Denitrocyclization in Synthesis of Dibenzo[*b*,*f*][1,4]thiazepin-11(10*H*)-ones and Their Derivatives

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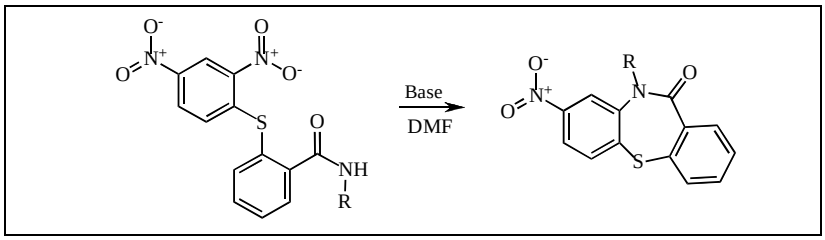

A convenient synthesis of the novel dibenzo[*b*,*f*][1,4]thiazepin-11(10*H*)-ones is reported. As a key step, the synthetic route includes intramolecular aromatic denitrocyclization of 2-(2,4-dinitro-phenylsulfanyl)-benzoic acid amides. Efficient procedures for denitrocyclization in the presence of different bases are developed. Reduction of the nitro group in the obtained heterocycles resulted in formation of primary amines, which were transformed into amides by acylation with different carboxylic acids. The synthesized compounds have a great potential of bioactivity and are useful objects for biomedicinal screening.

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INTRODUCTION

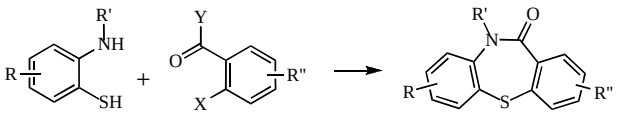
Benzo-fused seven-membered lactams (benzoazepine-2-ones) and their heterocyclic analogues represent well-known pharmacophoric scaffolds with a wide portfolio of interesting physiological activities. For example, they were reported as potential Ca-channel blockers [1], NMDA glycine-site antagonists [2], anticoagulants [3], inhibitors of proteases [4,5] and antihypertensive agents [6-8]. Dibenzo[*b*,*f*][1,4]thiazepin-11-ones and some of their analogues were documented as novel non-nucleoside inhibitors of HIV-1 reverse transcriptase [9,10]. These recent examples reflect the ongoing interest in new benzo-fused seven-membered lactams and their heterocyclic analogues.

In this work we have developed an efficient strategy for synthesis of the novel dibenzo[*b*,*f*][1,4]thiazepin-11(10*H*)-ones and their 10-substituted derivatives which have a great potential of bioactivity and are useful objects for biomedicinal screening.

RESULTS AND DISCUSSION

Denitrocyclization is a well-documented synthetic approach for the synthesis of heterocyclic compounds [11]. However, this method has never been used for preparation of the dibenzo[*b*,*f*][1,4]thiazepin-11(10*H*)-ones, which were usually obtained by interaction of the substituted *ortho*-aminothiophenols with *ortho*-halogeno-benzoic acids derivatives (Scheme 1) In particular, this method was used for the synthesis of 8-nitro-10*H*-dibenzo[*b*,*f*][1,4]thiazepin-11-one [12], but in general this approach is rather limited.

Scheme 1

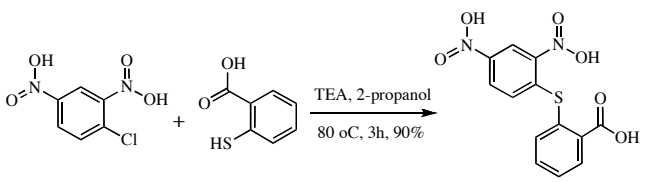


X = F, Cl, Br, I;
Y = Cl, OH, OAlk

We have developed a novel synthetic approach to dibenzo[*b*,*f*][1,4]thiazepin-11(10*H*)-ones based on intra-molecular nucleophilic substitution of nitro group (denitrocyclization) as a key step.

Reaction of equimolar amounts of 1-chloro-2,4-dinitrobenzene (**1**) and 2-mercapto-benzoic acid (**2**) in the presence of TEA (2 equiv.) afforded 2-(2,4-dinitro-phenylsulfanyl)-benzoic acid (**3**) (Scheme 2). The reaction proceeded in 2-propanol at 80 ºC. The pure resulting product was precipitated from the reaction mixture after neutralization with hydrochloric acid.

Scheme 2

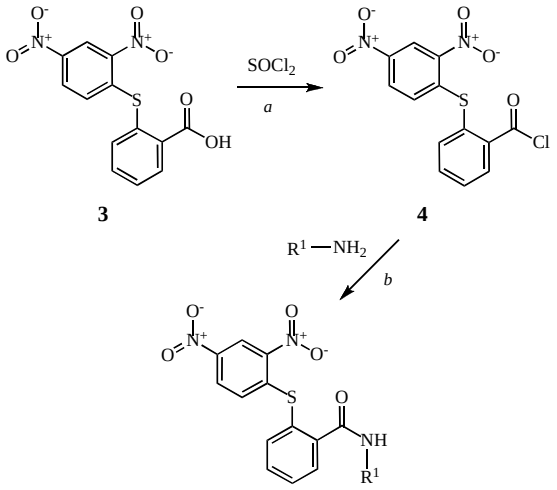


1 **2** **3**

The resulting acid was transformed into the acid chloride (**4**) by treatment of (**3**) with thionyl chloride in

dry dioxane. The reaction proceeded smoothly at 50 ºC. The resulting solution of (**4**) was used for synthesis of amides in parallel without isolation of the acid chloride (Scheme 3). Treatment of (**4**) with primary amines in dioxane in the presence of TEA afforded the desired amides (**5a-e**) which were used for the following denitrocyclization.

Scheme 3

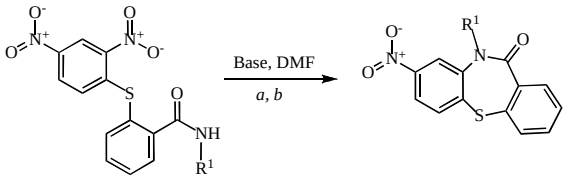


R^1 = **a** - CH_3, **b** - C_2H_5, **c** - *n*-C_3H_7, **d** - cyclo-C_5H_9, **e** - cyclo-C_3H_5
a - dioxane, 50 ºC, 2 h; *b* - TEA, dioxane, 20 ºC, 2 h

The obtained amides (**5a-e**) were considered as objects for intramolecular nucleophilic substitution of nitro group with amide nitrogen (Scheme 4). This reaction proceeded only in the presence of a base. Thus, the reaction proceeded even at room temperature in the presence of such strong bases as sodium hydride, sodium amide or potassium *tert*-butoxide in dry DMF. The reaction products afforded in good yields only when sodium hydride or potassium *tert*-butoxide were used. It can be suggested that, under the described conditions, sodium amide initiated Chichibabin amination [13].

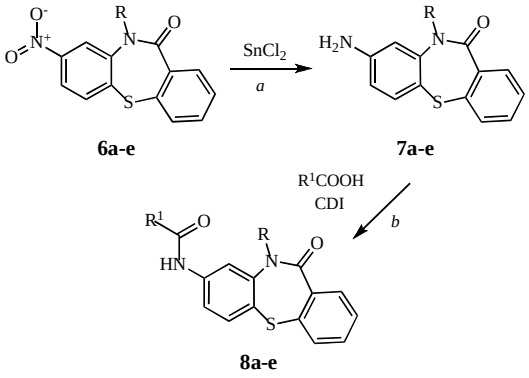
We have found that denitrocylcization of (**5a-e**) can also proceed in the presence of potassium carbonate as deprotonating agent in a solution of wet DMF at 120 ºC. This procedure allows one to obtain the desired products in 80-90% yields.

Scheme 4



a - 0-20 ºC, 2h, $R^1 = CH_3$, Base = NaH (80%), $NaNH_2$ (23%), $KO(CH_3)_3$ (88%)
b - 120 ºC, 5h, $R^1 = CH_3$, Base = K_2CO_3 (90%)

Scheme 5



a - HCl, 80 ºC, 2 h
b - dioxane, 50-100 ºC, 5 h

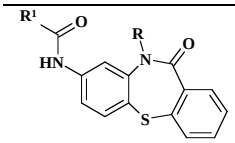
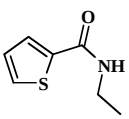
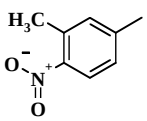
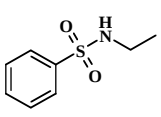
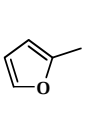
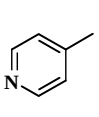
The resulting compounds (**6a-e**) were transformed to the corresponding amines (**7a-e**) *via* reduction of the nitro group by treatment with tin (II) chloride in the presence of hydrochloric acid at 80 ºC followed by neutralization of the mixture with NaOH (Scheme 5). The desired amines (**7a-e**) precipitated from the reaction mixture and then were purified by reprecipitating from DMF in 80-90% yields.

The synthesized amines (**7a-e**) were used as building-blocks for synthesis of amides in parallel. Reaction of equimolar amounts of the corresponding acid with *N*,*N*'-carbonyldiimidazole (CDI) afforded the corresponding imidazolides which were transformed into the desired amides (**8a-e**) (Table 1) by addition of the amines (**7a-e**) *in situ*.

The assignment of these structures was made on the basis of elemental analysis and ^{1}H NMR spectroscopy data. ^{1}H NMR spectra of the resulting compounds were

Table 1

Structure of compounds (**8a-e**)

Structure	Entry	**8a**	**8b**	**8c**	**8d**	**8e**
	R^1	Me	Et	Pr	Cyclo-C_5H_9	Cyclo-C_3H_5
	R^2					

clean and showed characteristic signals from protons of two benzene rings and corresponding substituents at both nitrogen atoms.

EXPERIMENTAL

Melting points were measured with a Buchi B-520 melting point apparatus and were not corrected. ^{1}H NMR spectra were recorded on Bruker DRX-500 spectrometers in DMSO-d_6 or $CDCl_3$ using TMS as an internal standard.

2-(2,4-Dinitro-phenylsulfanyl)-benzoic acid (**3**). A mixture of 20.26 g (0.1 mol) of 1-chloro-2,4-dinitrobenzene (**1**), 15.42 g (0.1 mol) of 2-mercapto-benzoic acid (**2**), 20.24 g (0.2 mol) of TEA and 150 ml of 2-propanol was stirred at 80 ºC for 3 h. Then the mixture was cooled down to a room temperature and poured into 300 ml of 15% hydrochloric acid. The formed precipitate was collected by filtration, washed with water and dried to afford pure reaction product (**3**) as yellow crystals, 28.8 g (90%), mp 220-223º; ^{1}H nmr (DMSO-d_6): δ 7.06 (d, 1H, J= 7.9 Hz, ArH), 7.65 (m, 3H, 3ArH), 8.00 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 8.20 (dd, 1H, J_o= 8.1 Hz, J_m=1.1 Hz, ^{5}CH), 8.92 (d, J_m= 1.1 Hz, ^{3}CH). *Anal.* Calcd. for $C_{13}H_8N_2O_6S$: C, 48.75; H, 2.52; N, 8.73; S, 10.01. Found: C, 48.65; H, 2.52; N, 8.70, S, 10.02.

General Procedure for Synthesis of 2-(2,4-dinitro-phenylsulfanyl)-benzamides (**5a-e**). Thionyl chloride (13.09 g, 0.11 mol) was added to a suspension of 32.03 g (0.1 mol) of compound (**3**) in 100 ml of dry dioxane. The mixture was treated at 50 ºC for 2 h. Then the mixture was cooled down to a room temperature and added dropwise to a solution of 0.11 mol of a primary amine and 11.13 g (0.11 mol) of TEA in 200 ml of dioxane. The mixture was stirred at room temperature for 2 h and then poured into water. The formed precipitate was collected by filtration, washed with water and dried to afford pure reaction product (**5a-e**).

2-(2,4-Dinitro-phenylsulfanyl)-*N*-methyl-benzamide (**5a**). This compound was obtained as yellow solid in 79% yield, mp 174-176°; ^{1}H nmr (DMSO-d_6): δ 2.70 (d, 3H, J=5.3 Hz, NCH_3), 7.00 (d, 1H, J_o=8.1Hz, ^{5}CH), 7.60 (m, 4H, 4ArH), 8.20 (m, 2H, ^{3,5}CH), 8.95 (q, 1H, J=5.3 Hz, NH). *Anal.* Calcd. for $C_{14}H_{11}N_3O_5S$: C, 50.45; H, 3.33; N, 12.61; S, 9.62. Found: C, 50.37; H, 3.33; N, 12.65; S, 9.63.

2-(2,4-Dinitro-phenylsulfanyl)-*N*-ethyl-benzamide (**5b**). This compound was obtained as yellow solid in 82% yield, mp 143-145°; ^{1}H nmr (DMSO-d_6): δ 1.02 (t, 3H, J=7.1 Hz, CH_3), 3.21 (m, 2H, NCH_2), 7.02 (d, 1H, J_o=8.1Hz, ^{5}CH), 7.63 (m, 4H, 4ArH), 8.20 (m, 2H, ^{3,5}CH), 8.97 (t, 1H, J=5.2 Hz, NH). *Anal.* Calcd. for $C_{15}H_{13}N_3O_5S$: C, 51.87; H, 3.77; N, 12.1; S, 9.23. Found: C, 51.78; H, 3.78; N, 12.09; S, 9.24.

2-(2,4-Dinitro-phenylsulfanyl)-*N*-propyl-benzamide (**5c**). This compound was obtained as yellow solid in 86% yield, mp 93-95°; ^{1}H nmr (DMSO-d_6): δ 0.80 (t, 3H, J=7.0 Hz, CH_3), 1.40 (m, 2H, CH_2), 3.08 (m, 2H, NCH_2), 7.00 (d, 1H, J_o=8.1Hz, ^{6}CH), 7.58 (m, 4H, 4ArH), 8.20 (dd, 1H, J_o=8.1Hz, J_m=1.1 Hz, ^{5}CH), 8.32 (m, 1H, NH), 8.94 (d, 1H, J_m=1.1 Hz, ^{3}CH). *Anal.* Calcd. for $C_{16}H_{15}N_3O_5S$: C, 53.18; H, 4.18; N, 11.63; S, 8.87. Found: C, 53.14; H, 4.19; N, 11.60; S, 8.88.

***N*-Cyclopentyl-2-(2,4-dinitro-phenylsulfanyl)-benzamide** (**5d**). This compound was obtained as yellow solid in 90% yield, mp 140-142°; ^{1}H nmr (DMSO-d_6): δ 1.60 (m, 8H, $4CH_2$). 4.05 (m, 1H, NCH), 7.01 (d, 1H, J= 8.1 Hz, ^{6}CH), 7.61 (m, 4H, 4ArH), 8.21 (dd, 1H, J_o=8.1 Hz, J_o=1.1 Hz, ^{5}CH), 8.37 (d, 1H, J= 8.5Hz, NH), 8.95 (d, 1H, J_o=1.1 Hz, ^{3}CH), 1H). *Anal.* Calcd. for $C_{18}H_{17}N_3O_5S$: C, 55.80; H, 4.42; N, 10.85; S, 8.28. Found: C, 55.09; H, 4.43; N, 10.82; S, 8.29.

***N*-Cyclopropyl-2-(2,4-dinitro-phenylsulfanyl)-benzamide** (**5e**). This compound was obtained as yellow solid in 60% yield, mp 131-133°; ^{1}H nmr (DMSO-d_6): δ 1.58 (m, 4H, $2CH_2$). 4.08 (m, 1H, NCH), 7.05 (d, 1H, J= 8.1 Hz, ^{6}CH), 7.64 (m, 4H, 4ArH), 8.23 (dd, 1H, J_o=8.1 Hz, J_o=1.1 Hz, ^{5}CH), 8.36 (d, 1H, J= 8.5Hz, NH), 8.96 (d, 1H, J_o=1.1 Hz, ^{3}CH), 1H). *Anal.* Calcd. for $C_{16}H_{13}N_3O_5S$: C, 53.48; H, 3.65; N, 11.69; S, 8.92. Found: C, 53.43; H, 3.65; N, 11.67; S, 8.93.

General Procedure for Synthesis of 10-substituted 8-nitro-dibenzo[*b,f*][1,4]thiazepin-11-ones (**6a-e**). Potassium carbonate (27.64 g, 0.2 mol) was added to a solution of 0.1 mol (**5a-e**) in DMF (100 ml). The mixture was stirred at 120 ºC for 5 h. Then the mixture was cooled down to room temperature and poured into water. The formed precipitate was collected by filtration, washed with water, dried and purified by crystallization from a mixture of ethanol and DMF to afford pure reaction product (**6a-e**).

10-Methyl-8-nitro-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**6a**). This compound was obtained as yellow solid in 90% yield, mp 187-189°; ^{1}H nmr (DMSO-d_6): δ 3.60 (s, 3H, NCH_3), 7.36 (m, 2H), 7.47 (m, 1H), 7.58(m, 1H), 7.66 (d, 1H, J_o= 8.0 Hz, ^{6}CH), 8.22 (dd, 1H, J_o= 8.0 Hz, J_m= 1.1 Hz, ^{7}CH), 8.38 (d, 1H, J_m= 1.1 Hz, ^{9}CH). *Anal.* Calcd. for $C_{14}H_{10}N_2O_3S$: C, 58.73; H, 3.52; N, 9.78; S, 11.20. Found: C, 58.66; H, 3.52; N, 9.80; S, 11.22.

10-Ethyl-8-nitro-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**6b**). This compound was obtained as yellow solid in 85% yield, mp 119-121°; ^{1}H nmr (DMSO-d_6): δ 1.21 (t, 3H, J=7.1 Hz, CH_3), 4.57 (q, 2H, J=7.1 Hz, NCH_2), 7.34 (m, 2H, 2ArH), 7.45 (m, 1H, ArH), 7.56 (m, 1H, ArH), 7.63 (d, 1H, J_o=8.0 Hz, ^{6}CH), 8.20 (dd, 1H, J_o=8.0 Hz, J_m=1.1 Hz, ^{7}CH), 8.37 (d, 1H, J_m=1.1 Hz, ^{9}CH). *Anal.* Calcd. for $C_{15}H_{12}N_2O_3S$: C, 59.99; H, 4.03; N, 9.33; S, 10.67. Found: C, 59.89; H, 4.03; N, 9.37; S, 10.69.

8-Nitro-10-propyl-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**6c**). This compound was obtained as yellow solid in 80% yield, mp 117-119°; ^{1}H nmr (DMSO-d_6): δ 0.90 (t, 3H, J=6.8 Hz, CH_3), 1.60 (m, 2H, CH_2), 3.70 (m, 1H, CH), 4.60 (m, 1H, CH), 7.42 (m, 2H, 2ArH), 7.52 (m, 1H, ArH), 7.60 (m, 1H, ArH), 7.86 (d, 1H, J_o=8.0 Hz, ^{6}CH), 8.22 (dd, 1H, J_o=8.0 Hz, J_o=1.1 Hz, ^{7}CH), 8.40 (d, 1H, J_o=1.1 Hz, ^{9}CH). *Anal.* Calcd. for $C_{16}H_{14}N_2O_3S$: C, 61.13; H, 4.49; N, 8.91; S, 10.20. Found: C, 61.05; H, 4.49; N, 8.88; S, 10.21.

10-Cyclopentyl-8-nitro-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**6d**). This compound was obtained as yellow solid in 87% yield, mp 157-159°; ^{1}H nmr (DMSO-d_6): δ 1.75 (m, 8H, $4CH_2$), 4.50 (m, 1H, NCH), 7.41 (m, 2H, 2ArH), 7.51 (m, 1H, ArH), 7.61 (m, 1H, ArH), 7.85 (d, 1H, J_o=8.0 Hz, ^{6}CH), 8.21 (dd, 1H, J_o=8.0 Hz, J_m=1.1 Hz, ^{7}CH), 8.40 (d, 1H, J_m=1.1 Hz, ^{9}CH). *Anal.* Calcd. for $C_{18}H_{16}N_2O_3S$: C, 63.51; H, 4.74; N, 8.23; S, 9.42. Found: C, 63.46; H, 4.74; N, 8.20; S, 9.43.

10-Cyclopropyl-8-nitro-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**6e**). This compound was obtained as yellow solid in 82% yield, mp 153-155°; ^{1}H nmr (DMSO-d_6): δ 1.71 (m, 4H, $2CH_2$), 4.52 (m, 1H, NCH), 7.40 (m, 2H, 2ArH), 7.53 (m, 1H, ArH), 7.60 (m, 1H, ArH), 7.82 (d, 1H, J_o=8.0 Hz, ^{6}CH), 8.22 (dd, 1H, J_o=8.0 Hz, J_m=1.1 Hz, ^{7}CH), 8.42 (d, 1H, J_m=1.1 Hz, ^{9}CH). *Anal.* Calcd. for $C_{16}H_{12}N_2O_3S$: C, 61.53; H, 3.87; N, 8.97; S, 10.26. Found: C, 61.47; H, 3.88; N, 8.95; S, 10.27.

General Procedure for Synthesis of 10-substituted 8-aminodibenzo[*b,f*][1,4]thiazepin-11-one (**7a-e**). Tin (II) chloride dihydrate (78.96 g, 0.35 mol) and 85 ml (0.7 mol) of

30% hydrochloric acid were added to a solution of 0.1 mol (**6a-e**) in 100 ml of ethanol. The mixture was stirred at 80 ºC for 2 h. Then the mixture was cooled down to room temperature and added to a solution of 40 g (1 mol) of NaOH in 300 ml of water. The formed precipitate was collected by filtration, washed with water, dried, reprecipitated from DMF and dried to afford pure reaction product (**7a-e**).

8-Amino-10-methyl-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**7a**). This compound was obtained as white solid in 93% yield, mp 227-229°; ^{1}H nmr (DMSO-d_6): δ 3.52 (s, 3H, CH_3), 5.26 (s, 2H, NH_2), 6.50 (m, 1H, ArH), 6.72 (m, 1H, ArH), 7.11 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.29 (m, 2H, 2ArH), 7.41 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 7.50 (d, 1H, J_o=1.0 Hz). *Anal.* Calcd. for $C_{14}H_{12}N_2OS$: C, 65.60; H, 4.72; N, 10.93; S, 12.51. Found: C, 65.50; H, 4.72; N, 10.95; S, 12.52.

8-Amino-10-ethyl-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**7b**). This compound was obtained as white solid in 84% yield, mp 181-183°; ^{1}H nmr (DMSO-d_6): δ 1.18 (t, 3H, J=7.1 Hz, CH_3), 4.50 (q, 2H, J=7.1 Hz, CH_2), 4.90 (s, 2H, NH_2), 6.52 (m, 1H, ArH), 6.72 (m, 1H, ArH), 7.13 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.28 (m, 2H, 2ArH), 7.42 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 7.51 (d, 1H, J_o=1.0 Hz). *Anal.* Calcd. for $C_{15}H_{14}N_2OS$: C, 66.64; H, 5.22; N, 10.36; S, 11.86. Found: C, 66.57; H, 5.22; N, 10.33; S, 11.88.

8-Amino-10-propyl-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**7c**). This compound was obtained as white solid in 82% yield, mp 172-174°; ^{1}H nmr (DMSO-d_6): δ 0.90 (t, 3H, J=6.8 Hz, CH_3), 1.50 (m, 2H, CH_2), 3.36 (m, 1H, CH), 4.45 (m, 1H, CH), 5.30 (s, 2H, NH_2), 6.50 (m, 1H, ArH), 6.72 (m, 1H, ArH), 7.11 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.29 (m, 2H, 2ArH), 7.41 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 7.50 (d, 1H, J_o=1.0 Hz). *Anal.* Calcd. for $C_{16}H_{16}N_2OS$: C, 67.58; H, 5.67; N, 9.85; S, 11.27. Found: C, 67.53; H, 5.68; N, 9.82; S, 11.29.

8-Amino-10-cyclopentyl-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**7d**). This compound was obtained as white solid in 92% yield, mp 248-250°; ^{1}H nmr (DMSO-d_6): δ 1.6 (m, 8H, $4CH_2$), 4.55 (m, 1H, NCH), 4.85 (s, 2H, NH_2), 6.52 (m, 1H, ArH), 6.72 (m, 1H, ArH), 7.13 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.28 (m, 2H, 2ArH), 7.42 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 7.51 (d, 1H, J_o=1.0 Hz). *Anal.* Calcd. for $C_{18}H_{18}N_2OS$: C, 69.65; H, 5.84; N, 9.02; S, 10.33. Found: C, 69.58; H, 4.85; N, 9.05; S, 10.34.

8-Amino-10-cyclopropyl-10*H*-dibenzo[*b,f*][1,4]thiazepin-11-one (**7e**). This compound was obtained as white solid in 78% yield, mp 215-217°; ^{1}H nmr (DMSO-d_6): δ 1.6 (m, 4H, $2CH_2$), 4.56 (m, 1H, NCH), 4.84 (s, 2H, NH_2), 6.53 (m, 1H, ArH), 6.74 (m, 1H, ArH), 7.12 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.29 (m, 2H, 2ArH), 7.43 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 7.52 (d, 1H, J_o=1.0 Hz). *Anal.* Calcd. for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N, 9.92; S, 11.35. Found: C, 67.99; H, 5.00; N, 9.95; S, 11.37.

General Procedure for Synthesis of 10-substituted *N*-(11-oxo-11*H*-dibenzo[*b,f*][1,4]thiazepin-8-yl-amides (**8a-e**). A mixture of 0.0011 mol of the corresponding carboxylic acid, 0.0011 mol of CDI and 3 ml of dry dioxane was stirred at 50 ºC for 1 h. Then 0.001 mol of (**7a-e**) was added to the reaction mixture; it was refluxed for 5 h, then cooled down to a room temperature and poured into 5% water solution of sodium bicarbonate. The formed precipitate was collected by filtration, washed with water, dried and purified by crystallization from a mixture of ethanol and DMF to afford pure reaction product (**8a-e**).

Thiophene-2-carboxylic acid [(10-methyl-11-oxo-10,11-dihydrodibenzo[*b,f*][1,4]thiazepin-8-ylcarbamoyl)-methyl]-amide (**8a**). This compound was obtained as white solid in 80% yield, mp 171-173°; ^{1}H nmr (DMSO-d_6): δ 3.48 (s, 3H, NCH_3), 4.00 (d, 2H, J=6.5 Hz, NCH_2), 7.05 (t, 1H, J=6.5 Hz, NH), 7.30 (m, 3H, Th), 7.42 (m, 1H, ArH), 7.49 (m, 1H, ArH), 7.60 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.75 (m, 2H, 2ArH), 7.92 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 8.65 (d, 1H, J_o=1.0 Hz, ^{9}CH), 10.05 (s, 1H, NH). *Anal.* Calcd. for $C_{21}H_{17}N_3O_3S_2$: C, 59.56; H, 4.05; N, 9.92; S, 15.14. Found: C, 59.48; H, 4.05; N, 9.96; S, 15.16.

***N*-(10-Ethyl-11-oxo-10,11-dihydro-dibenzo[*b,f*][1,4]thiazepin-8-yl)-3-methyl-4-nitro-benzamide** (**8b**). This compound was obtained as yellow solid in 72% yield, mp 257-259°; ^{1}H nmr (DMSO-d_6): δ 1.25 (t, 3H, J=7.1 Hz, CH_3), 3.22 (s, 3H, CH_3), 3.65 (m, 1H, CH), 4.52 (m, 1H, CH), 7.25 (t, 2H), 7.42 (m, 1H, ArH), 7.49 (m, 1H, ArH), 7.60 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.63 (d, 1H, J_o=8.0 Hz, $^{5'}$CH), 7.75 (m, 2H, 2ArH), 7.92 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 8.20 (dd, 1H, J_o=8.0 Hz, J_m=1.1 Hz, $^{6'}$CH), 8.37 (d, 1H, J_m=1.1 Hz, $^{2'}$CH), 8.65 (d, 1H, J_o=1.0 Hz), 10.22 (s, 1H, NH). *Anal.* Calcd. for $C_{23}H_{19}N_3O_4S$: C, 63.73; H, 4.42; N, 9.69; S, 7.40. Found: C, 63.66; H, 4.42; N, 9.71; S, 7.41.

2-Benzenesulfonylamino-*N*-(11-oxo-10-propyl-10,11-dihydro-dibenzo[*b,f*][1,4]thiazepin-8-yl)-acetamide (**8c**). This compound was obtained as white solid in 65% yield, mp 208-210°; ^{1}H nmr (DMSO-d_6): δ 0.90 (t, 3H, CH_3), 1.55 (m, 2H, CH_2), 3.42 (m, 1H, CH), 3.54 (d, 2H, J= 6.2Hz, NCH_2), 4.50 (m, 1H, CH), 7.26 (m, 4H, 4ArH), 7.45 (m, 5H, Ph), 7.52 (t, 1H, J=6.2 Hz, NH), 7.62 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.94 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 8.65 (d, 1H, J_o=1.0 Hz, ^{9}CH), 10.15 (s, 1H, NH). *Anal.* Calcd. for $C_{24}H_{23}N_3O_4S_2$: C, 59.86; H, 4.81; N, 8.73; S, 13.32. Found: C, 59.81; H, 4.82; N, 8.75; S, 13.33.

Furan-2-carboxylic acid (10-cyclopentyl-11-oxo-10,11-dihydro-dibenzo[*b,f*][1,4]thiazepin-8-yl)-amide (**8d**). This compound was obtained as white solid in 58% yield, mp 103-105°; ^{1}H nmr (DMSO-d_6): δ 1.60 (m, 2H, CH_2), 1.80 (m, 2H, CH_2), 1.95 (m, 2H, CH_2), 2.10 (m, 2H, CH_2), 4.50 (m, 1H, CH), 6.80 (m, 3H, Fu), 7.26 (m, 4H, 4ArH), 7.60 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.92 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 8.66 (d, 1H, J_o=1.0 Hz, ^{9}CH), 10.10 (s, 1H, NH). *Anal.* Calcd. for $C_{23}H_{20}N_2O_3S$: C, 68.30; H, 4.98; N, 6.93; S, 7.93. Found: C, 68.26; H, 4.99; N, 6.89; S, 7.94.

***N*-(10-Cyclopropyl-11-oxo-10,11-dihydro-dibenzo[*b,f*][1,4]-thiazepin-8-yl)-isonicotinamide** (**8e**). This compound was obtained as white solid in 50% yield, mp >300°; ^{1}H nmr (DMSO-d_6): δ 0.20 (m, 1H, CH), 0.80 (m, 2H, CH_2), 1.20 (m, 1H, CH), 3.35 (m, 1H, CH), 7.26 (m, 4H, 4ArH), 7.62 (d, 1H, J_o= 8.1 Hz, ^{6}CH), 7.75 (d, 2H, J=7.9 Hz, 2PyH), 7.94 (dd, 1H, J_o=8.1 Hz, J_m=1.0 Hz, ^{7}CH), 8.65 (d, 1H, J_o=1.0 Hz, ^{9}CH), 8.70 (d, 2H, J=7.9 Hz, 2PyH), 10.31 (s, 1H, NH). *Anal.* Calcd. for $C_{22}H_{17}N_3O_2S$: C, 68.20; H, 4.42; N, 10.85; S, 8.27. Found: C, 68.12; H, 4.43; N, 10.72; S, 8.28.

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