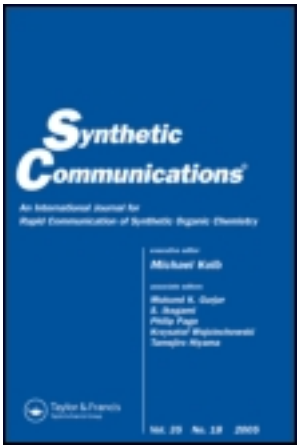


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Microwave-Induced Rapid Access to Aromatic and Heteroaromatic Sulfonamides Under Solvent-Free Conditions Without Using External Base

Ashwani Kumar Sharma [a] & Saibal Kumar Das [a]
[a] Discovery Chemistry, Dr. Reddy's Laboratories Ltd., Discovery Research, Bollaram Road, Miyapur, Hyderabad, 500049, India
Published online: 19 Apr 2010.

SYNTHETIC COMMUNICATIONS®
Vol. 34, No. 20, pp. 3807–3819, 2004

Microwave-Induced Rapid Access to Aromatic and Heteroaromatic Sulfonamides Under Solvent-Free Conditions Without Using External Base[#]

Ashwani Kumar Sharma and Saibal Kumar Das*

Discovery Chemistry, Dr. Reddy's Laboratories Ltd.,
Discovery Research, Bollaram Road, Miyapur, Hyderabad 500049, India

ABSTRACT

Microwave-induced syntheses of sulfonamides, without using base under solvent-free conditions, have been developed. The process finds its utility because of its simple operational procedure and high yields. Moreover, the process is fast and accommodative to different substituents on aromatic as well as heteroaromatic rings rendering sulfonamides (28 examples).

Key Words: Aromatic; Heteroaromatic; Solvent-free; Sulfonamide.

[#]DRL-Publication No. 327.

*Correspondence: Saibal Kumar Das, Discovery Chemistry, Dr. Reddy's Laboratories Ltd., Discovery Research, Bollaram Road, Miyapur, Hyderabad 500049, India; Tel.: +91-40-23045439 ; Fax: + 91-40-23045438; E-mail: saibalkumardas@drreddys.com.

DOI: 10.1081/SCC-200032530 0039-7911 (Print); 1532-2432 (Online)

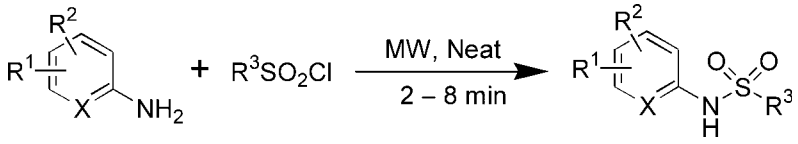
INTRODUCTION

Sulfonyl groups have been widely used to protect amines and other nitrogenous functionality in organic syntheses.[1] Sulfonamides are also an important class of compounds in organic chemistry. Research is going on in drug development, where the sulfonamides are proved to be a separate class of therapeutic agents used in different areas as cholesterol modulator,[2] antiarrhythmic drug and β–adrenergic blocker,[3] antitumor agents against multidrug resistant tumors,[4] selective Cox-II inhibitors,[5] endothelin receptor antagonists,[6] etc. Although there are a number of methods[3,7] available to prepare sulfonamides, one often uses a base, and the reactions take a long time for completion. Our interest in the total synthesis of biologically significant molecules containing sulfonamide moiety in general has opened the avenue for newer methodologies for the introduction of sulfonyl groups. Herein, we report some of our investigational findings in the microwave-assisted sulfonamide synthesis without using base and solvent, as shown in Sch. 1 and 2, which could be an attractive alternative to hitherto reported methods.

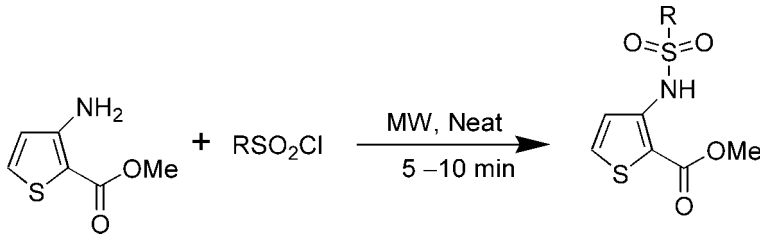
The benefits of microwave-assisted reactions in the field of organic chemistry are increasingly making the technique more established worldwide, as is evident from the number of reviews that have appeared in the literature since 1991.[8] Microwave irradiation has proved its efficiency in rate enhancement over classical heating methods, and there has been tremendous advance in the synthesis of organic compounds using microwave irradiation.[9]

RESULTS AND DISCUSSION

Although there are several methods available in the literature[3,7] to make these kinds of sulfonamides, at our hands, all those methods did not work well. Either low or no yields and even disulfonamide formation were observed. The compound in entry 1 (Table 1) was reported in 59.7% yield based on benzene sulfonyl chloride (0.8 equivalent with respect to the substrate) used.[2b] Using classical techniques, we could not even achieve 50% yields



Scheme 1.



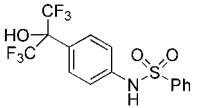
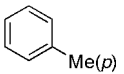
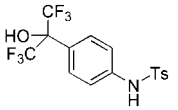
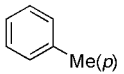
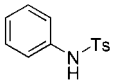
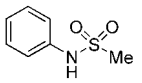
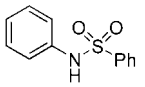
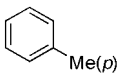
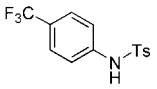
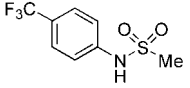
Scheme 2.

for the compounds in entries 2 and 3, Table 1. For the compound in entry 2, we also obtained disulfonamide when the reaction was performed using triethyl amine in dichloromethane. Because we are using microwave techniques for other organic reactions, we wanted to explore this possibility.

To our surprise, the reactions afforded the products easily under solvent-free conditions in the absence of an external base. But, the use of even a stoichiometric amount of sulfonyl chlorides afforded a loss in yields. The optimum condition ultimately determined was the use of 0.65 equivalents of sulfonyl chlorides. The yields were calculated based on the amount of sulfonyl chlorides used. In most of the cases, we could achieve high yields, although where the anilines were very high melting, the yields were relatively low. If there were electron-withdrawing groups (EWGs) or no group at *p*-position of the substrate, the yields were high in contrast to the presence of electron-donating groups (EDGs) at the same position. This may be because the EWG lowers the availability of lone pairs on nitrogen, thereby reducing the probability of forming salts; instead, it reacts with the sulfonyl group under forced conditions. Bulky molecules showed the same deviations. Steric hindrance was prominent in entries 12, 13, 14, and 16 (Table 1); although, moderate yields were observed in entries 11 and 15. In general, poor yields have been observed for the free carboxylic acid substituents at the *ortho*-position. This observation was also reflected in reactions with 3-amino thiophene-2-carboxylic acid. Very low yields (20–30%) were observed with free acids against very high yields in case of esters (Table 2). Typically, both the reactants were placed in an open vessel and irradiated with microwaves for an appropriate time (Tables 1 and 2) without any solvent. All the compounds were characterized based on their hydrogen nuclear magnetic resonance (^{1}H-NMR), infrared (IR), and liquid chromatography-mass spectrometry (LC-MS) data.

To conclude, the present methodology is operationally simple and requires no external base; the reactions are clean with no appreciable side product being detected; and it is cost effective and high yielding. In some

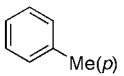
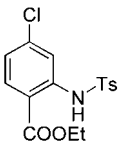
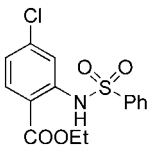
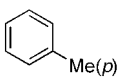
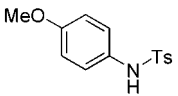
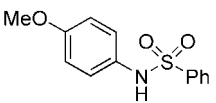
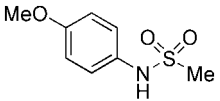
Table 1. Preparation of various sulfonamides using six-membered ring scaffold (Sch. 1).

Entry	R^1	R^2	X	R^3	Product	Time (min)	%Yield	Ref.
1	*p*-$C(CF_3)_2OH$	H	CH			6	92	[2b]
2	*p*-$C(CF_3)_2OH$	H	CH			6	84	—
3	H	H	CH			5	88	[10a]
4	H	H	CH	Me		6	76	[7b]
5	H	H	CH			6	68	[10b]
6	*p*-CF_3	H	CH			6	92	—
7	*p*-CF_3	H	CH	Me		6	66	[10c]

8	*p*-CF_3	H	CH			6	92	[10d]
9	H	H	N			6	29	[10e]
10	H	H	N			2	56	[10e]
11	*p*-OMe	*o*-COOH	CH			6	62	—
12	*p*-OMe	*o*-COOH	CH			6	31	—
13	H	*o*-Cl	CH			5	46	—
14	*m*-F	*o*-COOH	CH			7	30	—

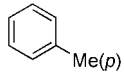
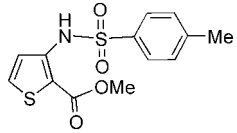
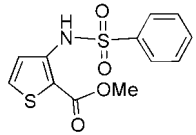
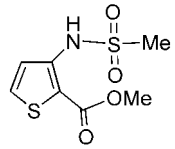
(*continued*)

Table 1. Continued.

Entry	R^1	R^2	X	R^3	Product	Time (min)	%Yield	Ref.
15	*m*-Cl	*o*-COOEt	CH			8	68	—
16	*m*-Cl	*o*-COOEt	CH			8	45	—
17	*p*-OMe	H	CH			6	78	[7a]
18	*p*-OMe	H	CH			6	88	[7c]
19	*p*-OMe	H	CH	Me		6	90	[7d]

20	*m*-Br	H	CH			6	88	[7a]
21	*m*-Br	H	CH			6	85	[10f]
22	*m*-Br	H	CH	Me		6	94	[7a]
23	*p*-COOH	H	CH			6	63	[10h]
24	*p*-COOH	H	CH			8	60	—
25	*p*-COOH	H	CH	Me		8	54	[10i]

Table 2. Preparation of various sulfonamides using thiophene ring structure (Sch. 2).

Entry	R	Product	Time (min)	%Yield	Ref.
1			5	75	[10g]
2			10	75	—
3	Me		10	80	[10g]

cases, yields are higher than those obtained through existing methods. The absence of catalyst and solvent, easy workup procedure, and short reaction time impart greater merit to this procedure over those existing.

EXPERIMENTAL

The ^{1}H-NMR spectra were recorded with tetramethylsilane (TMS, δ 0.00) as internal standards on a Varian Gemini 200 MHz FT NMR spectrometer. Mass spectra were measured on Hewlet Packard-5989A mass spectrometer (CI, 20 eV). The IR spectra were recorded using Perkin–Elmer 1650 Fourier transform-infrared (FT-IR) spectrophotometer. Melting points were measured in a glass capillary on a digital melting point apparatus model No. Büchi-535, and they are uncorrected. All the chromatography solvents were distilled before use. Silica gel (100–200 mesh, SRL, India) was used for column purification.

General Procedure

Aniline derivative (100 mg) and aryl (or methyl) sulfonyl chloride (0.65 equiv) were placed in an open vessel, and the mixture was irradiated

with microwaves (LG model: MC-804AAR) for the appropriate time (see Tables 1 and 2). The reaction mixture was then treated with ethyl acetate to remove the solid particles (mostly salts of remaining starting material). The supernatant was evaporated to dryness. The residue was purified on silica gel (100–200 mesh) using ethyl acetate-pet ether to afford the desired products as summarized in Tables 1 and 2.

Table 1, entry **2**

Mp. 185–187°C; ^{1}H-NMR ($CDCl_3$ + DMSO-d_6, 200 MHz): δ 2.37 (s, 3H, CH_3), 7.16 (d, 2H, $J = 8.6$ Hz, Ph), 7.30 (d, 2H, $J = 8.1$ Hz, Ph), 7.54 (d, 2H, $J = 8.3$ Hz, Ph), 7.68 (d, 2H, $J = 7.8$ Hz, Ph); IR (KBr): ν_{max} (cm^{-1}) 3390, 3241, 1615, 1517, 1467, 1228, 1165; LC-MS (CI): m/z 414 ($M^+ + 1$). Anal calculated for $C_{16}H_{13}F_6NO_3S$: C 46.49; H 3.17; N 3.39. Found: C 46.48; H 3.42; N 3.23.

Table 1, entry **6**

Mp. 70–72°C; ^{1}H-NMR (CD_3OD, 200 MHz): δ 2.37 (s, 3H, CH_3), 7.25 (d, 2H, $J = 8.8$ Hz, Ph), 7.31 (d, 2H, $J = 8.6$ Hz, Ph), 7.50 (d, 2H, $J = 8.3$ Hz, Ph), 7.71 (d, 2H, $J = 8.3$ Hz, Ph); IR (Neat): ν_{max} (cm^{-1}) 3264, 1619, 1517, 1328, 1162; LC-MS (CI): m/z 316 ($M^+ + 1$). Anal calculated for $C_{14}H_{12}F_3NO_2S$: C 53.32; H 3.95; N 4.44. Found: C 53.20; H 4.21; N 4.41.

Table 1, entry **11**

^{1}H-NMR ($CDCl_3$, 200 MHz): δ 2.32 (s, 3H, CH_3), 3.76 (s, 3H, CH_3), 7.01–7.23 (m, 3H, Ph), 7.64 (d, 4H, $J = 8.1$ Hz, Ph); IR (Neat): ν_{max} (cm^{-1}) 3424, 3222, 2926, 1682, 1498, 1241, 1229, 1164, 1039; LC-MS (CI): m/z 321 (M^+), 322 ($M^+ + 1$). Anal calculated for $C_{15}H_{15}NO_5S$: C 56.06; H 4.70; N 4.36. Found: C 55.80; H 4.88; N 4.66.

Table 1, entry **12**

^{1}H-NMR ($CDCl_3$ + DMSO-d_6, 200 MHz): δ 3.75 (s, 3H, CH_3), 7.03 (dd, 1H, $J = 8.9$ and 2.9 Hz, Ph), 7.40 (d, 1H, $J = 2.7$ Hz, Ph), 7.41–7.54 (m, 3H, Ph), 7.69 (d, 1H, $J = 5.5$ Hz, Ph), 7.73 (d, $J = 7.3$ Hz, Ph); IR (Neat): ν_{max} (cm^{-1}) 3419, 1659, 1499, 1027, 1006; LC-MS (CI): m/z 308 ($M^+ + 1$). Anal calculated for $C_{14}H_{13}NO_5S$: C 54.72; H 4.26; N 4.56. Found: C 54.49; H 3.97; N 4.85.

Table 1, entry **13**

Mp. 100–102°C; ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 2.38 (s, 3H, CH_3), 6.92–7.08 (m, 1H, Ph), 7.15–7.28 (m, 4H, Ph), 7.65 (d, 3H, $J = 8.3$ Hz, Ph); IR (KBr): ν_{max} (cm^{-1}) 3440, 3265, 1595, 1482, 1396, 1167; LC-MS (CI): m/z 282 ($M^+ + 1$ with ^{35}Cl), 284 ($M^+ + 1$ with ^{37}Cl). Anal calculated for $C_{13}H_{12}ClNO_2S$: C 55.42; H 4.29; N 4.97. Found: C 55.08; H 4.42; N 5.23.

Table 1, entry **14**

Mp. 140–142°C; ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 2.36 (s, 3H, CH_3), 6.80 (t, 1H, $J = 8.8$ Hz, Ph), 7.22 (d, 2H, $J = 7.8$ Hz, Ph), 7.35–7.54 (m, 2H, Ph), 7.73 (d, 2H, $J = 8.1$ Hz, Ph), 10.34 (br s, D_2O exchangeable); IR (KBr): ν_{max} (cm^{-1}) 3437, 2927, 1667, 1613, 1467, 1259, 1164; LC-MS (CI): m/z 310 ($M^+ + 1$). Anal calculated for $C_{14}H_{12}FNO_4S$: C 54.36; H 3.91; N 4.53. Found: C 54.28; H 3.79; N 4.43.

Table 1, entry **15**

Mp. 116–118°C; ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 1.37 (t, 3H, $J = 7.1$ Hz, CH_2CH_3), 2.38 (s, 3H, CH_3), 4.33 (q, 2H, $J = 7.2$ Hz, CH_2CH_3), 6.99 (dd, 1H, $J = 8.8$ and 2.0 Hz, Ph), 7.25 (d, 2H, $J = 7.8$ Hz, Ph), 7.70–7.79 (m, 3H, Ph), 7.85 (d, 1H, $J = 8.6$ Hz, Ph), 10.77 (br s, D_2O exchangeable); IR (KBr): ν_{max} (cm^{-1}) 3438, 1687, 1595, 1491, 1253, 1157; LC-MS (CI): m/z 354 ($M^+ + 1$ with ^{35}Cl), 356 ($M^+ + 1$ with ^{37}Cl). Anal calculated for $C_{16}H_{16}ClNO_4S$: C 54.31; H 4.56; N 3.96. Found: C 54.58; H 4.48; N 3.72.

Table 1, entry **16**

Mp. 110–112°C; ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 1.35 (t, 3H, $J = 7.2$ Hz, CH_2CH_3), 4.33 (q, 2H, $J = 7.1$ Hz, CH_2CH_3), 6.99 (dd, 1H, $J = 8.6$ and 1.9 Hz, Ph), 7.40–7.56 (m, 3H, Ph), 7.72 (d, 1H, $J = 1.6$ Hz, Ph), 7.80–7.96 (m, 3H, Ph), 10.80 (br s, D_2O exchangeable); IR (KBr): ν_{max} (cm^{-1}) 3424, 2925, 1691, 1574, 1492, 1248, 1160; LC-MS (CI): m/z 340 ($M^+ + 1$ with ^{35}Cl), 342 ($M^+ + 1$ with ^{37}Cl). Anal calculated for $C_{15}H_{14}ClNO_4S$: C 53.02; H 4.15; N 4.12. Found: C 53.38; H 3.92; N 4.43.

Table 1, entry **24**

Mp. 128–130°C; ^{1}H-NMR (CD_3OD, 200 MHz): δ 7.17 (d, 2H, $J = 8.6$ Hz, Ph), 7.45–7.58 (m, 3H, Ph), 7.80–7.88 (m, 4H, Ph); IR (KBr): ν_{max} (cm^{-1}) 3424, 3279, 1681, 1606, 1337, 1291, 1090; LC-MS (CI): m/z

278 ($M^+ + 1$). Anal calculated for $C_{13}H_{11}NO_4S$: C 56.31; H 4.0; N 5.15. Found: C 56.04; H 4.10; N 4.85.

Table 2, entry **2**

Mp. 88–90°C; ^{1}H-NMR (CD_3OD, 200 MHz): δ 3.80 (s, 3H, CH_3), 6.57 (d, 1H, $J = 5.4$ Hz, thiophene), 7.39 (t, 1H, $J = 4.6$ Hz, Ph), (d, 2H, $J = 7.8$ Hz, Ph), 7.59 (d, 1H, $J = 7.3$ Hz, Ph), 7.64 (d, 1H, $J = 5.4$ Hz, thiophene), 7.83 (d, 2H, $J = 7.3$ Hz, Ph); IR (KBr): ν_{max} (cm^{-1}) 3453, 2951, 1700, 1682, 1550, 1447, 1374, 1242, 1174, 1091; LC-MS (CI): m/z 238 (M^+- COOMe). Anal calculated for $C_{12}H_{11}NO_4S_2$: C 48.47; H 3.73; N 4.71. Found: C 48.08; H 3.55; N 5.00.

ACKNOWLEDGMENTS

We express our esteemed gratitude to Professor J. Iqbal and Dr. R. Rajagopalan for their continuous encouragement to this work.

REFERENCES

1. For review, see: Green, T.W.; Wuts, P.G. *Protective Groups in Organic Synthesis*, 2nd Ed.; Wiley: New York, 1991; 379–386.
2. (a) Repa, J.J.; Turley, S.D.; Lobaccaro, J.-M.A.; Medina, J.; Li, L.; Lustig, K.; Shan, B.; Heyman, R.A.; Dietschy, J.M.; Mangelsdorf, D.J. Regulation of absorption and ABC1-mediated efflux of cholesterol by RXR heterodimers. Science **2000**, *289*, 1524–1529; (b) Li, L.; Medina, J.C.; Hasegawa, H.; Liu, J.; Zhu, L.; Shan, B.; Lustig, K. Preparation of *bis*(trifluoromethyl)hydroxymethylbenzenesulfonamides, -ureas, and -carbamates as liver X receptor modulators. PCT Patent No. WO 00/054759, 2000; Chem. Abstr. **2000**, *133*, 237693.
3. Lumma, W.C., Jr.; Wohl, R.A.; Davey, D.D.; Argentieri, T.M.; De Vita, R.J.; Gomez, R.P.; Jain, V.K.; Marisca, A.J.; Morgan, T.K., Jr.; Reiser, H.J.; Sullivan, M.E.; Wiggins, J.; Wong, S.S. Rational design of 4-[(methylsulfonyl)amino]benzamides as class III antiarrhythmic agents. J. Med. Chem. **1987**, *30*, 755–758.
4. Shan, B.; Medina, J.C.; Santha, E.; Frankmoelle, W.P.; Chou, T.-C.; Learned, R.M.; Narbut, M.R.; Stott, D.; Wu, P.; Jaen, J.C.; Rosen, T.; Timmermans, P.B.M.W.M.; Beckmann, H. Selective, covalent modification of β-tubulin residue Cys-239 by T138067, an antitumor agent with in vivo efficacy against multidrug-resistant tumors. Proc. Natl. Acad. Sci. USA **1999**, *96*, 5686–5691.

5. (a) Penning, T.D.; Talley, J.J.; Bertenshaw, S.R.; Carter, J.S.; Collins, P.W.; Docter, S.; Graneto, M.J.; Lee, L.F.; Malecha, J.W.; Miyashiro, J.M.; Rogers, R.S.; Rogier, D.J.; Yu, S.S.; Anderson, G.D.; Berton, E.G.; Cogburn, J.N.; Gregory, S.A.; Koboldt, C.M.; Perkins, W.E.; Seibert, K.; Veenhuizen, A.W.; Zhang, Y.Y.; Isakson, P.C. Synthesis and biological evaluation of the 1,5-diarylpyrazole class of cyclooxygenase-2 inhibitors: Identification of 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl]benzenesulfonamide (SC-58635, Celecoxib). J. Med. Chem. **1997**, *40*, 1347–1365; (b) Talley, J.J.; Brown, D.L.; Carter, J.S.; Graneto, M.J.; Koboldt, C.M.; Masferrer, J.L.; Perkins, W.E.; Rogers, R.S.; Shaffer, A.F.; Zhang, Y.Y.; Zweifel, B.S.; Seibert, K. 4-[5-Methyl-3-phenylisoxazol-4-yl]-benzenesulfonamide, Valdecoxib: A potent and selective inhibitor of COX-2. J. Med. Chem. **2000**, *43*, 775–777.
6. For review, see: Iqbal, J.; Sanghi, R.; Das, S.K. Endothelin receptor antagonists: An overview of their synthesis and structure–activity relationship. Mini Rev. Med. Chem. **2004**, *in press*.
7. (a) Tokuyama, H.; Sato, M.; Ueda, T.; Fukuyama, T. A practical route to quinolines from anilines. Heterocycles **2001**, *54*, 105–108; (b) Baxter, N.J.; Rigoreau, L.J.M.; Laws, A.P.; Page, M.I. Reactivity and mechanism in the hydrolysis of β-sultams. J. Am. Chem. Soc. **2000**, *122*, 3375–3385; (c) Boulos, L.S.; Hennawy, I.T.; Arsanious, M.H.N. Reactions of phosphites with 1,4-benzoquinone monoimines. Liebigs Ann. Chem. **1993**, 351–354; (d) Kim, S.Y.; Sung, N.-D.; Choi, J.-K.; Kim, S.S. 1*H*-benzotriazol-1-yl methanesulfonate: a regioselective *N*-mesylating reagent. Tetrahedron Lett. **1999**, *40*, 117–120.
8. (a) Mingos, D.M.P.; Baghurst, D.R. Applications of microwave dielectric heating effects to synthetic problems in chemistry. Chem. Soc. Rev. **1991**, *20*, 1–47; (b) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. Microwave assisted organic synthesis—A review. Tetrahedron **2001**, *57*, 9225–9283; (c) Perreux, L.; Loupy, A. A tentative rationalization of microwave effects in organic synthesis according to the reaction medium, and mechanistic considerations. Tetrahedron **2001**, *57*, 9199–9223.
9. (a) Das, S.K.; Reddy, K.A.; Abbineni, C.; Roy, J.; Rao, K.V.L.N.; Sachwani, R.H.; Iqbal, J. Microwave-induced, $InCl_3$-catalyzed Ferrier rearrangement of acetylglycals: synthesis of 2,3-unsaturated *C*-glycosides. Tetrahedron Lett. **2003**, *44*, 4507–4509; (b) Das, S.K.; Reddy, K.A.; Roy, J. Microwave-induced, $InCl_3$-catalyzed Ferrier rearrangement of acetylglycals: synthesis of 2,3-unsaturated glycopyranosides. Synlett **2003**, 1607–1610.

10. (a) Schantl, J.G.; Hebeisen, P.; Karpellus, P. *N*-(Arenesulfonyl)-*N*-phenylhydrazones. Synth. Commun. **1989**, *19*, 39–48; (b) Katritzky, A.R.; Zhang, G.; Wu, J. 1-Phenylsulfonylbenzotriazole: a novel and convenient reagent for the preparation of benzenesulfonamides and aryl benzenesulfonates. Synth. Commun. **1994**, *24*, 205–216; (c) Kondo, K.; Sekimoto, E.; Nakao, J.; Murakami, Y. Studies on development of sufficiently chemoselective *N*-acylation reagents: *N*-acyl-*N*-(2,3,4,5,6-pentafluorophenyl)-methanesulfonamides. Tetrahedron **2000**, *56*, 5843–5856; (d) Burger, A.; Hornbaker, E.D. Some aromatic trifluoromethyl derivatives. The Rosenmund reduction of trifluoromethyl benzoic acids. J. Org. Chem. **1953**, *18*, 192–195; (e) Mastrukova, T.A.; Sheinker, Y.N.; Kuznetsova, I.K.; Peresleni, E.M.; Sakharova, T.B.; Kabachnik, M.I. The application of the Hammett equation to the theory of tautomeric equilibrium-II: Tautomerism of α-arylsulphaminopyridines. Tetrahedron **1963**, *19*, 357–372; (f) Kaplan, H.; Leubner, G.W. Some halogenated sulfonanilides. J. Am. Chem. Soc. **1945**, *67*, 1076–1077; (g) Coutts, I.G.C.; Edwards, M.; Richards, D.J. Mild selective hydrolysis of the methyl esters of some *ortho*-substituted aromatic carboxylic acids. Synthesis **1981**, 487–489; (h) Weisblat, D.I.; Magerlein, B.J.; Hanze, A.R.; Myers, D.R.; Rolfson, S. Synthesis of pteroic and pteroylglutamic acids. J. Am. Chem. Soc. **1953**, *75*, 3625–3629; (i) Hu, H.; Mendoza, J.S.; Lowden, C.T.; Ballas, L.M.; Janzen, W.P. Synthesis and protein kinase C inhibitory activities of balanol analogs with modification of 4-hydroxybenzamido moiety. Bioorg. Med. Chem. **1997**, *5*, 1873–1882.

Received in the UK June 20, 2004