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SYNTHESES AND REACTIONS OF 2-CYCLOHEXYL-1,3,4,5-TETRAHYDRO-10*H*-PYRROLO[3,4-*b*][1,5]BENZODIAZEPINE-1,4-DIONE AND 4-ARYL-2-CYCLOHEXYL-1,3,4,10-TETRAHYDROPYRROLO[4,3-*c*][1,5]BENZOTHIAZEPIN-1-ONES

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Abstract- 2-Cyclohexyl-1,3,4,5-tetrahydro-10*H*-pyrrolo[3,4-*b*][1,5]benzodiazepine-1,4-dione was synthesized by heating a solution of ethyl 1-cyclohexyl-2,3-dioxopyrrolidine-4-carboxylate and *o*-phenylenediamine in acetic acid. Alkylation and acylation of the synthesized compound were examined. 4-Aryl-2-cyclohexyl-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-ones were synthesized by Michael addition of 2-aminothiophenol to 4-arylidene-1-cyclohexyl-2,3-dioxopyrrolidines and concomitant dehydrative cyclization.

In the course of our synthetic studies on the biologically active heterocyclic compounds using tetronic acids, tetramic acids and thiotetronic acid, we reported that the synthesis and biological activities, namely antimicrobial and analgesic activities, of 10-aryl-3,3-dimethyl-3,4,9,10-tetrahydro-1*H*-pyrrolo[4,3-*b*]-[1,5]benzodiazepin-1-ones (**1**),[1] 10-aryl-3,3-dimethyl-1,3,4,10-tetrahydropyrrolo[3,4-*c*][1,5]benzothiazepin-1-ones (**2**),[2] and 10-aryl-3,3-dimethyl-1,3,3a,9-tetrahydrofuro[4,3-*b*][1,5]benzothiazepin-1-ones (**3**).[3] As a continuation of our work on the structure-activity relationships of benzodiazepinones and benzothiazepinones, we plan to synthesize 2-cyclohexyl-1,3,4,5-tetrahydro-10*H*-pyrrolo[3,4-*b*][1,5]-benzodiazepine-1,4-dione (**4**),[4] 4-aryl-2-cyclohexyl-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-one (**5**),[5] and their derivatives (Figure 1).

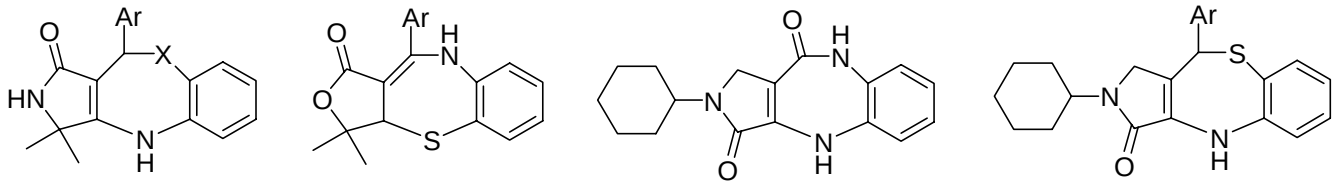
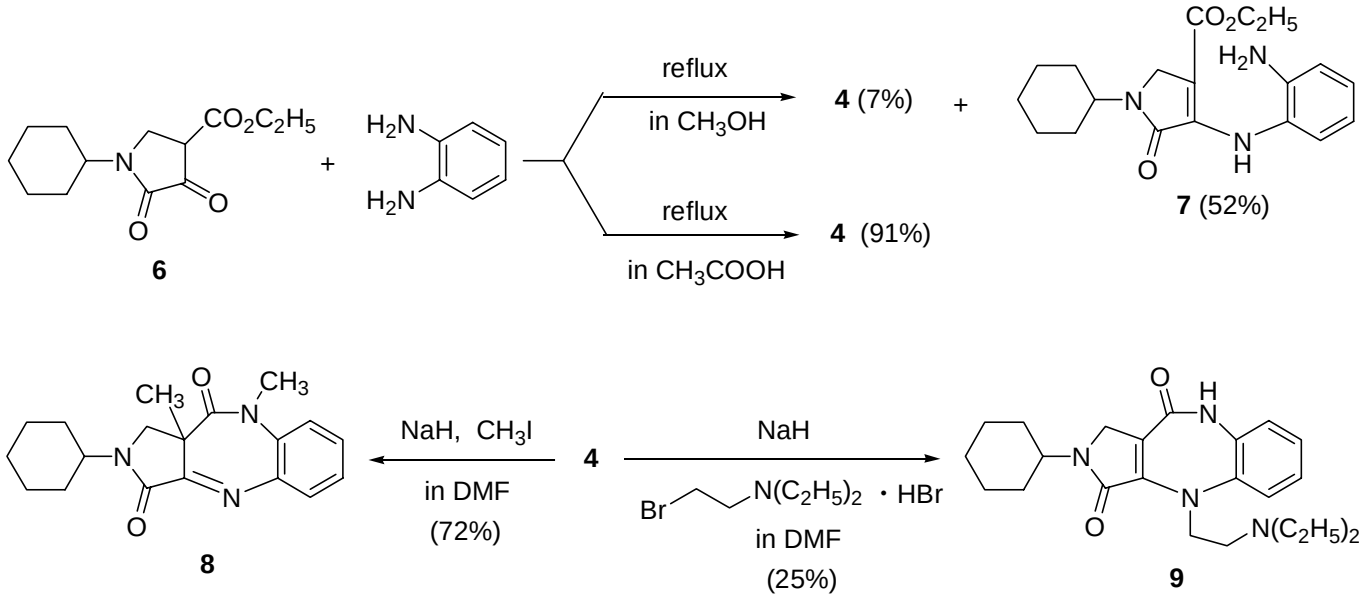


Figure 1

For the synthesis of **4** and **5**, ethyl 1-cyclohexyl-2,3-dioxopyrrolidine-4-carboxylate (**6**)[6] was used as the starting material. Treatment of **6** with *o*-phenylenediamine in methanol at refluxing temperature for 8 h

gave the desired compound (**4**) in only 7% yield, and the major product was the intermediate (**7**) (52%). When the above reaction was carried out in acetic acid at refluxing temperature for 1 h, **4** was obtained in 91% yield (Scheme 1).

For the chemical modifications of **4**, alkylation of **4** was tried first. Reaction of **4** with methyl iodide in DMF in the presence of NaH afforded an unexpected methylation product (**8**) in 72% yield as a sole product.[7] In the ^{1}H-NMR spectrum, 3a-CH_3 and *N*-CH_3 signals appeared at δ 0.95 and 3.47 ppm, respectively. When diethylaminoethylation was performed by treatment of **4** with 2-diethylaminoethyl bromide hydrobromide in DMF in the presence of NaH at room temperature, the desired compound (**9**) was obtained in 25% yield and the most of the starting material was recovered (Scheme 1).



Scheme 1

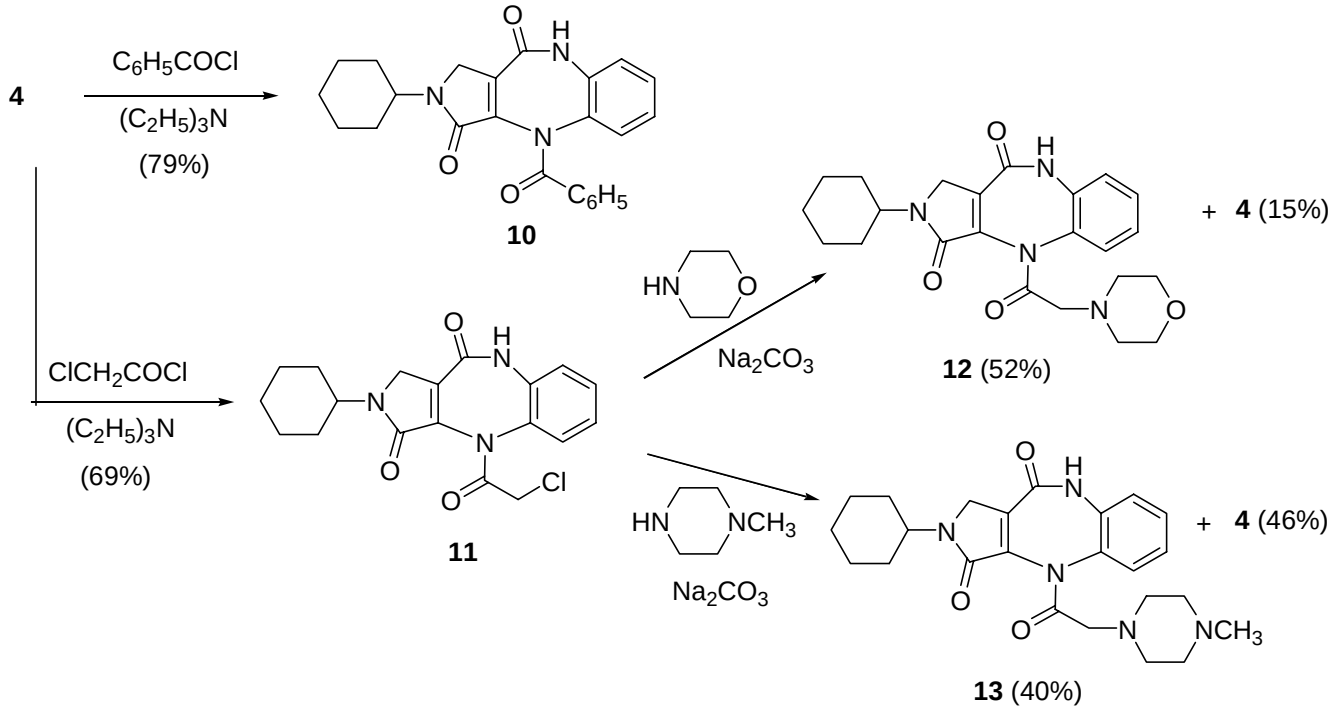
Next, we examined acylation of **4**. Reaction of **4** with benzoyl chloride in dioxane in the presence of triethylamine at refluxing temperature overnight gave the amide (**10**) in 79% yield. Similarly, when **4** was treated with chloroacetyl chloride, the chloroacetamide derivative (**11**) was obtained in 69% yield.

The product (**11**) was further reacted with morpholine in acetonitrile in the presence of Na_2CO_3 at refluxing temperature for 3 h to give **12** in 52% yield.[8] In this reaction, the compound (**4**) was obtained in 15% as the byproduct. Treatment of **11** with *N*-methylpiperazine under the same condition as above afforded **13** and **4** in 40 and 46% yields, respectively (Scheme 2).

For the preparation of **5**, we thought that it might be obtained by Michael addition of 2-aminothiophenol to 4-arylidene-1-cyclohexyl-2,3-dioxopyrrolidines (**14**). 4-Benzylidene-1-cyclohexyl-2,3-dioxopyrrolidine (**14a**)[9] was synthesized by the reaction of **6** with benzaldehyde in the presence of 20% HCl in 73% yield. The other derivatives (**14b-e**) were synthesized by the similar method.

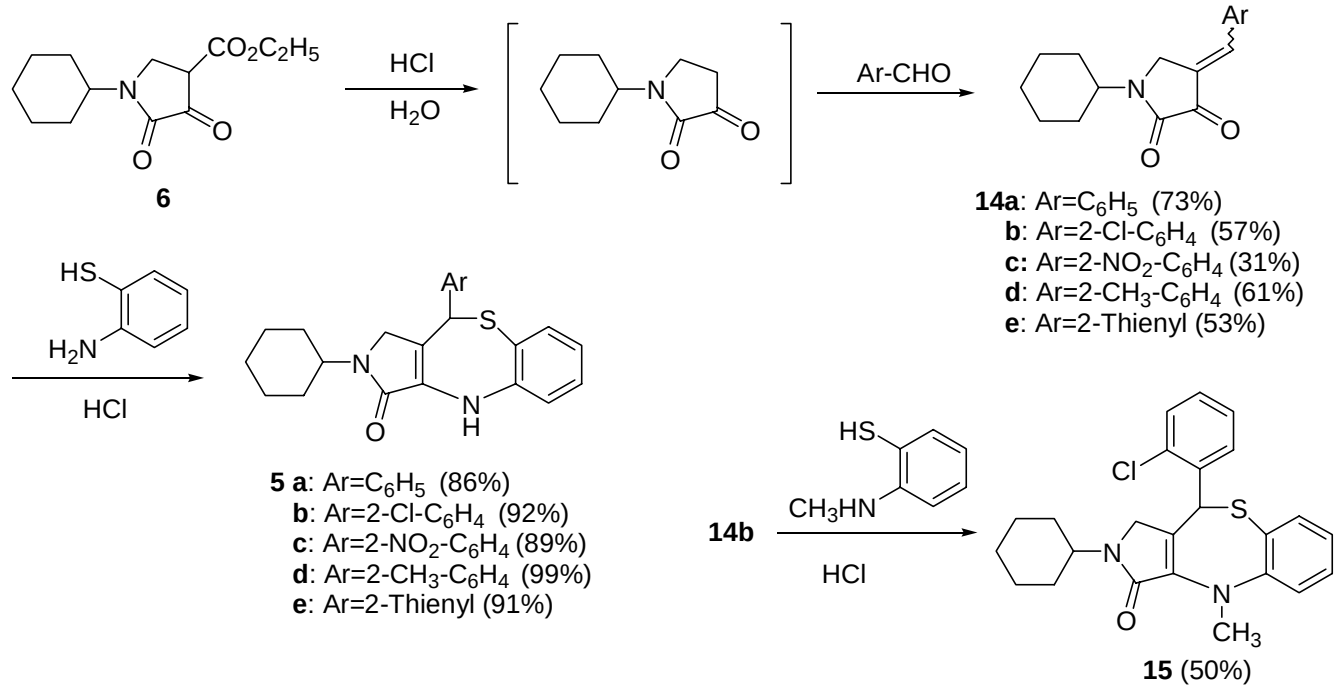
The synthesis of 4-aryl-2-cyclohexyl-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-one (**5**) was performed by a similar procedure used in the preparation of 10-aryl-3,3-dimethyl-1,3,4,10-tetrahydropyrrolo[3,4-*c*][1,5]benzothiazepin-1-ones (**2**).[2] Thus, a mixture of **14a**, 2-aminothiophenol and conc. HCl in ethanol was heated under reflux to give **5a** in 86% yield. Similarly, the other derivatives (**5b-e**) were prepared in good yields (Scheme 3). As a chemical modification of **5**, methylation of **5b** was examined.

Treatment of **5b** with methyl iodide in the presence of potassium carbonate in acetone at refluxing temperature resulted in recovery of the starting material. When **5b** was reacted with methyl iodide in the



Scheme 2

presence of NaH in DMF at room temperature, a complex mixture was obtained. Therefore, we thought to use 2-methylaminothiophenol[10] as a Michael donor. Thus, when an ethanol solution of **14b**, 2-methyl-aminothiophenol and conc. HCl was refluxed, the *N*-methyl derivative (**15**) was obtained in 50% yield.



Scheme 3

Thus, we synthesized new heterocyclic compounds, 2-cyclohexyl-1,3,4,5-tetrahydro-10*H*-pyrrolo[3,4-*b*]-[1,5]benzodiazepine-1,4-dione (**4**), 4-aryl-2-cyclohexyl-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-one (**5**), and their derivatives (Scheme 3).

EXPERIMENTAL

Melting points were determined using a Yanagimoto micro-melting point apparatus, model MP-S3, and are uncorrected. IR spectra were measured with a Hitachi 260-30 infrared spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL JNM-GSX270 (270 MHz) spectrometer using tetramethylsilane as the internal standard. High-resolution MS (HRMS) spectra were measured with a JEOL JMS-HX100 instrument at 70 eV.

2-Cyclohexyl-1,3,4,5-tetrahydro-10*H*-pyrrolo[3,4-*b*][1,5]benzodiazepine-1,4-dione (4) and ethyl 3-(2-aminophenylamino)-1-cyclohexyl-2*H*,5*H*-2-oxopyrrol-4-ylcarboxylate (7)

A mixture of **6** (2.000 g, 7.90 mmol) and *o*-phenylenediamine (0.854 g, 7.90 mmol) in CH_3OH (10 mL) was heated under reflux for 6 h. After addition of more **6** (0.40 g, 1.58 mmol), the mixture was heated under reflux for further 2 h. The crystals formed by cooling were collected by filtration to give **4** (0.195 g, 7%). The filtrate was concentrated under reduced pressure to give the residue, which was recrystallized from 2-propanol-hexane to afford **7** (1.686 g, 52%). **4**: mp 288-290 ℃. IR (Nujol): 3260, 1660 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.05-1.80 (10H, m, cyclohexyl), 3.79 (1H, m, NCH), 3.92 (2H, s, NCH_2), 6.70-7.10 (4H, m, ArH), 8.08 and 8.58 (each 1H, br s, 2 x NH). HRMS (*m/z*): Calcd for $C_{17}H_{19}N_3O_2$: 297.1477. Found: 297.1458. **7**: mp 131-135 ℃. IR (Nujol): 3225, 1660, 1245, 1220, 1130 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.17 (3H, t, *J*=7.0 Hz, CH_2CH_3), 1.30-1.86 (10H, m, cyclohexyl), 4.01 (2H, s, NCH_2C), 4.00 (1H, m, NCH), 4.00 (2H, br s, NH_2), 4.12 (2H, q, *J*=7.0 Hz, OCH_2CH_3), 6.68-7.07 (4H, m, ArH), 7.45 (1H, br s, NH). *Anal*. Calcd for $C_{19}H_{25}N_3O_3$: C, 66.45; H, 7.34; N, 12.24. Found: C, 66.56; H, 7.30; N, 12.21.

2-Cyclohexyl-1,3,4,5-tetrahydro-10*H*-pyrrolo[3,4-*b*][1,5]benzodiazepine-1,4-dione (4)

A solution of **6** (5.000 g, 19.74 mmol) and *o*-phenylenediamine (2.134 g, 19.73 mmol) in acetic acid (25 mL) was heated under reflux for 1 h. After cooling and addition of water, the crystals formed were collected by filtration to give **4** (5.368 g, 91%).

2-Cyclohexyl-3a,5-dimethyl-3,3a,4,5-tetrahydro-1*H*-pyrrolo[3,4-*b*][1,5]benzodiazepine-1,4-dione (8)

To a suspension of NaH (205 mg, 60%, 5.10 mmol) in dry DMF (10 mL) was added **4** (500 mg, 1.68 mmol) and the whole was stirred at rt for 30 min. Iodomethane (0.40 mL, 7.09 mmol) was added to the above solution and then the reaction mixture was stirred at rt overnight. After addition of water, the precipitates formed were collected by filtration. The crude products were purified by SiO_2 column chromatography (hexane-acetone=5:3) to give **8** (0.392 g, 72%). mp 199.5-201 ℃ (2-propanol-hexane). IR ($CHCl_3$): 1695, 1665, 1600, 1310, 1270, 1210, 1110 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, s, CCH_3), 1.10-1.90 (10H, m, cyclohexyl), 3.19 (1H, d, *J*=11.0 Hz, NCH_2), 3.47 (3H, s, NCH_3), 4.25 (1H, tt, *J*=12.0, 3.5 Hz, NCH), 4.83 (1H, d, *J*=11.0 Hz, NCH_2), 7.25-7.39 (3H, m, ArH), 7.64 (1H, d, *J*=8.5 Hz, ArH). *Anal*. Cacd for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91. Found: C, 69.88; H, 7.18; N, 12.96.

2-Cyclohexyl-10-(2-diethylaminoethyl)-1,3,4,5-tetrahydropyrrolo[3,4-*b*][1,5]benzodiazepine-1,4-dione (9)

To a suspension of NaH (0.194 g, 60%, 5.05 mmol) in dry DMF (10 mL) was added **4** (0.500 g, 1.68 mmol) and the mixture was stirred at rt for 15 min. *N*,*N*-Diethylaminoethyl bromide hydrobromide (0.528 g, 2.02 mmol) was added to the above mixture and the whole was stirred at rt for 1.5 h. After addition of water, the precipitates formed were collected by filtration (0.322 g). These were identical with the starting **4**. The filtrate was extracted with $CHCl_3$ and the combined extracts were washed with water and brine, and then dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave the residue which was purified by SiO_2 column chromatography ($CHCl_3$-CH_3OH=9:1) to give **9** (59 mg, 25%). mp 192-195 ℃ (2-propanol-hexane). IR (Nujol): 3230, 1690, 1660, 1630, 1270 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (6H, t, *J*=7.0 Hz, 2 x NCH_2CH_3), 1.10-1.90 (10H, m, cyclohexyl), 2.51 (4H, q, *J*=7.0Hz, 2 x CH_2CH_3), 2.63 (2H, t, *J*=7.0 Hz, $NCH_2CH_2N(C_2H_5)_2$), 3.97 (2H, t, *J*=7.0 Hz, $NCH_2CH_2N(C_2H_5)_2$), 4.00 (1H, m, NCH), 4.08 (2H, s, NCH_2C), 6.49 (1H, br s, NH), 6.80-7.22 (4H, m, ArH). HRMS (*m/z*): Calcd for $C_{23}H_{32}N_4O_2$: 396.2525. Found: 396.2542.

10-Benzoyl-2-cyclohexyl-1,3,4,5-tetrahydropyrrolo[3,4-*b*][1,5]benzodiazepine-1,4-dione (10)

A solution of **4** (0.500 g, 1.68 mmol), benzoyl chloride (0.24 mL, 2.02 mmol) and triethylamine (0.28 mL, 2.02 mmol) in dioxane (40 mL) was heated under reflux for 9 h. After addition of more benzoyl chloride (0.12 mL, 1.03 mmol) and triethylamine (0.14 mL, 1.01 mmol), the mixture was heated again under reflux for 4 h. The solution was concentrated under reduced pressure and the residue was dissolved in $CHCl_3$. The solution was washed with water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave the crude product which was recrystallized from 2-propanol to give **10** (0.532, 79%). mp 258-261 ℃. IR (Nujol): 1680, 1630, 1300, 1260, 1220 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10-1.90 (10H, m, cyclohexyl), 4.09 (3H, s, NCH_2, NCH), 7.26-7.57 (9H, m, ArH), 8.29 (1H, s, NH). *Anal*. Calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47. Found: C, 71.86; H, 5.93; N, 10.51.

10-Chloroacetyl-2-cyclohexyl-1,3,4,5-tetrahydropyrrolo[3,4-*b*][1,5]benzodiazepine-1,4-dione (11)

A solution of **4** (3.445 g, 11.59 mmol), chloroacetyl chloride (1.11 mL, 13.91 mmol) and triethylamine (2.52 mL, 18.08 mmol) in dry dioxane (240 mL) was heated under reflux for 5 h. After addition of more chloroacetyl chloride (1.11 mL, 13.91 mmol) and triethylamine (2.52 mL, 18.08 mmol), the solution was heated under reflux for further 5 h. After cooling, the reaction mixture was concentrated under reduced pressure to give the residue, which was dissolved in $CHCl_3$. The solution was washed with water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave the residue, which was recrystallized from 2-propanol to give **11** (2.989 g, 69%). mp 250.5-252 ℃. IR (Nujol): 3200, 1690, 1665, 1630, 1595, 1260, 1230 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10-1.92 (10H, m, cyclohexyl), 4.08 (1H, m, NCH), 4.17 (2H, s, NCH_2C), 4.48 (2H, s, $COCH_2Cl$), 7.30-7.42 (4H, m, ArH), 8.54 (1H, br s, NH). *Anal*. Calcd for $C_{19}H_{20}N_3O_3Cl$: C, 61.04; H, 5.39; N, 11.24. Found: C, 60.87; H, 5.45; N, 10.99.

2-Cyclohexyl-10-(morpholin-4-ylethanoyl)-1,3,4,5-tetrahydropyrrolo[3,4-*b*][1,5]benzodiazepine-1,4-dione (12)

A mixture of **11** (0.500 g, 1.34 mmol), morpholine (0.116 g, 1.33 mmol) and Na_2CO_3 (0.142 g, 1.34

mmol) in dry acetonitrile (10 mL) was heated under reflux for 1 h. After cooling, the insoluble materials were filtered off and washed with acetonitrile. The insoluble materials were dissolved in water and the solution was extracted with $CHCl_3$. The extract was washed with water and brine, and then dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave the residue which was recrystallized from 2-propanol to give **4** (61 mg, 15%). The original filtrate and washings were combined and the whole was concentrated under reduced pressure. The residue was dissolved in $CHCl_3$ and the solution was washed with water and brine, and then dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave the residue which was recrystallized from 2-propanol to give **12** (0.295 g, 52%). **12**: mp 213-215 ℃. IR (Nujol): 3230, 1675 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.18-1.92 (10H, m, cyclohexyl), 2.39 (4H, t, *J*=5.0 Hz, 2 x NCH_2CH_2O), 3.47 (4H, t, *J*=5.0 Hz, 2 x NCH_2CH_2O), 3.49 (2H, s, $COCH_2N$), 4.12 (1H, m, NCH), 4.19 (2H, s, NCH_2C), 7.14-7.42 (4H, m, ArH), 7.73 (1H, s, NH). *Anal*. Calcd for $C_{23}H_{28}N_4O_4$: C, 65.08; H, 6.65; N, 13.20. Found: C, 64.69; H, 6.60; N, 13.14. HRMS (*m/z*): Calcd for $C_{23}H_{28}N_4O_4$: 424.2111. Found: 424.2121.

2-Cyclohexyl-10-(4-methylpiperazin-1-ylethanoyl)-1,3,4,5-tetrahydropyrrolo[3,4-*b*][1,5]benzodiazepine-1,4-dione (13)

A mixture of **11** (0.500 g, 1.34 mmol), *N*-methylpiperazine (0.134 g, 1.34 mmol) and Na_2CO_3 (0.142 g, 1.34 mmol) in dry acetonitrile (10 mL) was heated under reflux for 6 h. After addition of more *N*-methylpiperazine (0.134 g, 1.34 mmol) and Na_2CO_3 (0.142 g, 1.34 mmol), refluxing was continued for 1 h. After cooling, the insoluble materials were filtered off and washed with acetonitrile. The filtrate and washings were combined and the whole was concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography ($CHCl_3$-CH_3OH=9:1) to give **13** (0.236 g, 40%) and **4** (0.184 g, 46%). **13**: mp 240-243 ℃ (2-propanol). IR (Nujol): 3250, 1680, 1650 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10-2.00 (10H, m, cyclohexyl), 2.17 (3H, s, NCH_3), 2.41 (8H, br s, 2 x NCH_2CH_2N), 3.47 (2H, br s, $COCH_2N$), 4.14 (1H, m, NCH), 4.19 (2H, s, NCH_2C), 7.20-7.42 (4H, m, ArH), 8.02 (1H, br s, NH). *Anal*. Calcd for $C_{24}H_{31}N_5O_3$: C, 65.88; H, 7.14; N, 16.01. Found: C, 65.81; H, 7.15; N, 15.83.

4-Benzylidene-1-cyclohexyl-2,3-dioxopyrrolidine (14a)[9]

The diketo ester (**6**) (5.000 g, 19.74 mmol) was dissolved in C_2H_5OH (38 mL) by warming. To this solution were added 20% HCl (125 mL) and benzaldehyde (2.750g, 25.91 mmol) and the whole was heated under reflux for 2 h. After cooling, the crystals formed were collected by filtration and recrystallized from 2-propanol- hexane to give **14a** (3.87 g, 73%). mp 208-209 ℃ (lit.,[9] 204-205.5 ℃). IR (Nujol): 1710, 1670, 1610, 1580, 11270, 1140 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.12-1.68 (6H, m, cyclohexyl), 1.82-1.96 (4H, m, cyclohexyl), 4.32 (1H, m, NCH), 4.52 (2H, d, *J*=2.0 Hz, NCH_2C), 7.50 (5H, br s, ArH), 7.70 (1H, t, *J*=2.0 Hz, =CH).

The other derivatives (**14b-14e**) were synthesized by the similar method

4-(2-Chlorobenzylidene)-1-cyclohexyl-2,3-dioxopyrrolidine (14b)

Yield: 57%. mp 200-202 ℃ (C_2H_5OH). IR (Nujol): 1720, 1680, 1620, 1580, 1285, 1160, 1120, 1030, 1000, 920 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10-1.90 (10H, m, cyclohexyl), 4.31 (1H, tt, *J*=12.0, 4.0 Hz, NCH), 4.44 (2H, d, *J*=2.0 Hz, NCH_2C), 7.33-7.55 (5H, m, ArH), 8.11 (1H, t, *J*=2.0 Hz, =CH). *Anal*. Calcd for

$C_{17}H_{18}NO_2Cl$: C, 67.21; H, 5.97; N, 4.61. Found: C, 67.27; H, 6.00; N, 4.67.

1-Cyclohexyl-4-(2-nitrobenzylidene)-2,3-dioxopyrrolidine (14c)

Yield: 31%. mp 169.5-170.5 ℃ (2-propanol). IR (Nujol): 1725,1690, 1630, 1575, 1525, 1290, 1210, 1165, 1145, 1005 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.14-1.92 (10H, m, cyclohexyl), 4.27 (2H, d, *J*=2.0 Hz, NCH_2C), 4.28 (1H, m, NCH), 7.51 (1H, dd, *J*=7.5, 1.0 Hz, ArH), 7.66 (1H, dt, *J*=7.5, 1.0 Hz, ArH), 7.77 (1H, dt, *J*=7.5, 1.0 Hz, ArH), 8.04 (1H, br t, *J*=2.0 Hz, =CH), 8.21 (1H, dd, *J*=7.5, 1.0 Hz, ArH). *Anal*. Calcd for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.91. Found: C, 64.97; H, 5.67; N, 8.95.

1-Cyclohexyl-4-(2-methylbenzylidene)-2,3-dioxopyrrolidine (14d)

Yield: 61%. mp 200-201 ℃ (CH_3OH). IR (Nujol): 1725, 1690, 1620, 1600, 1290, 1220, 1170, 1005 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10-1.90 (10H, m, cyclohexyl), 2.46 (3H, s, $ArCH_3$), 4.30 (1H, tt, *J*=12.0, 4.0 Hz, NCH), 4.45 (2H, d, *J*=2.0 Hz, NCH_2C), 7.27-7.43 (4H, m, ArH), 7.99 (1H, t, *J*=2.0 Hz, =CH). *Anal*. Calcd for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.94. Found: C, 76.18; H, 7.42; N, 5.07.

1-Cyclohexyl-4-(2-thienylmethylene)-2,3-dioxopyrrolidine (14e)

Yield: 53%. mp 199-201 ℃ (C_2H_5OH). IR (Nujol): 3070, 1710, 1680, 1605, 1280, 1150, 1000 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10-1.95 (10H, m, cyclohexyl), 4.30 (1H, tt, *J*=12.0 3.0 Hz, NCH), 4.37 (2H, d, *J*=2.0 Hz, NCH_2C), 7.24 (1H, dd, *J*=5.0, 4.0 Hz, ArH), 7.49 (1H, br d, *J*=4.0 Hz, ArH), 7.73 (1H, d, *J*=5.0 Hz, ArH), 7.92 (1H, br t, *J*=2.0 Hz, =CH). *Anal*. Calcd for $C_{15}H_{17}NO_2S$: C, 65.43; H, 6.22; N, 5.09. Found: 65.29; H, 6.22; N, 5.13.

2-Cyclohexyl-4-phenyl-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-one (5a)

A solution of **14a** (0.500 g, 1.86 mmol), *o*-aminothiophenol (0.230 g, 1.86 mmol) and conc. HCl (1 drop) in C_2H_5OH (15 mL) was heated under reflux for 2 h. After cooling, the precipitates formed were collected by filtration and recrystallized from benzene-hexane to give **5a** (0.600 g, 86%). mp 230-235 ℃. IR (Nujol): 3250, 1660, 1530, 1260, 1210 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.02-1.44 (6H, m, cyclohexyl), 1.74-1.84 (4H, m, cyclohexyl), 3.64 (2H, s, NCH_2C), 4.02 (1H, m, NCH), 4.96 (1H, s, ArCH), 6.95 (1H, br s, NH), 7.08-7.24 (9H, m, ArH). *Anal*. Calcd for $C_{23}H_{24}N_2OS$: C, 73.42; H, 6.42; N, 7.44. Found: C, 73.38; H, 6.52; N, 7.37.

The other derivatives (**5b-5e and 15**) were synthesized by the similar method.

4-(2-Chlorophenyl)-2-cyclohexyl-4-phenyl-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-one (5b)

Yield: 92%. mp 211-212 ℃ (C_2H_5OH). IR (Nujol): 3340, 1670, 1580, 1510, 1250, 1210, 1160, 1120, 1040 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00-1.95 (10H, m, cyclohexyl), 3.60 (1H, d, *J*=18.0 Hz, NCH_2C), 3.74 (1H, d, *J*=18.0 Hz, NCH_2C), 4.03 (1H, tt, *J*=11.5, 3.0 Hz, NCH), 6.67 (1H, dd, *J*=8.0, 2.0 Hz, ArH), 6.75 (1H, dt, *J*=8.0, 1.0 Hz, ArH), 6.90-7.08 (2H, m, ArH, NH), 7.12 (1H, dt, *J*=8.0, 2.0 Hz, ArH), 7.22 (1H, dt, *J*=8.0, 2.0 Hz, ArH), 7.39 (1H, dt, *J*=8.0, 1.0 Hz, ArH). HRMS (*m/z*): Calcd for $C_{23}H_{23}N_2OClS$: 410.1219. Found: 410.1245. *Anal*. Calcd for $C_{23}H_{23}N_2OClS \cdot 1/5H_2O$: C, 66.64; H, 5.69; N, 6.76. Found: C, 66.62; H, 5.58; N, 6.76.

2-Cyclohexyl-4-(2-nitrophenyl)-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-one (5c)
Yield: 89%. mp: 209-210.5 ℃ (C_2H_5OH). IR (Nujol): 3250, 1670, 1580, 1525, 1250, 1220 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00-1.90 (10H, m, cyclohexyl), 3.69 (1H, d, *J*=18.0 Hz, NCH_2C), 3.85 (1H, d, *J*=18.0 Hz, NCH_2C), 4.05 (1H, tt, *J*=12.0, 4.0 Hz, NCH), 5.92 (1H, s, ArCH), 6.71 (1H, dt, *J*=8.0, 1.0 Hz, ArH), 6.80 (1H, dd, *J*=8.0, 1.0 Hz, ArH), 6.95 (1H, dd, *J*=8.0, 1.0 Hz, ArH), 7.00 (1H, dd, *J*=8.0, 1.0 Hz, ArH), 7.04 (1H, br s, NH), 7.17-7.24 (2H, m, ArH), 7.29 (1H, dt, *J*=8.0, 1.0 Hz, ArH), 7.92 (1H, dd, *J*=8.0, 1.0 Hz, ArH). *Anal*. Calcd for $C_{23}H_{23}N_3O_3S$: C, 65.54; H, 5.50; N, 9.97. Found: C, 65.27; H, 5.58; N, 9.73.

2-Cyclohexyl-4-(2-methylphenyl)-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-one (5d)
Yield: 99%. mp 202.5-203 ℃ (C_2H_5OH). IR (Nujol): 3270, 1665, 1585, 1530, 1255, 1220, 1200, 1170, 1140, 1090, 1040 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00-1.85 (10H, m, cyclohexyl), 2.50 (3H, s, $ArCH_3$), 3.63 (2H, s, NCH_2C), 4.03 (1H, tt, *J*=12.0, 3.5 Hz, NCH), 5.09 (1H, s, ArCH), 6.68 (1H, dd, *J*=8.0, 1.0 Hz, ArH), 6.75 (1H, dt, *J*=8.0, 1.5 Hz, ArH), 6.93 (2H, m, ArH, NH), 7.01 (1H, dd, *J*=8.0, 1.0 Hz, ArH), 7.04-7.24 (4H, m, ArH). *Anal*. Calcd for $C_{24}H_{26}N_2OS$: C, 73.81; H, 6.71; N, 7.17. Found: C, 73.51; H, 6.69; N, 7.10.

2-Cyclohexyl-4-(2-thienyl)-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-one (5e)
Yield: 91%. mp 212-213 ℃ (C_2H_5OH). IR (Nujol): 3250, 1665, 1585, 1530, 1255, 1215, 1190, 1160, 1075, 1040 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00-1.90 (10H, m, cyclohexyl), 3.73 (1H, d, *J*=18.0 Hz, NCH_2C), 3.82 (1H, d, *J*=18.0 Hz, NCH_2C), 4.03 (1H, tt, *J*=11.5, 3.5 Hz, NCH), 5.25 (1H, s, ArCH), 6.65 (1H, dt, *J*=3.5, 1.0 Hz, ArH), 6.76-6.85 (2H, m, ArH), 6.95 (1H, br s, NH), 6.97-7.02 (1H, m, ArH), 7.11 (1H, dd, *J*=5.5, 1.0 Hz, ArH), 7.20 (2H, d, *J*=7.5 Hz, ArH). *Anal*. Calcd for $C_{21}H_{22}N_2OS_2$: C, 65.94; H, 5.80; N, 7.32. Found: C, 65.66; H, 5.80; N, 7.18.

4-(2-Chlorophenyl)-2-cyclohexyl-10-methyl-1,3,4,10-tetrahydropyrrolo[4,3-*c*][1,5]benzothiazepin-1-one (15)
Yield: 50%. mp 143-143.5 ℃ (2-propanol-hexane). IR (Nujol): 1690, 1580, 1260, 1120 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.00-1.80 (10H, m, cyclohexyl), 2.71 (3H, s, NCH_3), 3.76 (1H, m, NCH), 4.09 (1H, dd, *J*=15.0, 2.0 Hz, NCH_2C), 4.40 (1H, dd, *J*=15.0, 3.0 Hz, NCH_2C), 6.49 (1H, d, *J*=8.0 Hz, ArH), 6.65 (1H, t, *J*=7.5 Hz, ArH), 6.99 (2H, d, *J*=7.5 Hz, ArH), 7.18 (1H, br t, *J*=2.0 Hz, ArCH), 7.33-7.54 (4H, m, ArH). *Anal*. Calcd for $C_{24}H_{25}NOClS \cdot 1/5H_2O$: C, 67.26; H, 5.97; N, 6.54. Found: 67.25; H, 6.01; N, 6.45. HRMS (*m/z*): Calcd for $C_{24}H_{25}NOClS$: 424.1376. Found: 424.1354.

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