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ELECTROCHEMICAL HETEROCYCLIZATION OF o-TOLUENESULFONAMIDES TO 3-ALKYL-4,5-DIHYDRO-1,2,4-BENZOTHIADIAZEPINE-1,1-DIOXIDES

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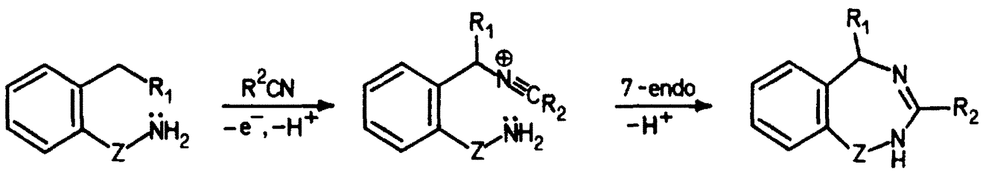
Controlled potential oxidation of a variety of substituted o-toluenesulfonamides at a Pt anode in MeCN using a divided cell provides 3-methyl -4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxides selectively and in generally good yields. The scope and limitations of this one-step heterocyclization sequence are also discussed.

The electrochemical functionalization of organic compounds have been the subject of intense efforts over the last decades during which time a reasonable understanding of the scope and limitations of this topic have been determined.[1]

In the context of our studies in the electro-organic synthesis[2], we have investigated the anodic oxidation of o-alkyl-benzenesulfonamides A($Z=SO_2$), -benzamides A(Z=CO) and -thiobenzamides A($Z=SO_2$) in the presence of nitriles as solvents. At the outset of this work, we were attracted by the possibility that anodically generated positive species (radical cations and/or carbenium ions) might react with nucleophilic solvents (nitriles) leading to a nitrilium ion B. This intermediate could, in turn, undergo a facile intramolecular attack by the neighbouring nucleophilic terminus $Z\text{-}NH_2$ (7-*endo* cyclization) to give diazepine ring systems C (Scheme 1).



A B C

SCHEME 1

While we were unsuccessful in finding a high-yield method for oxidative ring closure of o-alkylbenzamides A(Z=CO) and their thiono analogues A(Z=CS)[3], we disclose here that A($Z=SO_2$) can be cleanly converted to the corresponding benzothiadiazepine-S,S-dioxide ring system

$C(Z=SO_2)$ merely by electrochemical oxidation in the presence of a nitrile RCN.

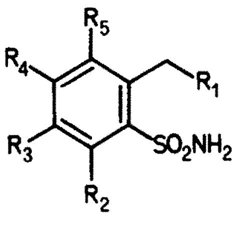
Eberson and Nyberg[4] were the first to shown that it is possible to trap electrolitically generated benzyl cations with wet MeCN giving, through the intermediacy of acetonitrilium ion and subsequent hydration, side-chain acetamidated products and it may be well considered analogous to the Ritter reaction[5]. Despite the intense activity in this field, the exploration of the anodic acetamidation of alkyl-arenes having a nucleophilic group(suitably located in *ortho* position) and its potential for preparative purpose have been completely neglected.

The oxidative behaviour of the checked o-alkylbenzenesulfonamides in MeCN is characterized , by a single broad and poorly defined irreversible voltammetric wave at a Pt electrode. For p-substituted 1a-h the half-wave oxidation potentials $E_{1/2}$ range from +1.70V for 1h(p-NHAc) to +2.79V for the p-NO_2 compound 1e and the trend in $E_{1/2}$ may be expressed by an extrathermodynamic relationship and a better fit (r=0.96) was obtained with Brown's electrophilic substituent constants σ^{+}[6] [$E_{1/2}$= 0.709(± 0.08)σ^{+}+2.20(± 0.03)].

Large-scale controlled-potential electrolysis of 1a-l have been performed on a Pt gauze anode at potential near to the diffusion plateau of the oxidation response in a MeCN-$LiClO_4$ medium (anodic limit:2.5V *vs* SCE) in an H-type cell equipped with ion-exchange membrane. After much experimentation to find optimum conditions, it was apparent that a proton source was needed for the reaction to proceed smoothly. Neverthless, current density decayed rapidly due to electrode inhibition by insulating polymeric film. Continuous pulsing to 0V(1 s)every 20 s was necessary in order to keep the anode uncoated and maintain a reasonable current flow. Electrolyses were generally halted after depletion of the starting material (TLC check). In practice, 1a(30 mmol) was electrolysed at +2.0V *vs* Ag/0.01N $AgNO_3$ using 1M $LiClO_4$ solution in nominally dry MeCN (125 mL) containing 70% $HClO_4$ (0.5 mL) at ambient temperature. After transfer of 2.2 F/mol the anolyte was purified by flash chromatography leading to 3-methyl-4,5-dihydro-1,2,4-benzothia-diazepine-1,1-dioxide 2a in 87% isolated yield.The EI-MS of 2a exhibited a molecular ion at m/z 210($C_9H_{10}N_2O_2S$)[7] while its IR spectrum (nujol mull) was devoid of any carbonyl band but had a broad NH absorption at 3300 cm^{-1}.Salient features in the ^1H NMR spectrum (DMSO-d_6)were the doublet (J=5Hz) at 4.80 ppm and a broad triplet (exchangeable with D_2O) at 9.46 ppm, due to benzylic methylene C(5) and coupled NH proton, respectively, thus implying that, at least in DMSO-d_6 and at 330K, the tautomer with a proton residing on the N(4)-nitrogen ,*i.e.*2a,is preferred over the 2*H*-tautomer 2a*. Significantly, ^{13}C NMR spectrum (DMSO-d_6) of 2a included the appearance of signals at 24.4(q), 45.4(t) and 161.0 (s) ppm assigned to Me-C(3), C(5) and C(3),respectively.

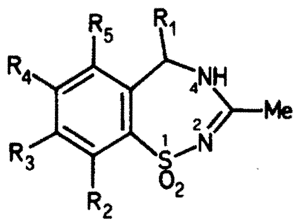
Although examples of 1,2,4-benzothiadiazepine-1,1-dioxides have been described [8,9],monosubstituted compounds at C(3) appear to have been prepared for the first time in our laboratory. For the sake of comparison, we have converted 2a by regioselective methylation [NaH, DMF, MeI,r.t.] into N(2)-methyl derivative 3(68%), whose N-Me proton signal appeared relatively downfield (0.25 ppm) as compared to that of N(4)-methyl analogue 4, unambiguously prepared according to Lora-Tamayo procedure.[9,10]

In order to determine the scope and limitations of this one-step heterocyclisation sequence, some of o-alkylbenzenesulfonamides were examined in different nitrile solvents(*e.g.*, propionitrile, n-butyronitrile, 2-methylpropionitrile and benzonitrile). As can be seen from the results summarised in Table, the isolated yields of seven-membered heterocyclic compounds are, in general, acceptable ranging from 55 to 87%.Furthermore, we attributed the formation of significant amount of o-acetamidomethylbenzenesulfonamides 5 to the hydrolysis by water adventitiously present in the solvent or added during work-up of intermediate nitrilium ion B(Z=SO_2)(Ritter reaction)[11]. As previously noted by Eberson[12] in his study of the anodic acetamidation, the partitioning of B(Z=SO_2) between 2 and 5 most probably reflects the abnormal greater selectivity of the more stable ions (*e.g.*,p-NO_2 vs p-Me) toward the internal weaker nucleophile SO_2NH_2, leading preferentially to heterocyclisation compounds.



1

	R_1	R_2	R_3	R_4	R_5
a	H	H	H	H	H
b	H	H	H	F	H
c	H	H	H	Cl	H
d	H	H	H	Br	H
e	H	H	H	NO_2	H
f	H	H	H	Me	H
g	H	H	H	iPr	H
h	H	H	H	NHAc	H
i	H	H	Me	H	Me
j	H	Me	H	Me	Me
k	H	Me	H	OMe	H
l	Me	H	H	NO_2	H



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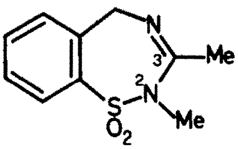

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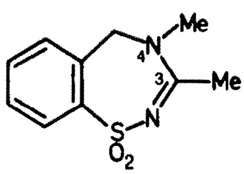
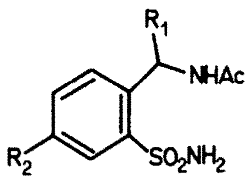
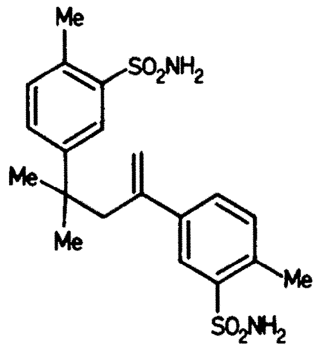


4

Product studies indicated that electro-oxidation of polymethylated benzenesulfonamides (1f,1i and 1j) involve preferential or exclusive functionalisation of the Me group at the *ortho* position to SO_2NH_2. If we assume that anodic oxidation of these compounds produce cation radicals $1^{+\cdot}$ (by removing an electron from HOMO), the observed positional selectivity is likely rationalizable in terms of the degree of lowest occupied MO(LUMO) electron density on the aromatic carbon atom (C-2) adjacent to the Me group relative to that in the other positions of 1^{+} . However, when 1g and 1k were subjected to anodic oxidation in MeCN, a seemingly different result was obtained.For example, 1g did not produce the expected 2g but the dehydrodimer 6 in 45% yield. The electrochemical formation of 6 apparently proceeds through an initial electron transfer yielding the radical-cation $1g^{+\cdot}$ .This then loses a proton in an ensuing rate-determining step to form a radical which undergoes rapidly further oxidation to 7. Under these conditions, the cation intermediate 7 suffers E_1-type deprotonation at the side-chain giving the styrene 8 capable of undergoing electrophilic attack by 7 ultimately leading to 6 (Scheme 2). The ease of side-chain oxidation of i-propyl group *vs* Me is likely explicable either by virtue of the LUMO electron density for $1g^{+\cdot}$ or by stabilisation of tertiary *vs* primary benzylic cations.Preparative electrolysis of 2,6-dimethyl-4-methoxybenzenesulfonamide 1k gave the ring-coupled dimer 9 in 42% yield as the main product. Attack of radical cation $1k^{+\cdot}$ on the starting material 1k rather than dimerisation of two radical cations appears preferred since the yield of 9 increases appreciably (up to 65%) using high concentration (1.5M) of 1k but is not affected by change in current density.



5c	R_1:H	R_2:Cl
5d	R_1:H	R_2:Br
5e	R_1:H	R_2:NO_2
51	R_1:Me	R_2:NO_2



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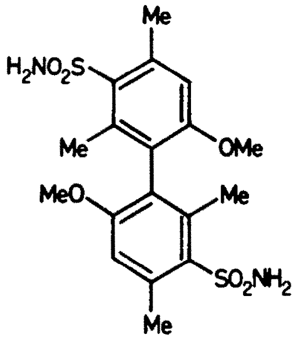

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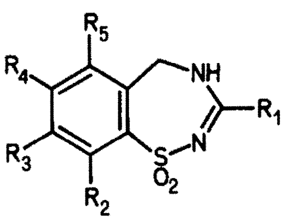
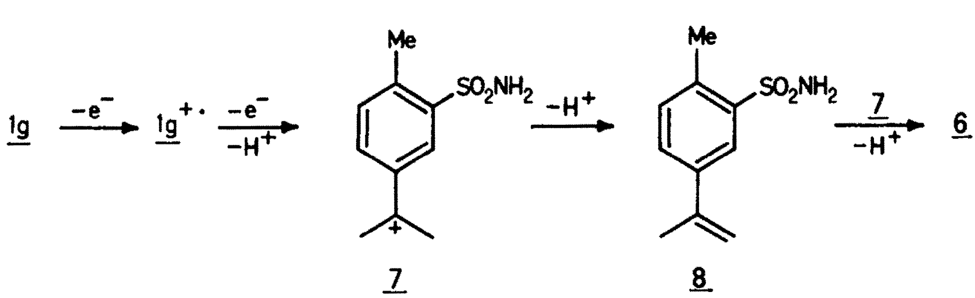


	R_1	R_2	R_3	R_4	R_5
10	Et	H	H	H	H
11	nPr	H	H	H	H
12	nPr	H	H	Cl	H
13	iPr	H	H	H	H
14	iPr	H	H	Cl	H
15	iPr	H	Me	H	Me
16	iPr	Me	H	Me	Me
17	Ph	H	H	H	H

The contrasting behaviour of 1k and 1i(where OMe is replaced by Me) deserves further comment. 1k forms a relatively stable radical cation intermediate $1k^{+\cdot}$ (stabilised by virtue of the electrodonating OMe group) and it has sufficient time to leave the electrode before it loses a proton and therefore coupling can become the main reaction pathway for $1k^{+\cdot}$ .Conversely, $1i^{+}$ undergoes proton loss much more readily, the radical is then further oxidised and the resulting cation displays only carbenium ion behaviour. Furthermore, electro- chemical oxidation required more than 4.2F/mol for the consumption of 1h without any major product being detected (TLC).



SCHEME 2

Finally, the electrochemical generation of a nitrilium ion and its intramolecular trapping provides a mild, selective and straightforward entry to benzothiadiazepine-S,S-dioxide ring system from readily available o-alkylbenzenesulfonamides.

Table. Results of Preparative Electrolysis of o-Alkylbenzenesulfonamides 1a-1 in RCN-1M $LiClO_4$

Compd(mM)	Solvent/RCN	Applied Potential	F/mol	Identified Products(%)
1a(240)	AN	2.0	2.2	2a(87)
1a(180)	PN	2.1	2.2	10(71)
1a(96)	BuN	2.2	3.5	11(59)
1a(100)	MPN	2.2	3.8	13(63)
1a(80)	BzN	2.1	4.0	17(58)
1b(190)	AN	1.8	2.1	2b(65)
1c(240)	AN	1.8	2.1	2c(79),5c(10)
1c(80)	BuN	2.0	3.5	12(65)
1c(80)	MPN	1.5	3.0	14(68)
1d(190)	AN	2.0	2.1	2d(72),5d(8)
1e(190)	AN	2.3	2.2	2e(55),5e(28)
1f(200)	AN	2.2	2.3	2f(61)
1g(200)	AN	1.7	2.8	6(45)
1h(200)	AN	1.6	4.2	d
1i(210)	AN	2.0	2.9	2i(68)
1i(80)	MPN	2.0	3.5	15(55)
1j(180)	AN	1.55	2.9	2j(63)
1j(100)	MPN	1.8	2.8	16(52)
1k(200)	AN	1.5	3.0	9(42)
1l(190)	AN	2.35	2.2	2l(59),5l(25)

[a] Acetonitrile,AN; propionitrile,PN; butyronitrile,BuN; 2-methylpropionitrile,

[b] Oxidation potential *vs* Ag/0.01M $AgNO_3$

[c] Faraday(per mol) consumed by the end of electrolysis when TLC indicated the depletion of the starting material.

[d] Unidentified complex mixture

EXPERIMENTAL SECTION

Melting points are uncorrected and were determined in open-ended capillaries. Infrared spectra were obtained on a Perkin-Elmer 681 spectrophotometer and UV are for solution in MeOH on a Perkin-Elmer 554 UV-VIS spectrophotometer, ^{1}H NMR spectra were recorded on a Bruker WP-80 (80 MHz) in DMSO-d_6 unless otherwise stated. ^{13}C NMR spectra were obtained on a Varian XL-200 (50.4 MHz). Chemical shifts are expressed in parts per million downfield from internal Me_4Si and coupling constants (J values) are given in Hz. Mass spectra (EI and positive FAB) were recorded on a VG 70-70 EQ instrument operating at 70 eV. Flash-chromatography (FC) was carried out as described by Still et al [14] and performed with silica gel S (230-400 mesh).

Materials Sulfonamides 1c[15], 1d[15], 1e[16], 1f[17], 1g[18], 1i[18] and 1j[18] were obtained according to the reported methods In a similar manner we prepared the following new sulfonamides:

2-Methyl-5-fluoro-benzenesulfonamide 1b: 55% yield. ^{1}H NMR: δ 2.51(s,Me-C(2)), 7.51(dd, J=7,2, H-C(6)) Anal. Calcd for $C_7H_8FNO_2S$: C,44.43; H,4.26;N,7.40. Found:C,44.52;H,4.20; N,7.61.

3-Nitro-6-ethyl-benzenesulfonamide 1l: 67% yield.M.p. 191°C(pentane-Et_2O); ^{1}H NMR : δ1.25

(t,J=7,Me-CH_2), 3.12(q,J=7,Me-CH_2),7.67(d,J=8,H-C(5)),7.72(s, SO_2NH_2).Anal.Calcd for $C_9H_{12}N_2O_4S$:C,41.73; H,4.38; N,12.16. Found:C,41.82; H,4.45; N,12.22.

5(Acetamido)-2-methyl-benzenesulfonamide 1h: 58% yield. ^{1}H NMR : δ 2.00(s,MeCO), 2.51 (s,Me-C(2)),7.25(d,J=7.5,H-C(3)), 7.30(br s,SO_2NH_2), 7.57 (dd ,J=7.5,2 ,H-C(4)) ,8.10(d,J=2 ,H-C(6)), 10.10 (br s,NHCO).Anal.Calcd for $C_9H_{12}N_2O_3S$: C,47.35; H,5.30; N,12.27. Found:C,47.41; H,5.33; N,12.28.

General Procedure of Anodic Oxidation. A general procedure is exemplified by the heterocyclization of 5-chloro-2-methyl-benzenesulfonamide 1c. In the anode chamber of a three-compartment cell with Pt electrodes and Ag/Ag+(0.1M) reference is introduced 5-chloro-2-methyl-benzenesulfonamide 1c(6.21 g,30 mmol) in 1M $LiClO_4$ (125 mL). In the cathode compartment is introduced a 1M $LiClO_4$ solution in MeCN (125 mL) containing 70% $HClO_4$(0.5 mL). The solution is magnetically stirred at room temperature and electrolyzed at 1.8V vs Ag/Ag+ (pulsing technique). When 2.1 F per mol of 1c has passed, the electrolysis is interrupted and the anolyte is neutralized with 5% $NaHCO_3$ solution and evaporated to dryness. The crystalline residue is taken up in water (250 mL) and exhaustively extracted with dichloromethane (3 x 100 mL). FC of the evaporated organic layer using EtOAc as eluent gave sequentially 5-chloro-2(acetamido)methyl-benzenesulfonamide 5c (0.84 g, 10%) and 8-chloro-3-methyl -4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide 2c (6.21 g, 79%).

5-Chloro-2(acetamido)methyl-benzenesulfonamide 5c M.p.173^{0}C(EtOAc); Rf0.27 (EtOAc); ^{1}H NMR : δ 1.95(s,MeCO), 4.65(d,J=4,CH_2NH), 7.70(br s,SO_2NH_2), 8.45 (t,J=4,CH_2NH).EI-MS: 262[M$^+$(^{35}Cl),2%], 219(6), 204(22), 202(23), 184(40), 182(100), 181(40), 168(34), 166(43), 141(42), 140(31), 139(48), 138(54). Anal.Calcd for$C_9H_{11}ClN_2O_3S$: C,41.14; H,4.22; N,10.66. Found:C,41.21 ; H,4.34; N,10.58.

8-Chloro-3-methyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide 2c:M.p.186^{0}C (Et_2O- propan-2-ol),Rf(EtOAc): 0.19; IR(nujol): 3310, 1575 cm^{-1}; ^{1}H NMR : δ 2.00(s,Me-C(5)), 4.80(d, J=3.5, CH_2N),7.50(d,J=8,H-C(6)),7.75(dd,J=8,3.5,H-C(7)),7.75(d,J=3.5,H-C(9)), 9.60(t, J=3.5, H-C(4)). EI-MS: 244[M$^+$(^{35}Cl),17%], 199(14), 179(11), 141(48), 140(52), 138(100), 111(28), 102(24), 89(38), 77(45). Anal.Calcd for $C_9H_9ClN_2O_2S$: C,44.14; H,3.67; N,11.44.Found :C,43.99; H, 3.71; N,11.38.

3-Methyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide 2a:M.p.203^{0}C(EtOAc);IR(nujol): 3300, 1575, 1460, 1280, 1130, 1080 cm^{-1}; UV(MeOH) :240 nm; ^{1}H NMR: δ 1.96(s,Me-C(3)), 4.80(d,J=5, H-C(5)),7.82(dd,J=8,1.5, H-C(9)),9.46(br t,J=5,H-N(4)).^{13}C NMR: 161.0(s), 142.1(s), 133.0(d), 131.8(s), 129.0(d), 128.6(d), 125.4(d), 45.4(t), 24.4(q).

8-Fluoro-3-methyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide 2b .Colorless glass, ^{1}H NMR δ 2.00(s,Me-C(3)), 4.78(br s,H-C(5)), 9.58(br s, SO_2NH_2). Anal. Calcd for $C_9H_9FN_2O_2S$: C,47.36; H,3.97; N,12.27. Found: C,47.41; H,4.05; N,12.32.

8-Bromo-3-methyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide 2d.M.p.217^{0}C(EtOAc), ^{1}H NMR δ 2.00(s,Me-C(3)), 7.50(d,J=7,H-C(6)), 7.65(dd,J=7,2,H-C(7)), 7.90(d,J=2,H-C(9)), 9.60(br t,J=4,H-N(4)).Anal.Calcd for $C_9H_9BrN_2O_2S$: C,37.35; H,3.11; N,9.68.Found: C,37.12; H,3.04; N,9.61.

3-Methyl-8-nitro-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide 2e.M.p. 278-80^{0}C; UV(EtOH) :237 nm; ^{1}H NMR : δ 2.12(s,Me-C(3)), 5.00(d,J=4,H-C(5)) ,7.72(d, J=8, H-C(6)), 8.51(dd, J=8,2,H-C(7)), 8.75(d,J=2,H-C(9)), 9.42(br t,J=4,H-N(4)) . Anal.Calcd for $C_9H_9N_3O_4S$: C,42.36; H,3.55; N,16.47.Found: C,42.21; H,3.49; N,16.38.

3,8-Dimethyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide 2f.M.p.167^{0}C (EtOAc); ^{1}H NMR ($CDCl_3$) : δ 2.08(s,Me-C(3)),2.42(s,Me-C(8)), 4.93(d,J=4,H-C(5) 7.28(d,J=8,H-C(6)), 7.41(br d,J=8,H-C(7)), 7.76(br s,H-C(9)), 8.16(br t, J=4, H-N(4)).Anal. Calcd for $C_{10}H_{12}N_2O_2S$: C,53.37; H,5.39; N,12.49.Found: C,53.39; H,5.42; N,12.53.

3,7,9-Trimethyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide 2i.M.p.167^{0}C (EtOAc);^{1}H NMR : δ 1.90(s,Me-C(3)), 2.33(s,Me-C(7)), 2.53(s,Me-C(9)),4.75 (d,J=4, H-C(5)), 7.16(m,H-C(6) and H-C(8)), 9.38(br t,J=4,H-N(4)).Anal. Calcd for $C_{11}H_{14}N_2O_2S$: C,55.46; H,5.92; N,11.76. Found: C,55.39; H,5.88; N,11.71.

3,6,8,9-Tetramethyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide 2j.M.p.213^{0}C(EtOAc); ^{1}H NMR :δ1.90(s,Me-C(3)), 2.25 and 2.37(2 x s,Me-C(6) and Me-C(8)), 2.50(s,Me-C(9)), 4.83 (d,J=4, H-C(5)), 7.30(s,H-C(7)), 9.42(br t,J=4,H-N(4)). Anal. Calcd for $C_{12}H_{16}N_2O_2S$: C,57.13; H,6.39;

N,11.10. Found:C,57.23;H,6.31; N,11.15.

3,5-Dimethyl-8-nitro-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **21**.M.p.280-2°C(EtOAc); ^{1}H NMR δ 1.81(d,J=6,Me-C(5)), 2.10(s,Me-C(3)), 6.03(dq,J=6,4, H-C(5)), 7.82(d,J=8,H-C(6)), 8.58 (dd,J=8,2,H-C(7)), 8.74(d,J=2,H-C(9)), 9.08 br d,J=4,H-N(4)). Anal. Calcd for $C_{10}H_{11}N_3O_4S$: C,44.62; H,4.12; N,15.61. Found :C,44.57; H,4.08; N,15.58.

3-Ethyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **10**.M.p.154°C(EtOAc);^{1}H NMR δ 1.04(t, J=7.5,CH_2Me),2.23(q,J=7.5,CH_2Me), 4.84(d,J=5,H-C(5)), 7.65(dt, J=7.5,1.5, H-C(8)), 7.67(dt, J=7.5,1.5,H-C(6)), 7.79(dt,J=7.5,1.5,H-C(7)),7.88 (dd,J=7.5,1.5,H-C(9)), 9.37(br t,J=5,H-N(4)). Anal Calcd for $C_{10}H_{12}N_2O_2S$: C,53.57 ; H,5.39; N,12.49.Found:C,53.41; H,5.29; N,12.37.

3-(n-Propyl)-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **11**.M.p.172°C (AcOEt); ^{1}H NMR δ 0.73(t,J=7,CH_2Me), 1.51(sext,J=7,CH_2Me), 2.12(t,J=7,H-C(3)) 4.75(d,J=5,H-C(5)), 7.4-7.8(m, H-C(6), H-C(7) and H-C(8)), 8.77(dd,J=8,3, H-C(9)) , 9.30(br t,J=5, H-N(4)).Anal.Calcd for $C_{11}H_{14}N_2O_4S$: C,55.46; H,5.92; N,11.76.Found:C,55.21; H,5.89; N,11.83.

8-Choro-3(n-propyl)-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **12** .M.p.165-8°C(AcOEt);^{1}H NMR:δ 0.80(t,J=7,MeCH_2), 1.51(sext,J=7,CH_2Me), 2.16(t,J=7,H-C(3)), 4.76(br s,H-C(5)), 9.51(br s,H-N(4)),Anal.Calcd for $C_{11}H_{13}ClN_2O_2S$: C,45.75; H,4.54; N,9.70. Found:C,45.69; H,4.59; N,9.61.

3(2-Methylethyl)-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **13**.M.p.181-2°C(EtOAc) ;IR ($CHCl_3$):3420,3300,1575 cm^{-1};^{1}H NMR:δ 1.00(d,J=7,Me_2CH),2.42 (sept, J=7,HCMe_2), 4.78(d, J=5, H-C(5)) , 9.28(br s,H-N(4)). Anal.Calcd for $C_{11}H_{14}N_2O_2S$ C,55.44; H,5.92; N,11.75. Found: C,55.61; H,5.98; N,11.69.

8-Chloro-3(2-methylethyl)-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **14**.M.p.138°C(EtOAc); ^{1}H NMR:δ 1.00(d,J=7,Me_2CH), 2.33(sept,J=7,H-CMe_2), 4.75(d,J=5,H-C(5)), 9.43(br t,J=5, H-N(4)). Anal.Calcd for $C_{11}H_{13}ClN_2O_2S$: C,48.44; H,4.80;N,10.27.Found:C,48.51; H,4.78; N,10.35.

7,9-Dimethyl-3(2-methylethyl)-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **15**.Amorphous glass;^{1}H NMR:δ 1.00(d,J=7,Me_2CH), 2.40(sept,J=7,Me_2CH), 2.31(s,Me-C(7)), 2.53(s,Me-C(9)), 4.70(d,J=5,H-C(5)), 7.11(2 x s,H-C(6) and H-C(8)), 9.20(br t,J=5,H-N(4)). Anal. Calcd for $C_{13}H_{17}N_2O_2S$:C,58.84; H,6.45; N,10.55.Found; C,58.91; H,6.41; N,10.65.

3(2-Methylethyl)-6,8,9-trimethyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **16**. Amorphous glass; ^{1}H NMR:δ 1.00(d,J=7,Me_2CH); 2.25,2.35 and 2.45(3 x s , Me-C(6) ,Me-C(8) and Me-C(9)), 4.85(d,J=7,H-C(5)), 7.31(s,H-C(7)), 9.25(br t,H-N(4)). Anal. Calcd for $C_{14}H_{19}N_2O_2S$:C,60.18; H,6.85; N,10.02. Found:C,60.25 H,6.79; N,9.95.

3-Phenyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **17**.Amorphous glass; ^{1}H NMR ($CDCl_3$):δ 5.08(d,J=5,H-C(2)),7.2-7.5(m,aromatic protons,6H),8.04(dd,J=8,2,H-C(9)),9.00(br d,J=5, H-N(4)). Anal. Calcd for $C_{14}H_{12}N_2O_2S$: C,61.76; H,4.44; N,10.29. Found: C,61.58;H,4.35; N,10.18.

2(Acetamido)methyl-5-bromo-benzenesulfonamide **5d** M.p.183°C(EtOAc); ^{1}H NMR:δ 1.98(s,MeCO), 4.68 (d,J=4.5, CH_2NH_2), 7.70(s,SO_2NH_2), 8.45(t,J=4.5,NHCO) .Anal.Calcd for $C_9H_{11}BrN_2O_3S$: C,35.14; H,3.60; N,9.12.Found:C, 35.20; H,3.65; N,9.21.

2(Acetamido)methyl-5-nitro-benzenesulfonamide **5e**. Amorphous pale yellow foam;^{1}H NMR: δ 2.02(s, MeCO), 4.90(d,J=5,CH_2NH), 7.70(s,SO_2NH_2),7.84 (d,J=7.5,H-C(3)), 8.10(t,J=5,NHCO), 8.38(dd, J=7.5,2,H-C(4)), 8.55(d, J=2,H-C(6)). Anal. Calcd for $C_9H_{11}N_3O_5S$:C, 39.56; H,4.06; N,15.37. Found:C, 39.61; H,4.10; N,15.40.

2(Acetamido)ethyl-5-nitro-benzenesulfonamide **51**. Amorphous pale yellow foam; ^{1}H NMR: δ 1.41 (d,J=7,MeCH), 1.85(s,MeCO), 5.70(dq,J_1≃J_2=7,MeCH), 7.70(br s,SO_2NH_2), 7.85(d,J=7.5,H-C(3)), 8.42(dd,J=7.5,3,H-C(4)), 8.50(d,J=3,H-C(6)), 9.00(br d,J=5,NHCO).Anal. Calcd for $C_{10}H_{13}N_3O_5S$:C, 41.80; H,4.56; N,14.62.Found:C,41.92; H,4.66; N,14.70.

2,3-Dimethyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **3** was prepared according to Fernandez-Tome *et al*[9] as an amorphous colorless glass; Rf0.32 (EtOAc-MeOH,9:1),^{1}H NMR:δ 2.10 (s, Me-C(3)), 3.00(s,Me-N(2)), 5.00 (s,H-C(5)). Anal.Calcd for $C_{10}H_{12}N_2O_2S$: C, 53.55; H,5.39; N,12.49. Found:C,53.65; H,5.43; N,12.51.

3,4-Dimethyl-4,5-dihydro-1,2,4-benzothiadiazepine-1,1-dioxide **4**. To a solution of **2a** (175 mg, 0.83 mmol) in dry DMF (10 mL) was added NaH(60% in oil)(38 mg,0.95 mmol), followed by MeI(60 μL,0.95 mmol).The mixture was stirred for 10 h at room temperature and the excess of NaH was quenched by dropwise addition of water (50 mL). The reaction mixture was then extracted with dichloromethane (3 x 15 mL) and the combined organic phase was dried ($MgSO_4$) and concentrated to give a yellowish foam. TLC(EtOAc-MeOH,9:1) showed the presence of a small amount of starting material 2a in addition to 4(Rf 0.24). Purification by PLC (silica) gave pure 4(127 mg,68%) as a colorless glass; ^{1}H NMR: δ 2.00(s ,Me-C(2) , 3.25(s,Me-N(4)), 5.02(s,H-C(5)). Anal.Calcd for $C_{10}H_{12}N_2O_2S$:C, 53.55; H,5.39; N,12.49. Found:C, 53.59; H,5.50; N,12.52.

Dehydrodimer 6. Amorphous glass; Rf 0.21($CHCl_3$-MeOH,95:5); ^{1}H NMR: δ 1.44(2 x s,Me_2C-aryl), 2.64(s,Me-Ar), 2.70(s,Me-Ar), 2.98(br s,CH_2-C=,2H), 5.13 and 5.24(2 x m,CH_2=), 6.36 and 6.43(2 x s,SO_2NH_2,4H), 7.70 and 7.85(2 x d,J=7, H-*ortho* to SO_2NH_2). Anal. Calcd for $C_9H_{12}NO_3S$:C,50.45; H,5.65; N,6.53. Found:C, 50.40; H,5.71; N,6.50.

Diphenyl compound 9. Amorphous glass;^{1}H NMR: δ 2.61(s,Me-Ar), 2.65(s,Me-Ar) 3.88(s,OMe), 6.98 (s,H-Ar), 7.31(s,SO_2NH_2).Anal. Calcd for $C_{15}H_{12}NO_3S$:C,62.93 ;H,4.19;N,4.89 .Found:C,63.05; H,4.24;N,4.75

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[3]Anodic oxidation of o-toluamide in MeCN/1M $LiClO_4$ using pulsing technique (20 s at 2.2 V/1 s at 0 V) is very clean, producing only 2(acetamido)methylbenzonitrile, m.p. 125°C(AcOEt) in 41% yield.For the sake of comparison,2-methylthiobenzamide was anodically oxidized under similar conditions(20s at 1.2V/1s at 0V) giving a complex mixture of products.These results will be reported in due course

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