, SO_2), 1089 (s, S=O). ^{1}H NMR ($CDCl_3$) δ: 7.47 (2H, d, *J* = 8.0, TsH_o), 7.13-7.03 (12H, m, ArH), 4.83 (2H, s, OCH_2), 3.10-2.99 (1H, m, H-1), 2.88-2.75 (1H, m, H-1), 2.47 (2H, t, *J* = 7.08, H-2), 2.18 (3H, s, $ArCH_3$). ^{13}C NMR ($CDCl_3$) δ: 145.2, 143.1, 135.0, 131.2, 129.9, 129.6, 129.4, 129.3, 128.9, 128.5, 123.9 (ArC), 79.5 (OCH_2), 54.0 (C-1), 47.1 (C-2), 21.6 ($ArCH_3$); MS (EI) *m/z* (rel. int., %): 274 $[M\text{-}Ts]^+$ (4); 155 $[Ts]^+$ (5); 167 $[C_8H_9NS]^+$ (0.4); 125 $[M\text{-}SOPh]^+$ (9); 107 $[C_7H_7O]^+$ (0.6); 91 $[C_7H_7]^+$ (100); 77 $[C_6H_5]^+$ (13); HRMS (EI): Found 430.115443 calcd. for $C_{22}H_{23}NO_4S_2$ 430.114677.

***N*-Phenoxy-*N*-(2-benzenesulfonylethyl)-4'-methylbenzenesulfonamide (4f).** Yield 93%. White solid. Mp 91-93 ºC (*n*-hexane); R_f 0.37 (Et_2O/*n*-hexane 1:1, three elutions; spray reagents: $KMnO_4$, negative; Dragendorff, orange spot); IR (KBr) ν_{max}: 1361 (s, SO_2), 1323 (s, SO_2), 1170

(s, SO_2), 1145 (s, SO_2). ^{1}H NMR ($CDCl_3$) δ 7.87 (2H, d, *J* = 7.4, ArH), 7.79-7.76 (3H, m, ArH), 7.65 (2H, t, *J* = 7.8, ArH), 7.5 (2H, d, *J* = 8.0, ArH), 7.29 (2H, t, *J* = 8.2, ArH), 7.07 (1H, t, *J* = 7.3, ArH), 6.99 (2H, d, *J* = 8.2, ArH), 3.46-3.39 (4H, m, H-1 + H-2), 2.49 (3H, s, $ArCH_3$). HRMS (FAB): Found 431.084244, calcd. for $C_{21}H_{21}NO_5S_2$ 431.086117.

***(E)*-*O*-Benzylbenzaldoxime [*(E)*-5].**[21] Yield 45% (calculated on Aza-Brook rearrangement of 1b to yield 6. N-Desulfinylation of 3 to yield 8.). Light yellow oil. Rf 0.74 (CH_2Cl_2/Et_2O 1:1); IR (film) ν_{max}: 1446 (w, C=N). ^{1}H NMR (CD_3CN) δ 8.19 (1H, s, no exchange with D_2O, N=CH), 7.61 (2H, bs, N=CHArH_o), 7.45-7.34 (8H, m, ArH), 5.19 (2H, s, OCH_2); MS (EI) *m/z* (rel. int., %): 211 $[M]^+$ (68); 91 $[C_7H_7]^+$ (97); 77 $[C_6H_6]^+$ (78).

Aza-Brook rearrangement of 1b to yield (6)

Yield 80%. White solid. Mp 75-78 ºC (*n*-hexane); R_f 0.28 (Et_2O/*n*-hexane 1:1, eluted twice; spray reagents: $PdCl_2$ and $KMnO_4$, negative); IR (KBr) ν_{max}: 3249 (s, NH), 1334 (s, SO_2), 1154 (s, SO_2). ^{1}H NMR ($CDCl_3$) δ 7.87 (2H, dd, *J* = 5.8, 1.5, ArH), 7.53-7.46 (3H, m, ArH), 4.43 (1H, bs, exchanges with D_2O, NH), 0.89 [9H, s, Si-C-$(CH_3)_3$], 0.21 [6H, s, Si-$(CH_3)_2$]. ^{13}C NMR ($CDCl_3$) δ: 143.7, 132, 128, 126 (ArC), 25.7 (Si-*t*-Bu), 17.3 (Si-CH_3); Anal. calcd for $C_{12}H_{21}SiNO_2S$: C, 53.10; H, 7.80; N, 5.16; S, 11.81; Found: C, 52.61; H, 7.60; N, 5.36; S, 12.07.

N-Desulfinylation of (3) to yield (8)

Compound **3** (1.0 equiv., 50 mg, 0.13 mmol) was dissolved at RT in dry CH_2Cl_2 (2.0 mL) under inert atmosphere and stirring. $BF_3.Et_2O$ (1.0 equiv., 16.5 μL, 0.13 mmol) was added and after 2 days of reaction (TLC indicating no evolution) the reaction was quenched by the addition of a 15% $NaHCO_3$ aqueous solution. The mixture was diluted with CH_2Cl_2, the organic phase dried and the solvent removed to dryness. Compound **8** was obtained as a light yellow oil which was purified by preparative chromatography. Yield 43.5% (14.2 mg). Light yellow oil. R_f 0.40 (Et_2O/*n*-hexane 7:3, eluted twice; spray reagents: Dragendorff, dark-orange spot; 2,4-DNP, orange spot; $PdCl_2$, negative); IR (film) ν_{max}: 3263 (s, NH), 1682 (s, C=O); ^{1}H-NMR (CD_3CN) δ: 7.96 (2H, d, *J* = 7.7, COArH_o), 7.62 (1H, t, *J* = 7.3, ArH_p), 7.51 (2H, t, *J* = 7.7, ArH_m), 7.36-7.28 (5H, m, ArH), 6.04 (1H, bs, exchanges with D_2O, NH), 4.63 (2H, s, OCH_2), 3.26-3.23 (2H, m, H-3), 3.19-3.16 (2H, m, H-2). HRMS (FAB): Found: 256.133349, calcd. for $C_{16}H_{17}NO_2$ 256.133754.

Acknowledgements

We acknowledge Fundação para a Ciência e a Tecnologia (FC&T, Lisbon, Portugal), PRAXIS program, for partial financial support. Two of us (V.D.B.B. and R.P.K) also acknowledge PRAXIS program for the award of research fellowships.

References and Notes

1. Maricich, T. J.; Jourdenais, R. A.; Albright, T. A. *J. Am. Chem. Soc*. **1973**, *95*, 5831.
2. Racemic benzenesulfinyl chloride was used. Chiral arylsulfinamides can be prepared using a cinchona alkaloid/sulfinyl choride system: Shibata, N.; Matsunaga, M.; Nakagawa, M.; Fukuzumi, T.; Nakamura, S.; Toru, T. *J. Am. Chem. Soc.* **2005**, *127*, 1374; or using commercial Andersen's menthyl sulfinate esters. The importance of enantio-enriched, sulfoxides has been recently reviewed: O'Mahony, G. E.; Kelly, P.; Lawrence, S. E.; Maguire, A. R. *Arkivoc.* **2011** (*i*), 1-110.
3. Enders, D.; Müller, S. F.; Raabe, G. *Angew. Chem. Int. Ed.* **1999**, *61*, 195.
4. The reaction between **1a** and methyl acrylate was also performed, however the isolated aza-Michael adduct had a persistent impurity which precluded complete microanalytic characterization. IR (film) ν_{max}: 1738 (s, C=O), 1107 (s, SO). ^{1}H NMR (CD_3CN) δ: 7.67-7.65 (2H, m, ArH), 7.60-7.58 (3H, m, ArH), 7.40-7.35 (5H, m, SOArH), 4.89 (1H, d, *J* = 10.6, OCH), 4.71 (1H, d, *J* = 10.6, OCH), 3.51 (3H, s, OCH_3), 3.22-3.17 (1H, m, H-1), 3.04-3.00 (1H, m, H-1), 2.48 (2H, m, H-2).
5. Compound **6** was isolated in 80% yield using NaH (1.0 equiv.) at 0 ºC in 15 min. The amount of base, temperature and time of reaction were found to influence the yield of the reaction. When prolonged reaction times were used only benzenesulfonamide was isolated.
6. These migrations are irreversible: Wolfgramm, R.; Muller, T.; Klingebiel, U. *Organometallics* **1998**, *17*, 3222.
7. One referee drew attention to the alternative nitrene mechanism of Maricich (ref. 1) which, after nucleophilic attack on sulfur by the alkoxide and *O* to *N* silyl migration, affords **6**.
8. For examples of aza-Brook rearrangements see: (a) Nielsen, L.; Lindsay, K. B.; Faber, J.; Nielsen, N. C.; Skrydstrup, T. *J. Org. Chem.* **2007**, *72*, 10035. (b) Liu, G.; Sieburth, S. McN. *Org. Lett.* **2003**, *5*, 4677. (c) Honda, T.; Mori, M. *J. Org. Chem.* **1996**, *61*, 1196.
9. (a) Bonifácio, V. D. B.; Gonzalez-Bello, C.; Rzepa, H. S.; Prabhakar, S.; Lobo, A. M. *Synlett* **2010**, *1*, 145. (b) Antunes, M. M.; Bonifácio, V. D. B.; Nascimento, S.; Branco, P. S.; Lobo, A. M.; Prabhakar, S. *Tetrahedron* **2007**, *63*, 7009. (c) Aires-de-Sousa, J.; Prabhakar, S.; Lobo, A. M.; Rosa, A. M.; Gomes, M. J. S.; Corvo, M. C.; Williams, D. J.; White, A. J. P. *Tetrahedron Asymm.* **2002**, *12*, 3349. (d) Antunes, M. M.; Marto, S. J. L.; Branco, P. C. S.; Prabhakar, S.; Lobo, A. M. *J. Chem. Soc. Chem. Commun.* **2001**, 405. (e) Aires-de-Sousa, J.; Lobo, A. M.; Prabhakar, S. *Tetrahedron Lett.* **1996**, *37*, 3183. (f) Pereira, M. M.; Santos, P. P. O.; Reis, L.V.; Lobo, A. M.; Prabhakar, S. *J. Chem. Soc., Chem. Commun.* **1993**, 38.
10. Hayase, T.; Osanai, S.; Shibata, T.; Soai, K. *Heterocycles* **1998**, *48*, 139.
11. Kato, Y.; Yen, D. H.; Fukudome, Y.; Hata, T.; Urabe, H. *Org. Lett.* **2010**, *12*, 3147.
12. (a) David, D. M.; O'Meara, G. W.; Pyne, S. G. *Tetrahedron Lett.* **1996**, *37*, 5417. (b) Gais, H.-J.; Scommoda, M.; Lenz, D. *Tetrahedron Lett.* **1994**, *35*, 7361. (c) Davis, F. A; Reddy, R. T; Reddy, R. E. *J. Org. Chem.* **1992**, *57*, 6387.

13. Davis, F. A.; Ramachandar, T.; Zhang, Y.; Chai, J.; Qiu, H.; Deng, J.; Velvadapu, V. *Tetrahedron Lett.* **2010**, *51*, 4042.
14. Evans, D. A.; Faul, M. M.; Colombo, L.; Bisaha, J. J.; Clardy, J.; Cherry, D. *J. Am. Chem. Soc.* **1992**, *114*, 5977.
15. Shi, M.; Li, C.-Q.; Jiang, J.-K. *Molecules* **2002**, *7*, 721.
16. (a) Chang, Y. H.; Chiu, F.-T. ; Zon, G. *J. Org. Chem.* **1981**, *46*, 342. (b) Robin, S.; Rousseau, G. *Eur. J. Chem.* **2000**, *17*, 3007.
17. Hassner, A. *J. Org. Chem.* **1970**, *35*, 1962.
18. Cooley, J. H.; Misra, B. N.; Throckmorton, J. R.; Bills, W. D. *J. Med. Chem.* **1968**, *11*, 196.
19. Endo, Y.; Shudo, K.; Okamoto, T. *J. Am. Chem. Soc.* **1982**, *104*, 6393.
20. Choi, J. H.; Lee, B. C.; Lee, H. W.; Lee, I. *J. Org. Chem*. **2002**, *67*, 1277.
21. (a) Miyabe, H.; Shibata, R.; Sangawa, M.; Ushiro, C.; Naito, T. *Tetrahedron* **1998**, *54*, 11431. (b) Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *J. Am. Chem. Soc.* **2004**, *126*, 5192.

