Derivatives of 2,3-Dihydroimidazo[1,5,4-*ef*][1,2,5]-benzothiadiazepin-6(4*H*,7*H*)-thione 1,1-Dioxide, a New Heterocyclic System Related to TIBO

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The synthesis of derivatives of 2,3-dihydroimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-thione 1,1-dioxide is reported starting from *N*-substituted ethyl 2-(5-chloro-2-nitrobenzenesulfonamido)-2-alkyl-acetates. Fundamental steps of the synthetic pathway were: i) intramolecular cyclization of *N*-substituted 2-(2-amino-5-chlorobenzenesulfonamido)-2-alkylacetic acids in the presence of *N*-(3-dimethyl-aminopropyl)-*N'*-ethyl carbodiimide hydrochloride-*N*,*N*-dimethylaminopyridine complex; ii) building of imidazole ring from 2-alkyl-8-chloro-2,3-dihydro-3-methyl-1,2,5-benzothiadiazepin-4(5*H*)-one 1,1-dioxide to achieve 2-alkyl-9-chloro-2,3-dihydro-3-methylimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-dioxide; iii) preparation of thiocarbonyl derivative by treatment with Lawesson's reagent. Introduction of a 3-methyl-2-butenyl chain at position 2 of above imidazobenzothiadiazepinone required protection at the 7 position with thermally removable *tert*-butoxycarbonyl moiety, due to the fact that alkylation of unprotected structure proved to be regioselective for the 7 position.

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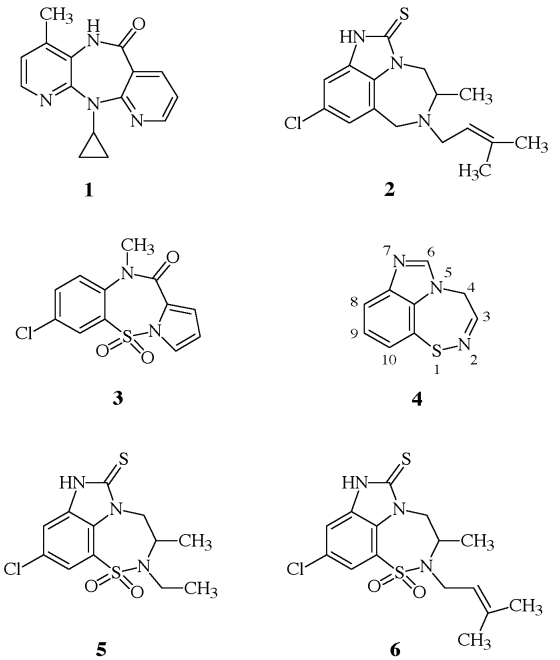
Search for novel tricyclic heteroaromatic ring systems have been deeply pursued after the discovery of potent anti-HIV-1 reverse transcriptase (RT) agents having a diazepine or benzodiazepine moiety annulated with other heterocyclic rings, such as pyridine, imidazole and pyrrole. Nevirapine (Viramune®, **1**) (Chart 1) [1], tetrahydroimidazobenzodiazepinethiones (TIBO) (**2**) [2-5] and pyrrolobenzothiadiazepines (PBTD) (**3**) [6] are derivatives of dipyridodiazepine, imidazo[4,5,1-*jk*]-[1,4]benzodiazepine and pyrrolo[1,2-*c*][1,2,5]-benzothiadiazepine rings, respectively. As a common feature, compounds **1**-**3** assume the "butterfly-like" spatial arrangement [7], a peculiar determinant for the biological activity.

Chart 1



1 **2** **3** **4** **5** **6**

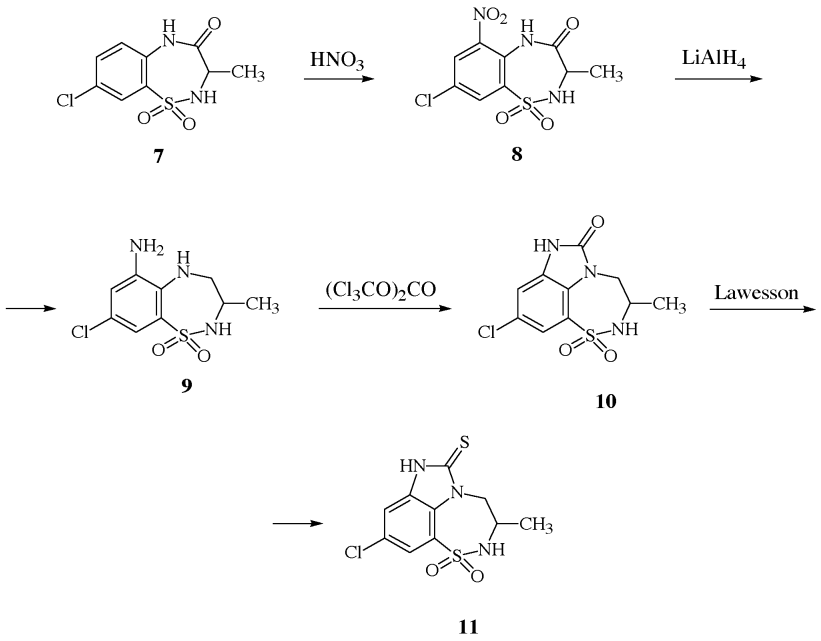
4*H*-Imidazo[1,5,4-*ef*][1,2,5]benzothiadiazepine (**4**), a new tricyclic ring system that shares chemical similarities with both imidazo[4,5,1-*jk*][1,4]benzodiazepine and pyrrolo[1,2-*c*][1,2,5]benzothiadiazepine, is a potential biophore for the design of novel antiretroviral agents useful for AIDS therapy.

Structure-activity relationship (SAR) studies on TIBO derivatives have shown that the presence of alkyl/alkenyl substituents at the position 2 of TIBO is a determinant for their anti-HIV-1 activity. Therefore, introduction of appropriate substituents at position 2 of the new TIBO-like structure **4** is a forced step for the design of new anti-HIV-1 agents. This reason pulsed us to synthesize derivatives **5** and **6** as cyclic sulfone analogues of potent antiretroviral TIBOs.

As a first approach we prepared 9-chloro-2,3-dihydro-3-methylimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-dioxide (**10**), a possible intermediate for achieving **5** and **6** by alkylation of the 2 position with ethyl iodide and 3-methyl-2-butenyl bromide, respectively.

For the synthesis of **10** we used 8-chloro-2,3-dihydro-3-methyl-1,2,5-benzothiadiazepin-4(5*H*)-one 1,1-dioxide (**7**) [8], which was nitrated with concentrated nitric acid to

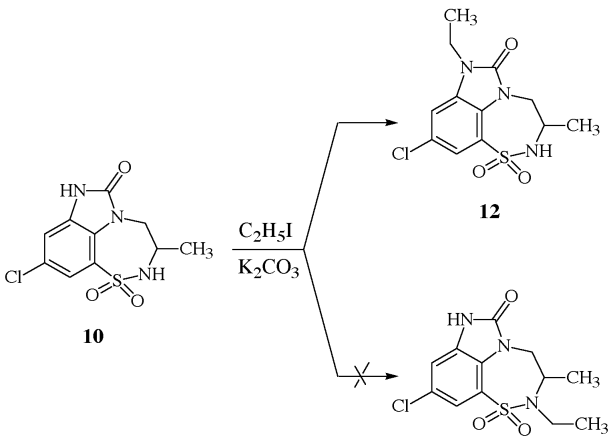
Scheme 1



afford 8-chloro-2,3-dihydro-3-methyl-6-nitro-1,2,5-benzothiadiazepin-4(5*H*)-one 1,1-dioxide (**8**). Reduction of both carbonyl and nitro groups of **8** was accomplished by treatment with lithium aluminum hydride. The diamine **9** which formed underwent cyclization with triphosgene with formation of the required 9-chloro-2,3-dihydro-3-methylimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-dioxide (**10**) (Scheme 1). Treatment of **10** with Lawesson's reagent led to the corresponding thiocarbonyl derivative **11**.

At this point we used compound **10** as an appropriate material for introducing substituents at position 2 by treatment with alkyl/alkenyl halides. However, when **10** was reacted with the equivalent amount of ethyl iodide in the presence of anhydrous potassium carbonate, alkylation occurred selectively at position 7 leaving position 2 unaffected and giving as the sole product derivative **12** (Scheme 2).

Scheme 2



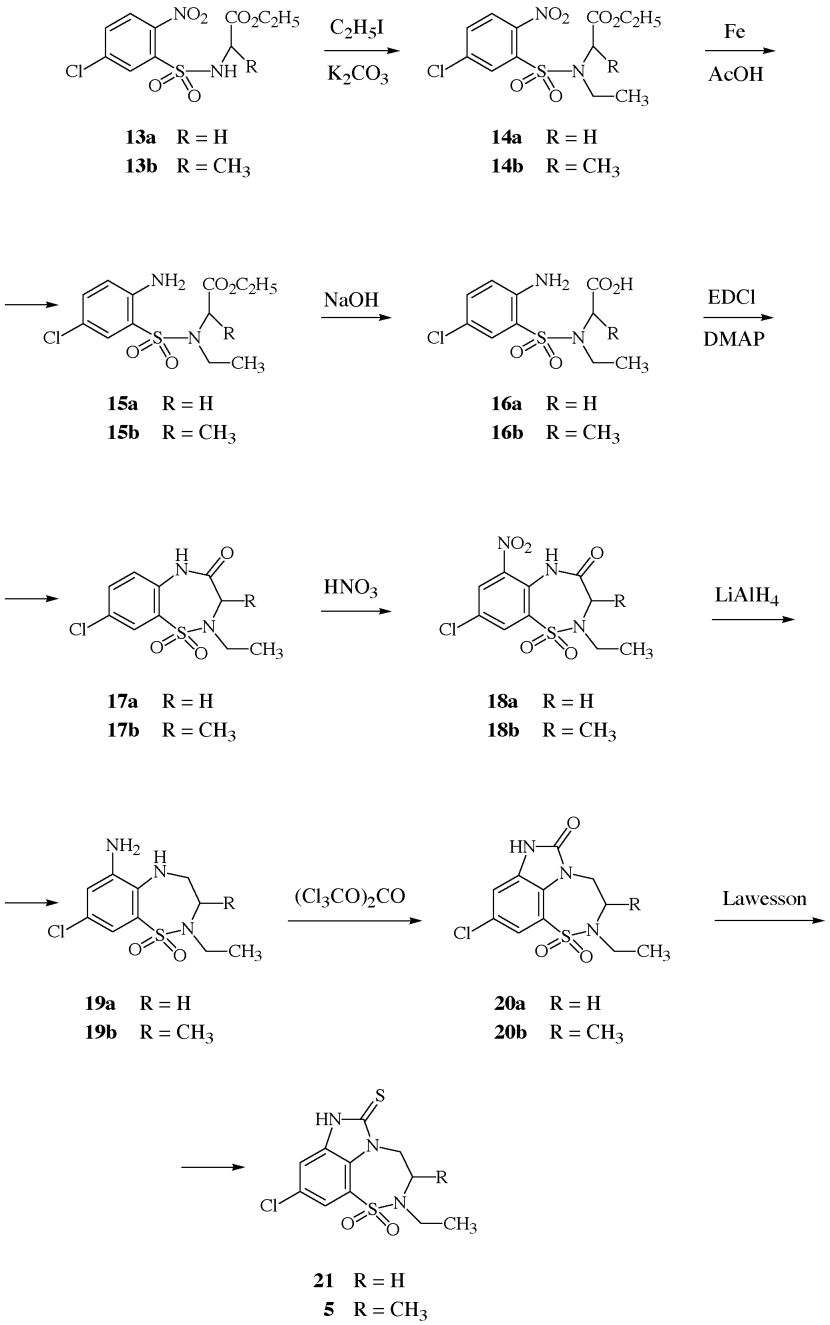
Failure of direct alkylation of **10** pulsed us to synthesize **5** by a different pathway as depicted in Scheme 3.

By this approach alkylation with ethyl iodide was performed before ring closure, thus assuring introduction of alkyl group only at position 2 of the tricyclic ring. As expected, ethylation of ethyl 2-(5-chloro-2-nitrobenzenesulfonamido)-2-propanoate (**13b**) [8] or the related acetate **13a** furnished ethyl 2-(5-chloro-*N*-ethyl-2-nitrobenzenesulfonamido)-2-alkylacetate derivatives **14**, which were reduced with iron powder in glacial acetic acid to amines **15**. Alkaline hydrolysis of the last derivatives afforded acids **16** which underwent intramolecular cyclization catalyzed by *N*-(3-dimethylaminopropyl)-*N'*-ethyl carbodiimide hydrochloride-*N*,*N*-dimethylaminopyridine complex to provide **17**.

Finally, transformation of benzothiadiazepinones **17** into tricyclic derivatives **5** and **21** was performed *via* the corresponding intermediates **18-20**.

Unfortunately, preparation of **6** by this procedure failed the goal (Scheme 4) because nitration of **25**, obtained starting from **13b** through the intermediates **22-24**, did not take place in the same conditions employed for the synthesis of **18**. In fact, only unworkable mixtures were obtained from nitration, probably as a consequence of disruption of the allylic unsaturated side-chain.

Scheme 3



13a R = H
13b R = CH_3

14a R = H
14b R = CH_3

15a R = H
15b R = CH_3

16a R = H
16b R = CH_3

17a R = H
17b R = CH_3

18a R = H
18b R = CH_3

19a R = H
19b R = CH_3

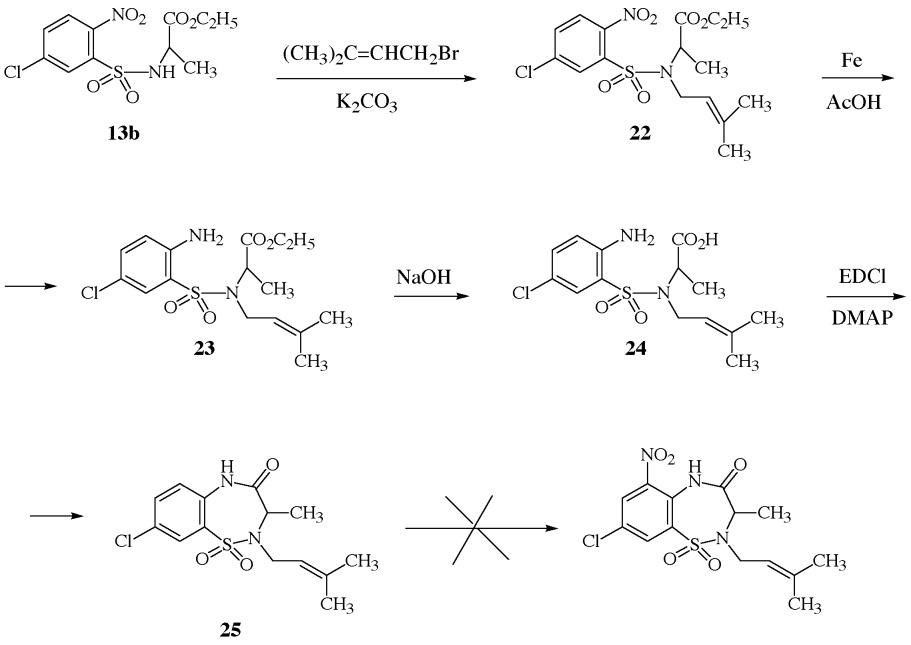
20a R = H
20b R = CH_3

21 R = H
5 R = CH_3

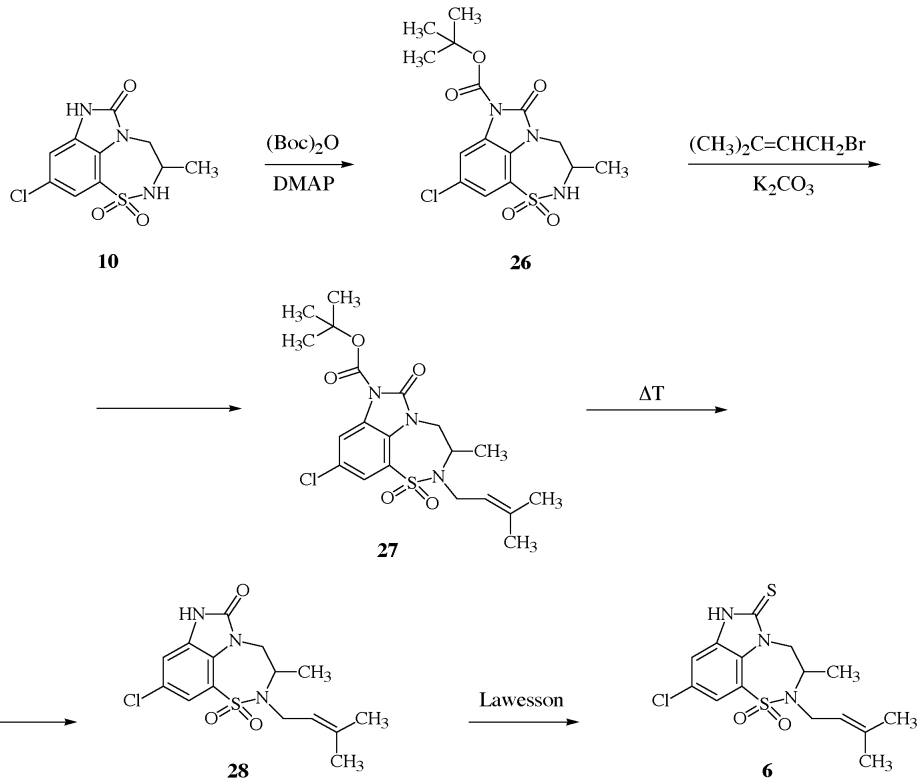
However, we were able to synthesize **6** by a protection/deprotection procedure as depicted in Scheme 5. 9-Chloro-2,3-dihydro-3-methylimidazo-[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-dioxide (**10**) was acylated at position 7 by treatment with di-*tert*-butyldicarbonate in the presence of *N*,*N*-dimethyl-aminopyridine.

7-*Tert*-butyloxycarbonyl-9-chloro-2,3-dihydro-3-methylimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6-(4*H*,7*H*)-one 1,1-dioxide (**26**) which formed was reacted with 3-methyl-2-butenyl bromide to afford 7-*tert*-butyl-oxycarbonyl-9-chloro-2,3-dihydro-3-methyl-2-(3-methyl-2-butenyl)imidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-dioxide (**27**).

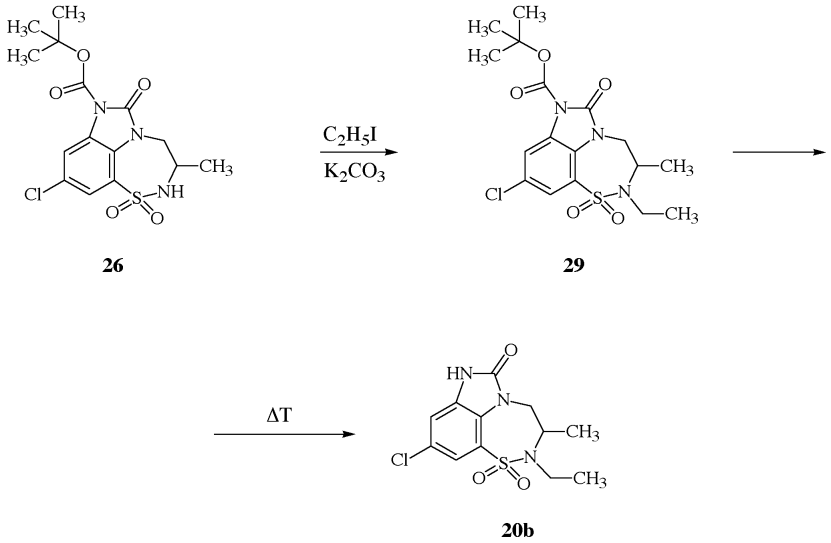
Scheme 4



Scheme 5



Scheme 6



26 **29** **20b**

Thermal decomposition of **27** gave the 7-deacyl derivative **28**, which was then treated with Lawesson's reagent to achieve the desired 9-chloro-2,3-dihydro-3-methyl-2-(3-methyl-2-butenyl)imidazo[1,5,4-*ef*][1,2,5]benzothiadia zepin-6(4*H*,7*H*)-thione 1,1-dioxide (**6**). This procedure was also useful for the synthesis of **5** starting from **26** (Scheme 6). Ethylation of this compound followed by thermal treatment of the intermediate 7-*tert*-butyloxycarbonyl-9-chloro-2,3-dihydro-3-methyl-2-ethylimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-dioxide (**29**) furnished compound **20b**, the precursor of **5**.

In conclusion, we have therein described a profitable procedure for obtaining derivatives of **4**, a novel tricyclic ring system useful as lead structure for the design of novel non-nucleoside reverse transcriptase (NNRT) agents of therapeutic interest. Furthermore, we have also remarked that alkylation of 9-chloro-2,3-dihydro-3-methyl-imidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-dioxide (**10**) with the equivalent amount of alkylating agent gave only 7-substituted derivatives, *e.g.* compound **12**, without formation of the related 2-mono substituted isomers. Similarly, acylation of **10** was regioselective for the 7 position with formation of **26** as the sole product.

EXPERIMENTAL

Melting points were determined on an Electrothermal IA6304 apparatus and are uncorrected. Infrared spectra (nujol mulls) were run on a Perkin Elmer 1310 spectrophotometer. The ^{1}H nmr spectra were recorded with a Bruker AC 200 (200 MHz) using tetramethylsilane as the internal standard. Column chromatography purifications were performed on silica gel Merck (70-230 Mesh). Silica gel/TLC-cards Fluka (silica gel precoated aluminum cards with fluorescent indicator 254 nm) were used for thin layer chromatography. Elemental analyses were performed by Dr. M. Zancato, Dipartimento di Scienze Farmaceutiche, Università degli Studi di Padova, Italy and were found within ± 0.4 of the theoretical values. Organic extracts were dried over anhydrous sodium sulfate. Evaporation of solvents after reactions and extractions involved the use of a rotatory evaporator (Büchi) operating at reduced pressure (approximately 20 bar).

8-Chloro-2,3-dihydro-3-methyl-6-nitro-1,2,5-benzothiadiazepin-4(5*H*)-one 1,1-Dioxide (**8**).

Finely powdered benzothiadiazepine **7** (1.0 g, 3.8 mmol) was carefully added into 90% nitric acid (15 ml) cooled at -10°. After stirring at this temperature for 1 hour, the solution was poured onto crushed ice and the mixture was extracted with ethyl acetate (3 x 50 ml). The organic extracts were collected, washed with brine (3 x 100 ml), saturated solution of sodium hydrogen carbonate (3 x 100 ml) and brine again (3 x 100 ml). The organic solution was then dried and the solvent was evaporated to obtain crude product which was chromatographed on silica gel column (chloroform/ethyl acetate 9:1 as eluent) to obtain 180 mg (15% yield) of **8**, mp 193-194° (from ethanol); ir: ν 3300 and 3150 (NH amide and NH sulfonamide), 1700 (CO) cm^{-1};^{1}H nmr (dimethylsulfoxide-d_6): δ 1.20 (d, 3H, CH_3), 4.95 (q, 1H, CH), 4.50 (s, broad, 1H, SO_2NH), 8.03 and 8.42 (2d, 2H, J_m = 1.8 Hz, benzothiadiazepine C7-H and C9-H), 9.55 (s, broad, 1H, CONH).

Anal. Calcd. for $C_9H_8ClN_3O_5S$: C, 35.36; H, 2.64; Cl, 11.60; N, 13.75; S, 10.49. Found: C, 35.41; H, 2.71; Cl, 11.75; N, 13.84; S, 10.54.

6-Amino-8-chloro-3-methyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine 1,1-Dioxide (**9**).

A solution of **8** (500 mg, 1.6 mmol) in anhydrous tetrahydrofuran (25 ml) was dropped into a well stirred suspension of lithium aluminum hydride (410 mg, 10.7 mmol) in the same solvent (9 ml), cooled at 0°. After stirring at room temperature for 15 minutes, crushed ice was carefully added and the inorganic

precipitate that formed was removed by filtration. The filtrate was evaporated and the residue was extracted with ethyl acetate (3 x 20 ml). The collected organic extracts were washed with brine (3 x 50 ml), dried and the solvent was removed to afford crude diamine **9** (420 mg, 100% yield), which was used for the next reaction without chromatographic purification because of its instability.

9-Chloro-2,3-dihydro-3-methylimidazo[1,5,4-*ef*][1,2,5]-benzothiadiazepin-6(4*H*,7*H*)-one 1,1-Dioxide (**10**).

A well stirred solution of **9** (2.6 g, 9.9 mmol) and triphosgene (3.0 g, 9.9 mmol) in chlorobenzene (50 ml) was heated at 120° for 15 minutes. Then the solvent was removed and the residue was treated with ethyl acetate (100 ml). The organic solution was washed with brine (3 x 100 ml), dried and the solvent was evaporated to afford the crude product which was chromatographed on a silica gel column (ethyl acetate as eluent) to obtain pure **10** (970 mg, 34% yield), mp >300° (from ethanol); ir: ν 3200 (NH imidazolone and NH sulfonamide), 1690 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 1.28 (d, 3H, CH_3), 3.72-4.37 (m, 3H, CH and CH_2), 7.22 (s, 2H, imidazobenzothiadiazepine C8-H and C10-H), 8.38 (d, J = 6.3 Hz, SO_2NH), 11.58 (s, broad, 1H, CONH).

Anal. Calcd. for $C_{10}H_{10}ClN_3O_3S$: C, 41.75; H, 3.50; Cl, 12.32; N, 14.60; S, 11.14. Found: C, 41.68; H, 3.47; Cl, 12.43; N, 14.81; S, 11.21.

9-Chloro-2,3-dihydro-3-methylimidazo[1,5,4-*ef*][1,2,5]-benzothiadiazepin-6(4*H*,7*H*)-thione 1,1-Dioxide (**11**).

A solution of **10** (200 mg, 0.7 mmol) and Lawesson's reagent (240 mg, 0.6 mmol) in anhydrous dioxane (2 ml) was heated at 100° for 10 hours. After cooling, the solvent was evaporated and the residue was chromatographed on a silica gel column (chloroform/ethyl acetate 1:5) to obtain pure **11** (130 mg, 66% yield), mp >270° (from ethanol); ir: ν 3280 (NH sulfonamide), 3080 (NH imidazolethione) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 1.32 (d, 3H, CH_3), 4.11 (m, 1H, CH), 4.45 (dd, 1H, J_{gem} = 14.9 Hz, J_1 = 11.8 Hz, CH_2CH), 5.67 (dd, 1H, J_{gem} = 14.9 Hz, J_2 = 4.5 Hz, CH_2CH), 7.42 (s, 2H, imidazobenzothiadiazepine C8-H and C10-H), 8.50 (d, 1H, J = 6.2 Hz, SO_2NH), 13.45 (s, broad, 1H, CSNH).

Anal. Calcd. for $C_{10}H_{10}ClN_3O_2S_2$: C, 39.54; H, 3.32; Cl, 11.67; N, 13.83; S, 21.11. Found: C, 39.57; H, 3.41; Cl, 11.84; N, 13.78; S, 21.10.

9-Chloro-2,3-dihydro-7-ethyl-3-methylimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-4,6(7*H*)-dione 1,1-Dioxide (**12**).

A mixture of **10** (250 mg, 0.9 mmol), anhydrous potassium carbonate (120 mg, 0.9 mmol) and ethyl iodide (140 mg, 0.9 mmol) in dry *N*,*N*-dimethylformamide (2 ml) was stirred at room temperature for 6 hours. Then water (30 ml) was added and the precipitate that formed was extracted with ethyl acetate (3 x 15 ml). The organic extracts were collected, washed with brine (3 x 30 ml) and dried. Evaporation of the solvent gave pure **12** (250 mg, 91% yield), mp 174-175° (from ethanol); ir: ν 3300 (NH), 1690 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.04 (t, 3H, CH_2CH_3), 1.31 (d, 3H, $CHCH_3$), 3.27 (q, 2H, CH_2CH_3), 3.83-4.00 (m, 3H, CH and CH_2CH), 7.22 (s, 2H, imidazobenzothiadiazepine C8-H and C10-H), 8.38 (d, 1H, J = 6.3 Hz, SO_2NH).

Anal. Calcd. for $C_{12}H_{14}ClN_3O_3S$: C, 45.64; H, 4.47; Cl, 11.23; N, 13.31; S, 10.15. Found: C, 45.70; H, 4.46; Cl, 11.20; N, 13.43; S, 10.21.

Ethyl 2-(5-Chloro-2-nitrobenzenesulfonamido)acetate (**13a**).

A solution of 5-chloro-2-nitrobenzenesulfonyl chloride (35 g, 0.136 mol) in dichloromethane (150 ml) was dropped into a well stirred solution of glycine ethyl ester hydrochloride (19.1 g, 0.136 mol) and triethylamine (27.7 g, 38.1 ml, 0.279 mol) in the same solvent (200 ml). After 2.5 hours water was added (300 ml) and the mixture was extracted with chloroform (3 x 200 ml). The organic extracts were collected, washed with brine (3 x 500 ml), dried and the solvent was evaporated. The crude product was chromatographed on silica gel column to obtain pure **13a** (43.9 g 100% yield), mp 109-110° (from benzene/cyclohexane); ir: ν 3300 (NH), 1730 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.19 (t, 3H, CH_3), 4.03-4.14 (m, 4H, CH_2COOC$_2H_5$ and OCH_2CH$_3$), 6.13 (s, broad, 1H, NH), 7.69 (dd, 1H, J_o = 8.5 Hz, J_m = 2.3 Hz, benzene C4-H), 7.93 (d, 1H, J_o = 8.5 Hz, benzene C3-H), 8.07 (d, 1H, J_m = 2.3 Hz, benzene C6-H).

Anal. Calcd. for $C_{10}H_{11}ClN_2O_6S$: C, 37.22; H, 3.44; Cl, 10.99; N, 8.68; S, 9.93. Found: C, 37.11; H, 3.41; Cl, 11.07; N, 8.70; S, 9.91.

Ethyl 2-(5-Chloro-*N*-ethyl-2-nitrobenzenesulfonamido)acetate (**14a**).

A mixture of **13a** (25.7 g, 80 mmol), anhydrous potassium carbonate (11 g, 80 mmol) and ethyl iodide (14.9 g, 96 mmol) in dry *N*,*N*-dimethylformamide (110 ml) was stirred at room temperature for 15 hours. Then water (300 ml) was added and the oily precipitate was extracted with ethyl acetate (3 x 150 ml). The organic extracts were collected, washed with brine (3 x 300 ml) and dried. Evaporation of the solvent gave pure **14a** (28 g, 100% yield), mp 39-41° (from benzene/cyclohexane); ir: ν 1730 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.16-1.26 (m, 6H, CH_3), 3.48 (m, 2H, NCH_2CH$_3$), 4.08-4.18 (m, 4H, CH_2COOC$_2H_5$ and OCH_2CH$_3$), 7.61 (m, 2H, benzene C3-H and C4-H), 8.08 (d, 1H, J_m = 2.0 Hz, benzene C6-H).

Anal. Calcd. for $C_{12}H_{15}ClN_2O_6S$: C, 41.09; H, 4.31; Cl, 10.11; N, 7.99; S, 9.14. Found: C, 41.15; H, 4.37; Cl, 10.03; N, 8.06; S, 9.20.

Ethyl 2-(2-Nitro-5-chloro-*N*-ethylbenzenesulfonamido)-propanoate (**14b**).

Derivative **14b** was obtained as reported for **14a**; evaporation of the solvent of organic extracts gave pure **14b** (90% yield) as a yellow oil; ir: ν 1720 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.17 and 1.26 (2t, 6H, CH_2CH_3), 1.55 (d, 3H, $CHCH_3$), 3.26 and 3.54 (2m, 2H, NCH_2CH$_3$), 4.08 (m, 2H, OCH_2CH$_3$), 4.75 (q, 1H, CH), 7.57 (d, 1H, J_o = 8.5 Hz, benzene C3-H), 7.64 (dd, 1H, J_o = 8.5 Hz, J_m = 2.0 Hz, benzene C4-H), 8.06 (d, 1H, J_m = 2.0 Hz, benzene C6-H).

Anal. Calcd. for $C_{13}H_{17}ClN_2O_6S$: C, 42.80; H, 4.70; Cl, 9.72; N, 7.68; S, 8.79. Found: C, 42.85; H, 4.70; Cl, 9.59; N, 7.71; S, 8.84.

Ethyl 2-(2-Amino-5-chloro-*N*-ethylbenzenesulfonamido)acetate (**15a**).

A well stirred solution of **14a** (29.7 g, 85 mmol) in glacial acetic acid (500 ml) was heated at 60°, then iron powder (37.8 g, 0.67 mol) was added portionwise over 1 hour. After evaporation of the solvent, the residue was treated with crushed ice and ethyl

acetate (3 x 200 ml) and the upper phases were separated. The organic extracts were collected, washed with brine (3 x 300 ml) and dried. Removal of the solvent provided pure **15a** (23.7 g, 87% yield), mp 78-80° (from benzene/cyclohexane); ir: ν 3440 and 3320 (NH_2), 1720 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.13 and 1.23 (2t, 6H, CH_3), 3.35 (q, 2H, NCH_2CH_3), 4.07 (s, 2H, $CH_2COOC_2H_5$), 4.13 (q, 2H, OCH_2CH_3), 5.06 (s, broad, 2H, NH_2), 6.65 (d, 1H, J_o = 8.7 Hz, benzene C3-H), 7.23 (dd, 1H, J_o = 8.7 Hz, J_m = 2.7 Hz, benzene C4-H), 7.66 (d, 1H, J_m = 2.7 Hz, benzene C6-H).

Anal. Calcd. for $C_{12}H_{17}ClN_2O_4S$: C, 44.93; H, 5.34; Cl, 11.05; N, 8.73; S, 9.99. Found: C, 44.98; H, 5.20; Cl, 11.00; N, 8.65; S, 9.87.

Ethyl 2-(2-Amino-5-chloro-*N*-ethylbenzenesulfonamido)-propanoate (**15b**).

Obtained as reported for **15a**. Compound **15b** was obtained in 82% yield, mp 114-115° (from benzene/cyclohexane); ir : ν 3440 and 3330 (NH_2), 1710 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.14-1.25 (m, 6H, CH_2CH_3), 1.48 (d, 3H, $CHCH_3$), 3.23 and 3.38 (2m, 2H, NCH_2CH_3), 4.05 (m, 2H, OCH_2CH_3), 4.64 (q, 1H, CH), 5.06, (s, broad, 2H, NH_2), 6.63 (d, 1H, J_o = 8.6 Hz, benzene C3-H), 7.21 (dd, 1H, J_o = 8.6 Hz, J_m = 2.6 Hz, benzene C4-H), 7.63 (d, 1H, J_m = 2.6 Hz, benzene C6-H).

Anal. Calcd. for $C_{13}H_{19}ClN_2O_4S$: C, 46.64; H, 5.72; Cl, 10.59; N, 8.37; S, 9.58. Found: C, 46.61; H, 5.84; Cl, 10.68; N, 8.23; S, 9.55.

2-(2-Amino-5-chloro-*N*-ethylbenzenesulfonamido)acetic Acid (**16a**).

A solution of **15a** (26.9 g, 83 mmol) in ethanol/tetrahydrofuran 1:1 (400 ml) was treated with 1 *N* sodium hydroxide (160 ml) and stirred at room temperature for 2.5 hours. After evaporation of the solvent the residue was treated with a saturated solution of sodium hydrogen carbonate and the mixture extracted with ethyl acetate (200 ml). Organic extract was discarded and the alkaline solution was made acid with 1 *N* hydrochloric acid until pH 4 and then extracted with ethyl acetate (3 x 200 ml). The organic extracts were collected, washed with brine (6 x 300 ml) and dried. Evaporation of the solvent afforded pure **16a** (21.1 g, 87% yield), mp 145-148° (from toluene); ir: ν 3440 and 3340 (NH_2), 2900 (OH), 1710 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 0.99 (t, 3H, CH_3), 3.20 (q, 2H, CH_2CH_3), 4.03 (s, 2H, CH_2COOH), 6.20 (s, broad, 2H, NH_2), 6.86 (d, 1H, J_o = 8.7 Hz, benzene C3-H), 7.31 (dd, 1H, J_o = 8.7 Hz, J_m = 2.5 Hz, benzene C4-H), 7.48 (d, 1H, J_m = 2.5 Hz, benzene C6-H), 12.77 (s, broad, 1H, OH).

Anal. Calcd. for $C_{10}H_{13}ClN_2O_4S$: C, 41.03; H, 4.48; Cl, 12.11; N, 9.57; S, 10.95. Found: C, 40.89; H, 4.45; Cl, 12.10; N, 9.61; S, 10.84.

2-(2-Amino-5-chloro-*N*-ethylbenzenesulfonamido)propanoic Acid (**16b**).

Derivative **16b** was synthesized as reported for **16a**. **16b** (15.9 g, 100% yield), mp 117-119° (from benzene); ir: ν 3460 and 3340 (NH_2), 2900 (OH), 1700 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 1.06 (t, 3H, CH_2CH_3), 1.35 (d, 3H, $CHCH_3$), 3.20 (m, 2H, CH_2CH_3), 4.53 (q, 1H, CH), 6.19 (s, broad, 2H, NH_2), 6.85 (d, 1H, J_o = 8.8 Hz, benzene C3-H), 7.30 (dd, 1H, J_o = 8.8 Hz, J_m = 2.4 Hz, benzene C4-H), 7.47 (d, 1H, J_m = 2.4 Hz, benzene C6-H), 12.60 (s, broad, 1H, OH).

Anal. Calcd. for $C_{11}H_{15}ClN_2O_4S$: C, 43.07; H, 4.93; Cl, 11.56; N, 9.13; S, 10.45. Found: C, 43.00; H, 4.90; Cl, 11.67; N, 9.15; S, 10.39.

8-Chloro-2,3-dihydro-2-ethyl-1,2,5-benzothiadiazepin-4(5*H*)-one 1,1-Dioxide (**17a**).

A solution of **16a** (19.4 g, 66 mmol) in dichloromethane (640 ml) was treated with *N*-(3-dimethylaminopropyl)-*N'*-ethyl carbodiimide hydrochloride (12.6 g, 66 mmol) and *N*,*N*-dimethylaminopyridine (8.1 g, 66 mmol). After stirring at room temperature for 15 hours, water was added (500 ml) and the mixture was extracted with ethyl acetate (3 x 300 ml). The organic extracts were collected, washed with brine (3 x 300 ml), 1 *N* hydrochloric acid (3 x 300 ml), saturated solution of sodium hydrogen carbonate (3 x 300 ml), with brine again (3 x 300 ml) and then dried. Removal of the solvent furnished pure **17a** (14.9 g, 82% yield), mp 193-195° (from ethanol); ir: ν 3200 (NH), 1670 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.21 (t, 3H, CH_3), 3.18 (q, 2H, CH_2CH_3), 4.39 (s, 2H, CH_2CO), 7.13 (d, 1H, J_o = 8.7 Hz, benzothiadiazepine C6-H), 7.46 (dd, 1H, J_o = 8.7 Hz, J_m = 2.4 Hz, benzothiadiazepine C7-H), 7.91 (d, 1H, J_m = 2.4 Hz, benzothiadiazepine C9-H), 9.53 (s, broad, 1H, NH).

Anal. Calcd. for $C_{10}H_{11}ClN_2O_3S$: C, 43.72; H, 4.04; Cl, 12.91; N, 10.20; S, 11.67. Found: C, 43.58; H, 4.02; Cl, 12.86; N, 10.11; S, 11.59.

8-Chloro-2,3-dihydro-2-ethyl-3-methyl-1,2,5-benzothiadiazepin-4(5*H*)-one 1,1-Dioxide (**17b**).

Derivative **17b** was synthesized with the same procedure reported for **17a**. **17b** (12.7 g, 87% yield), mp 212-214° (from benzene); ir: ν 3190 (NH), 1660 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.25 (t, 3H, CH_2CH_3), 1.65 (d, 3H, $CHCH_3$), 3.09-3.33 (m, 2H, CH_2), 4.56 (q, 1H, CH), 7.05 (d, 1H, J_o = 8.8 Hz, benzothiadiazepine C6-H), 7.45 (dd, 1H, J_o = 8.8 Hz, J_m = 2.4 Hz, benzothiadiazepine C7-H), 7.90 (d, 1H, J_m = 2.4 Hz, benzothiadiazepine C9-H), 9.01 (s, broad, 1H, NH).

Anal. Calcd. for $C_{11}H_{13}ClN_2O_3S$: C, 45.76; H, 4.54; Cl, 12.28; N, 9.70; S, 11.10. Found: C, 45.78; H, 4.61; Cl, 12.35; N, 9.67; S, 11.20.

8-Chloro-2,3-dihydro-2-ethyl-6-nitro-1,2,5-benzothiadiazepin-4(5*H*)-one 1,1-Dioxide (**18a**).

Synthesized as reported for **8**. Pure **18a** was obtained without chromatography (82% yield), mp 143-145° (the compound was not recrystallized because of its decomposition when heated in benzene/cyclohexane); ir: ν 3340 (NH), 1670 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.22 (t, 3H, CH_3), 3.22 (q, 2H, CH_2CH_3), 4.31 (s, 2H, CH_2CO), 8.23 and 8.38 (2d, 2H, J_m = 2.4 Hz, benzothiadiazepine C7-H and C9-H), 10.60 (s, broad, 1H, NH).

Anal. Calcd. for $C_{10}H_{10}ClN_3O_5S$: C, 37.57; H, 3.15; Cl, 11.09; N, 13.14; S, 10.03. Found: C, 37.60; H, 3.10; Cl, 11.01; N, 13.15; S, 10.09.

8-Chloro-2,3-dihydro-2-ethyl-3-methyl-6-nitro-1,2,5-benzothiadiazepin-4(5*H*)-one 1,1-Dioxide (**18b**).

Prepared as already shown for **18a**. **18b** (95% yield), mp 203-205° (from benzene); ir: ν 3280 (NH), 1670 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 1.05 (t, 3H, CH_2CH_3), 1.40 (d, 3H, $CHCH_3$), 3.20 (m, 2H, CH_2), 4.27 (q, 1H, CH), 8.08 and 8.45 (2d, 2H, J_m = 2.3 Hz, benzothiadiazepine C7-H and C9-H), 10.33 (s, broad, 1H, NH).

Anal. Calcd. for $C_{11}H_{12}ClN_3O_5S$: C, 39.59; H, 3.62; Cl, 10.62; N, 12.59; S, 9.61. Found: C, 39.66; H, 3.51; Cl, 10.54; N, 12.66; S, 9.60.

6-Amino-8-chloro-2-ethyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine 1,1-Dioxide (**19a**).

Title derivative was prepared as already reported for **9**; reaction time 45 minutes; chromatographic system: silica gel column (chloroform/ethyl acetate 1:1 as eluent). **19a** (39% yield), unstable in presence of the air; ir: ν 3350 (NH and NH_2) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.10 (t, 3H, CH_3), 2.95 (q, 2H, CH_2CH_3), 3.08 (m, 2H, $CH_2CH_2NSO_2$), 3.48 (m, 2H, $CH_2CH_2NSO_2$), 3.75 (s, broad, 3H, NH and NH_2), 6.75 (d, 1H, J_m = 2.3 Hz, benzothiadiazepine C7-H), 7.12 (d, 1H, J_m = 2.3 Hz, benzothiadiazepine C9-H).

6-Amino-8-chloro-2-ethyl-3-methyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine 1,1-Dioxide (**19b**).

Synthesized as above depicted for **19a**. **19b** (22% yield), unstable in presence of the air, mp 130° dec.; ir: ν 3370 (NH and NH_2) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 1.08 (t, 3H, CH_2CH_3), 1.22 (d, 3H, $CHCH_3$), 3.08 (m, 2H, CH_2CH_3), 3.20-3.72 (m, 3H, CH and $CHCH_2$), 5.35 and 5.48 (2s, broad, 3H, NH and NH_2), 6.72 and 6.78 (2d, 2H, J_m = 2.1 Hz, benzothiadiazepine C7-H and C9-H).

9-Chloro-2,3-dihydro-2-ethyl-imidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-Dioxide (**20a**).

Compound **20a** was obtained as shown for **10**; reaction time 5 minutes; chromatographic system: silica gel column (chloroform/ethyl acetate 1:1 as eluent). **20a** (52% yield), mp 235-237° (from ethanol); ir: ν 2900 (NH), 1690 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 1.10 (t, 3H, CH_3), 3.23 (q, 2H, CH_2CH_3), 3.83 and 4.10 (2m, 4H, CH_2CH_2), 7.23 (s, 2H, imidazobenzothiadiazepine C8-H and C10-H), 11.62 (s, broad, 1H, NH).

Anal. Calcd. for $C_{11}H_{12}ClN_3O_3S$: C, 43.79; H, 4.01; Cl, 11.75; N, 13.93; S, 10.62. Found: C, 43.84; H, 3.85; Cl, 11.83; N, 13.90; S, 10.70.

9-Chloro-2,3-dihydro-2-ethyl-3-methylimidazo[1,5,4-*ef*]-[1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-Dioxide (**20b**).

Method A.

Synthesized as reported for **20a** (56% yield).

Method B.

Derivative **29** (50 mg; 0.12 mmol) was heated neat at 185° for 5 minutes until the gas evolution stopped. After this time the product was stirred at the same temperature for 10 minutes more, then was cooled and chromatographed on silica gel column (chloroform as eluent) to afford pure **20b** (38 mg, 100% yield). **20b**, mp 215-216° (from ethanol); ir: ν 3100 (NH), 1710 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 0.94 (t, 3H, CH_2CH_3), 1.36 (d, 3H, $CHCH_3$), 3.13 (m, 2H, CH_2CH_3), 3.96-4.36 (m, 3H, CH and $CHCH_2$), 7.20 and 7.22 (2d, 2H, J_m = 1.8 Hz, imidazobenzothiadiazepine C8-H and C10-H), 11.62 (s, broad, 1H, NH).

Anal. Calcd. for $C_{12}H_{14}ClN_3O_3S$: C, 45.64; H, 4.47; Cl, 11.23; N, 13.31; S, 10.15. Found: C, 45.51; H, 4.53; Cl, 11.41; N, 13.20; S, 10.16.

9-Chloro-2,3-dihydro-2-ethylimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-thione 1,1-Dioxide (**21**).

Thioderivative **21** was prepared as already reported for **11**. Reaction time 22 hours; chromatographic system: silica gel column (chloroform/ethyl acetate 9:1 as eluent). **21** (93% yield), mp 252-254° (from ethanol); ir: ν 3100 (NH) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 1.08 (t, 3H, CH_3), 3.25 (q, 2H, CH_2CH_3), 3.89 and 4.60 (2m, 4H, CH_2CH_2), 7.42 (s, 2H, imidazobenzothiadiazepine C8-H and C10-H), 13.48 (s, broad, 1H, NH).

Anal. Calcd. for $C_{11}H_{12}ClN_3O_2S_2$: C, 41.57; H, 3.81; Cl, 11.16; N, 13.22; S, 20.18. Found: C, 41.71; H, 3.80; Cl, 11.15; N, 13.40; S, 20.10.

9-Chloro-2,3-dihydro-2-ethyl-3-methylimidazo[1,5,4-*ef*]-[1,2,5]benzothiadiazepin-6(4*H*,7*H*)-thione 1,1-Dioxide (**5**).

Synthesized as shown for **21**; reaction time 10 hours. **5** (29% yield), mp 230-232° (from ethanol); ir: ν 3080 (NH) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 0.89 (t, 3H, CH_2CH_3), 1.41 (d, 3H, $CHCH_3$), 3.14 (m, 2H, CH_2CH_3), 4.01 (m, 1H, CH), 4.42 (dd, 1H, J_{gem} = 14.8 Hz, J_1 = 11.9 Hz, $CHCH_2$), 5.05 (dd, 1H, J_{gem} = 14.8 Hz, J_2 = 4.6 Hz, $CHCH_2$), 7.39 (s, 2H, imidazobenzothiadiazepine C8-H and C10-H), 13.45 (s, broad, 1H, NH).

Anal. Calcd. for $C_{12}H_{14}ClN_3O_2S_2$: C, 43.43; H, 4.25; Cl, 10.68; N, 12.66; S, 19.32. Found: C, 43.56; H, 4.14; Cl, 10.70; N, 12.71; S, 19.25.

Ethyl 2-[5-Chloro-*N*-(3-methyl-2-butenyl)-2-nitrobenzenesulfonamido]propanoate (**22**).

A mixture of ethyl 2-(5-chloro-2-nitrobenzenesulfonamido)propanoate (11.5 g, 34 mmol) (**13b**), anhydrous potassium carbonate (4.7 g, 34 mmol) and 3-methyl-2-butenyl bromide (7.1 g, 48 mmol) in dry *N*,*N*-dimethylformamide (50 ml) was stirred at 70° for 4 hours. Then water was added (200 ml) and the precipitate that formed was extracted with ethyl acetate (3 x 150 ml). The organic extracts were collected, washed with brine (3 x 200 ml) and dried. Evaporation of the solvent gave pure **22** (13.6 g, 99% yield), mp 55-56° (from cyclohexane); ir: ν 1730 (CO) cm^{-1}; ^1H nmr (deutrochloroform): δ 1.23 (t, 3H, CH_2CH_3), 1.48 (d, 3H, $CHCH_3$), 1.61 and 1.67 (2s, 6H, =C-CH_3), 3.85 (m, 1H, NCH_2), 4.04-4.20 (m, 3H, NCH_2 and CH_2CH_3), 4.80 (q, 1H, $CHCH_3$), 5.07 (m, 1H, =CH-), 7.61 and 8.04 (2m, 3H, benzene H).

Anal. Calcd. for $C_{16}H_{21}ClN_2O_6S$: C, 47.47; H, 5.23; Cl, 8.76; N, 6.92; S, 7.92. Found: C, 47.56; H, 5.20; Cl, 8.66; N, 6.98; S, 7.89.

Ethyl 2-[2-Amino-5-chloro-*N*-(3-methyl-2-butenyl)benzenesulfonamido]propanoate (**23**).

Amine **23** was obtained as reported for **15a**: reaction time 5 hours, 88% yield. **23**, mp 78-79° (from benzene/cyclohexane); ir: ν 3460 and 3360 (NH_2), 1730 (CO) cm^{-1}; ^1H nmr (deutrochloroform): δ 1.21 (t, 3H, CH_2CH_3), 1.48 (d, 3H, $CHCH_3$), 1.54 and 1.61 (2s, 6H, =C-CH_3), 3.81 (m, 2H, NCH_2), 4.07 (q, 2H, CH_2CH_3), 4.63 (q, 1H, $CHCH_3$), 5.09 (m, 3H, =CH- and NH_2), 6.64 (d, 1H, J_o = 8.6 Hz, benzene C3-H), 7.21 (dd, 1H, J_o = 8.6 Hz, J_m = 2.4 Hz, benzene C4-H), 7.65 (d, 1H, J_m = 2.4 Hz, benzene C6-H).

Anal. Calcd. for $C_{16}H_{23}ClN_2O_4S$: C, 51.26; H, 6.18; Cl, 9.46; N, 7.47; S, 8.55. Found: C, 51.11; H, 6.24; Cl, 9.41; N, 7.53; S, 8.55.

2-[2-Amino-5-chloro-*N*-(3-methyl-2-butenyl)benzenesulfonamido]propanoic Acid (**24**).

Title compound was prepared as reported for **16a**; reaction time was 15 hours (100% yield). **24**, mp 115-116° (from benzene); ir: ν 3460 and 3360 (NH_2), 2950 (OH), 1720 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.40-1.65 (m, 9H, CH_3), 3.78 (m, 2H, CH_2), 4.65 (q, 1H, C*H*CH_3), 4.98 (m, 1H, =CH-), 6.50-6.80 (m, 3H, benzene C3-H and NH_2), 7.20 (dd, 1H, J_o = 8.5 Hz, J_m = 2.0 Hz, benzene C4-H), 7.60 (d, 1H, J_m = 2.0 Hz, benzene C6-H), 12.50 (s, broad, 1H, OH).

Anal. Calcd. for $C_{14}H_{19}ClN_2O_4S$: C, 48.48; H, 5.52; Cl, 10.22; N, 8.08; S, 9.24. Found: C, 48.49; H, 5.60; Cl, 10.15; N, 8.02; S, 9.21.

8-Chloro-2,3-dihydro-3-methyl-2-(3-methyl-2-butenyl)-1,2,5-benzothiadiazepin-4(5*H*)-one 1,1-Dioxide (**25**).

Obtained as reported for **17a**: reaction time 5 hours (72% yield). **25**, mp 157-158° (from benzene); ir: ν 3200 (NH), 1660 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.57-1.66 (m, 9H, CH_3), 3.79 (m, 2H, CH_2), 4.42 (q, 1H, C*H*CH_3), 5.03 (m, 1H, =CH-), 7.07 (d, 1H, J_o = 8.7 Hz, benzothiadiazepine C6-H), 7.44 (dd, 1H, J_o = 8.7 Hz, J_m = 2.4 Hz, benzothiadiazepine C7-H), 7.85 (d, 1H, J_m = 2.4 Hz, benzothiadiazepine C9-H), 9.21 (s, broad, 1H, NH).

Anal. Calcd. for $C_{14}H_{17}ClN_2O_3S$: C, 51.14; H, 5.21; Cl, 10.78; N, 8.52; S, 9.75. Found: C, 51.11; H, 5.27; Cl, 10.84; N, 8.60; S, 9.67.

7-*tert*-Butoxycarbonyl-9-chloro-2,3-dihydro-3-methylimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-Dioxide (**26**).

A solution of di-*tert*-butyldicarbonate (150 mg, 0.7 mmol) and *N*,*N*-dimethylaminopyridine (90 mg, 0.7 mmol) in anhydrous tetrahydrofuran (5 ml) was slowly dropped into a well stirred suspension of **10** (200 mg, 0.7 mmol) in the same solvent (5 ml). After stirring for 15 minutes at room temperature, the mixture was treated with 1 *N* hydrochloric acid (30 ml) and the precipitate which formed was extracted with ethyl acetate (3 x 30 ml). The collected organic extracts were washed with brine (6 x 50 ml) and dried. Evaporation of the solvent gave crude product which was then chromatographed on silica gel column (chloroform as eluent) to afford pure **26** (240 mg, 88% yield), mp > 300° (from ethanol); ir: ν 3280 (NH), 1800 (CO butoxycarbonyl), 1710 (CO imidazolone) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.47 (d, 3H, J = 6.6 Hz, CHC*H*$_3$), 1.71 (s, 9H, CCH_3), 4.04 (m, 1H, CH), 4.30 (dd, 1H, J_1 = 7.1 Hz, J_{gem} = 14.9 Hz, CH_2), 4.63 (dd, 1H, J_2 = 3.9 Hz, J_{gem} = 14.9 Hz, CH_2), 5.46 (d, 1H, J_3 = 4.5 Hz, NH), 7.50 and 7.98 (2d, 2H, J_m = 1.9 Hz, imidazobenzothiadiazepine C8-H and C10-H).

Anal. Calcd. for $C_{15}H_{18}ClN_3O_5S$: C, 46.45; H, 4.68; Cl, 9.14; N, 10.83; S, 8.27. Found: C, 46.40; H, 4.75; Cl, 9.14; N, 10.91; S, 8.41.

7-*tert*-Butoxycarbonyl-9-chloro-2,3-dihydro-3-methyl-2-(3-methyl-2-butenyl)imidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-Dioxide (**27**).

Compound **27** was obtained with a procedure similar to that reported for **22**, reaction time 15 hours in acetone at room temperature, 84% yield. **27**, mp 137-142° dec (from benzene); ir: ν 1730 (CO butoxycarbonyl and CO imidazolone) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.46 (d, 3H, J = 6.6 Hz, CHC*H*$_3$), 1.57 (m, 6H, C=CCH_3), 1.71 (s, 9H, CCH_3), 3.68-3.83 (m, 3H, C*H*CH_3 and C*H*$_2$CH=C), 4.48-4.55 (m, 2H, C*H*$_2$CH), 4.91 (m, 1H, CH=C), 7.55 and 8.00 (2d, 2H, J_m = 1.9 Hz, imidazobenzothiadiazepine C8-H and C10-H).

Anal. Calcd. for $C_{20}H_{26}ClN_3O_5S$: C, 52.68; H, 5.75; Cl, 7.78; N, 9.22; S, 7.03. Found: C, 52.71; H, 5.80; Cl, 7.82; N, 9.34; S, 7.09.

9-Chloro-2,3-dihydro-3-methyl-2-(3-methyl-2-butenyl)-imidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-Dioxide (**28**).

Derivative **28** was synthesized as reported for **20b**, method B. **28**: (100% yield), mp 197-199° (from toluene); ir: ν 3080 (NH), 1730 (CO) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.47-1.59 (m, 9H, CH_3), 3.78-3.85 (m, 3H, C*H*CH_3 and C*H*$_2$CH=C), 4.52 (m, 2H, C*H*$_2$CH), 4.95 (m, 1H, CH=C), 7.24 and 7.46 (2d, 2H, J_m = 1.9 Hz, imidazobenzothiadiazepine C8-H and C10-H), 10.58 (s, broad, 1H, NH).

Anal. Calcd. for $C_{15}H_{18}ClN_3O_3S$: C, 50.63; H, 5.10; Cl, 9.96; N, 11.81; S, 9.01. Found: C, 50.51; H, 5.15; Cl, 9.84; N, 11.89; S, 9.05.

9-Chloro-2,3-dihydro-3-methyl-2-(3-methyl-2-butenyl)-imidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-thione 1,1-Dioxide (**6**).

Compound **6** was obtained starting from **28**, as already reported for **5**. Chromatographic system: silica gel column, chloroform as eluent, 44% yield, mp 186-187° (from toluene); ir: ν 3080 (NH) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.52-1.57 (m, 9H, CH_3), 3.78-3.85 (m, 3H, C*H*CH_3 and C*H*$_2$CH=C), 4.79 (m, 2H, C*H*$_2$CH and CH=C), 5.21 (dd, 1H, J_{gem} = 14.9 Hz, J_1 = 5.0 Hz, C*H*$_2$CH), 7.38 and 7.59 (2d, 2H, J_m = 1.6 Hz, imidazobenzothiadiazepine C8-H and C10-H), 11.28 (s, broad, 1H, NH).

Anal. Calcd. for $C_{15}H_{18}ClN_3O_2S_2$: C, 48.44; H, 4.88; Cl, 9.53; N, 11.30; S, 17.24. Found: C, 48.50; H, 4.91; Cl, 9.48; N, 11.45; S, 17.11.

7-*tert*-Butoxycarbonyl-9-chloro-2,3-dihydro-2-ethyl-3-methylimidazo[1,5,4-*ef*][1,2,5]benzothiadiazepin-6(4*H*,7*H*)-one 1,1-Dioxide (**29**).

Title derivative was obtained as reported for **14a**. **29** was obatined in 87% yield, mp 138-139° dec (from benzene); ir: ν 1730 (CO butoxycarbonyl and CO imidazolone) cm^{-1}; ^1H nmr (deuterochloroform): δ 1.02 (t, 3H, CH_2CH_3), 1.31 (d, 3H, CHC*H*$_3$), 1.47 (m, 6H, C=CCH_3), 1.69 (s, 9H, CCH_3), 3.20 (q, 2H, C*H*$_2$CH$_3$), 3.75 (q, 1H, C*H*CH_3), 4.51 (m, 2H, C*H*$_2$CH), 7.56 and 7.98 (2d, 2H, J_m = 2.0 Hz, imidazobenzothiadiazepine C8-H and C10-H).

Anal. Calcd. for $C_{17}H_{22}ClN_3O_5S$: C, 49.10; H, 5.33; Cl, 8.52; N, 10.10; S, 7.71. Found: C, 49.20; H, 5.15; Cl, 8.47; N, 10.08; S, 7.84.

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