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**Dedicated to the memory of Professor Nicholas Alexandrou**

2-Substituted-amino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene derivatives **5** representing a novel ring system were synthesized. Their acylation led to exo-acylated derivatives **9** that could be converted to the corresponding glycine analogues **12**.

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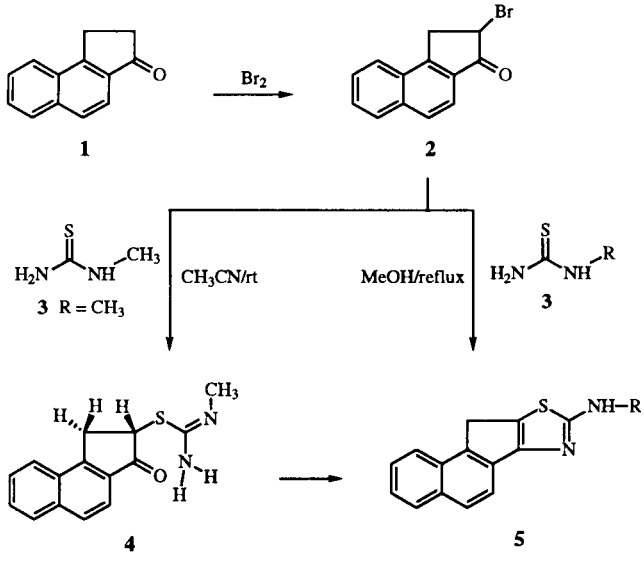
Our research efforts towards antiulcerogenic benz[*e*]-indenone derivatives [1] made available large quantities of the known [2-3] 1,2-dihydrobenz[*e*]inden-3-one (**1**) (Scheme 1).

In the hope to synthesize novel type *C-nor*-heterocyclic steroid analogues we elaborated a simple α-bromination procedure of **1** to yield the known [4] 2-bromo-1,2-dihydrobenz[*e*]inden-3-one (**2**) in good yield that was characterised by its pmr and cmr spectra (Experimental). Refluxing of derivative **2** with thiourea **3** (R = H) or *N*-methylthiourea **3** (R = methyl) in methanol as the solvent yielded the corresponding 2-amino-10*H*-thiazolo-[5,4-*b*]benz[*e*]indene **5** (R = H) and 2-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **5** (R = methyl), respectively, representing a novel ring system (Scheme 1).

Scheme 1

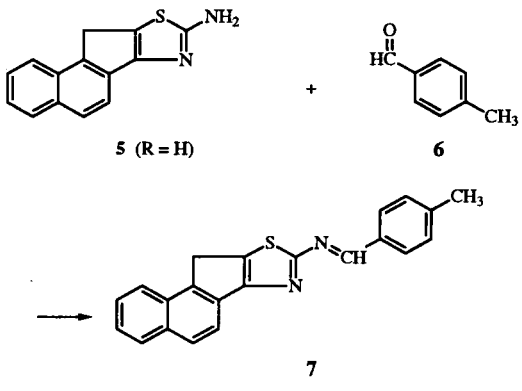



It was also possible to isolate the intermediate from the above reaction, the corresponding isothiourea derivative **4**, when the reaction of **2** with *N*-methylthiourea **3** (R = methyl) was provided in acetonitrile at room temperature. As expected, a short refluxing of derivative **4** in *n*-butanol yielded the corresponding derivative **5** (R = methyl).

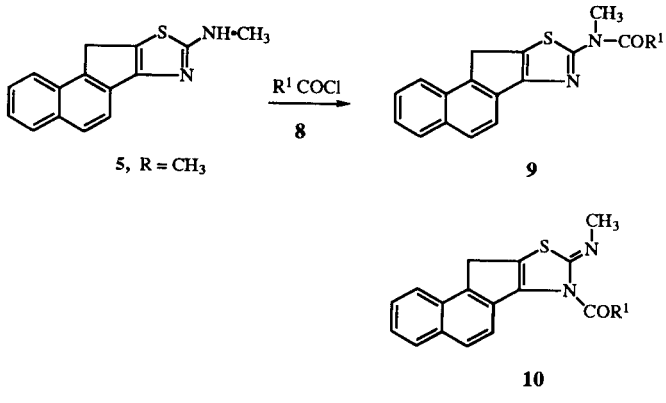
The structure proof of derivatives **5** (R = H and methyl, respectively) was based on the presence of the $CH_2$ group at position 10 that appeared in the pmr spectra as a singlet at 4.03 and 4.04 ppm, respectively, and in the cmr spectra at 31.3 and 31.1 ppm, respectively, as well as on the chemical shifts of the "thiazole" carbon atoms that appeared in the cmr at 173.5, 157.1 and 135.7 ppm and 174.2, 157.0 and 135.4 ppm, respectively. The above spectral data were also in accordance with the dominant tautomeric structure of derivatives **5** shown in Scheme 1, being further corroborated by the primary coupling of the $NHCH_3$ protons of **5** (R = methyl) appearing in the pmr spectrum as a quartet and a doublet.

The exo-amino structure of **5** (R = H) was also in agreement with the possibility to convert this material with 4-methylbenzaldehyde (**6**) to the corresponding Schiff

Scheme 2




Scheme 3

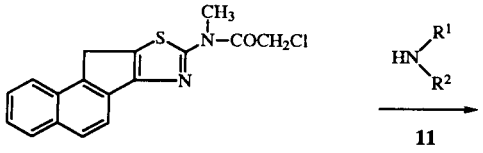


base **7** (Scheme 2).

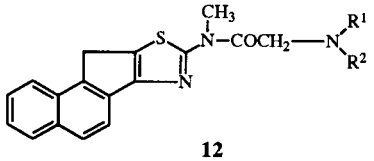
Derivative **5** (R = methyl) was acylated with different acyl chlorides **8** to yield the exo-acylated derivatives **9** (Scheme 3). However, in these acylation reactions ring-acylated derivatives **10** (Scheme 2) could also be formed, thus, the exo-acylated structure of derivatives **9** had to be proved. Structure **9** of the derivatives obtained is in agreement with the strong upfield shift of the *N*-methyl protons in **9** ($R^1$ = methyl and chloromethyl) appearing at 3.83 and 3.79 ppm, respectively, as compared with those of the starting material **5** (R = methyl) that appeared at 2.93 ppm and the practically unchanged chemical shifts of the "thiazole" carbon atoms 3a and 10a appearing between 155.0-155.2 and 134.3-134.8 ppm, respectively.

Ths reaction of derivatives **9** ($R^1$ = choromethyl) with secondary amines **11** led to the corresponding dialkylaminoacetyl derivatives **12**, (Scheme 3) having completely analogous pmr and cmr spectra to those of the corresponding derivatives **9** ($R^1$ = methyl and chloromethyl) (Experimental) further corroborating the exo-acylated structure of these compounds.

Scheme 4




**9**, $R^1 = CH_2Cl$




**12**

## EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are not corrected. The infrared spectra were obtained as potassium bromide pellets using a Perkin-Elmer 577 spectrometer. The pmr and cmr measurements were performed using a Bruker WM-250 instrument. All tlc determinations were performed on DC-Alufolien Kieselgel 60 $F_{254}$ (Merck) plates. The spots were detected by uv.

2,3-Dihydro-2-bromo-1*H*-benz[*e*]inden-3-one (**2**).

To a solution of 49.0 g (0.269 mole) of 2,3-dihydro-1*H*-benz-[*e*]inden-3-one (**1**) [2] in 100 ml of acetic acid a solution of 45.7 g (14.7 ml, 0.286 mole) of bromine in 50 ml of acetic acid was added dropwise at 55-60°. The mixture was stirred at 60° for 1 hour, then made free from the hydrogen bromide formed by bubbling a nitrogen stream through it. After cooling the mixture was diluted with 300 ml of methanol and poured into 1000 ml of water. The mixture obtained was stirred for 1 hour, the crystals that precipitated were filtered off and washed with water and ethanol to yield 64.8 g (92%) of 2,3-dihydro-2-bromo-1*H*-benz[*e*]inden-3-one (**2**), mp 124-126° that was pure enough for the further reactions. A sample recrystallised from methanol melted at 127-128°, lit [3] mp 132°; ir: ν C=O = 1705 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 3.68 [dd (J = 18.4 and 2.7 Hz), 1H, CH-1 eqv), 4.12 [dd (J = 18.4 and 7.3 Hz), 1H, CH-1ax), 4.78 [dd (J = 7.3 and 2.7 Hz), 1H, CH-2ax), 7.62 [dt (J = 7.1 and 1.3 Hz), 1H, CH-8], 7.68 [dt (J = 7.8 and 1.3 Hz), 1H, CH-7], 7.74-7.97 (m , 4H, CH-4, 5, 6 and 9]; cmr (deuteriochloroform): δ, ppm 36.1 (C-1) , 43.5 (C-2), 119.6 (C-4), 124.1*, 129.2* and 129.8* (C-5, 6 and 9), 127.3 (C-8), 128.8 (C-7), 129.5 (C-9a), 130.9 (C-5a), 136.7 (C-9b), 152.4 (C-3a), 199.3 (C=O).

*Anal.* Calcd. for $C_{13}H_9BrO$ (MW 261.13): C, 59.80; H, 3.47; Br , 30.60. Found: C, 59.91; H, 3.45; Br, 30.42.

*N*-Methyl-*S*-(2,3-dihydro-1*H*-benz[*e*]inden-3-on-2-yl)isothiourea (**4**).

To a solution of 1.30 g (0.005 mole) of 2,3-dihydro-2-bromo-1*H*-benz[*e*]inden-3-one (**2**) in 45 ml of acetonitrile a solution of 0.50 g (0.0055 mole) of *N*-methylisothiorea **3** (R = methyl) in 10 ml of acetonitrile was added at room temperature and stirred for 90 minutes. The crystals that precipitated were filtered off and washed with acetonitrile to yield 1.3 g (74%) of *N*-methyl-*S*-(2,3-dihydro-1*H*-benz[*e*]inden-3-one-2-yl)isothiourea hydrobromide (**4•HBr**), mp >350°. This was dissolved at room temperature in 110 ml of methanol; to the solution 1 ml of concentrated ammonium hydroxide and 20 ml of water were added, the crystals that precipitated were filtered off and washed with acetonitrile to yield 0.43 g (32%) of *N*-methyl-*S*-(2,3-dihydro-1*H*-benz[*e*]inden-3-on-2-yl)isothiourea (**4**), mp 221-223°; ir: ν C=N = 1587 $cm^{-1}$; pmr (DMSO-$d_6$): δ, ppm 2.72 (s, 3H, N-$CH_3$), 3.17 [dd (J = 17.1 and 4.3 Hz), 1H, CH-1 eqv], 3.86 [dd (J = 17.1 and 8.0 Hz), 1H, CH-1ax], 4.35 [dd (J = 8.0 and 4.3 Hz), 1H, CH-2ax], 6.27 (s, 1H, $NH_2$-H"out"], 6.84 (s, 1H, $NH_2$-H"in"), 7.51-7.94 (m, 6H, ArH); cmr (DMSO-$d_6$): δ, ppm 30.6 ($CH_3$), 38.2 ($CH_2$), 58.5 (CH), 122.8 (C-4), 124.4*, 126.0*, 126.5* (C-5, 6 and 9), 127.8 (C-8), 128.5 (C-7), 129.8 (C-9a), 133.4 (C-5a), 135.5 (C-9b), 142.9 (C-3a), 159.9 (S-*C*($NH_2$)$NCH_3$).

*Anal.* Calcd. for $C_{15}H_{14}N_2OS$ (MW 270.36): C, 66.64; H, 5.22; N, 10.36; S, 11.86. Found: C, 66.54; H, 5.44; N, 10.39; S, 11.75.

2-Amino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **5** (R = H).

To a solution of 10.45 g (0.04 mole) of 2,3-dihydro-2-bromo-1*H*-benz[*e*]inden-3-one (**2**) in 600 ml of hot methanol a solution of 3.35 g (0.044 mole) of thiourea in 100 ml of methanol was added and refluxed with stirring for 2 hours. After cooling, the reaction mixture was evaporated *in vacuo* to dryness, the residue was dissolved in 400 ml of water and made alkaline with concentrated ammonium hydroxide. The crystals that precipitated were filtered off and washed with water and acetone to yield 8.09 g (85%) of 2-amino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **5** (R = H), mp 217-220° dec; ir: ν $NH_2$ = 3430 and 3280 $cm^{-1}$, ν C=N = 1629 and 1531 $cm^{-1}$; pmr (DMSO-$d_6$): δ, ppm 4.03 (s, 2H, $CH_2$-10), 7.40 [dt (J = 7.5 and 1.1 Hz), 1H, CH-8], 7.51 [dt (J = 7 and 1.2 Hz), 1H, CH-7], 7.65 [d (J = 7.5 Hz), 1H, CH-9), 7.85-7.98 (m, 3H, CH-4, 5 and 6); cmr (DMSO-$d_6$): δ, ppm 31.3 (C- 10), 118.8 (C-4), 123.0*, 124.8* and 126.5* (C-5, 6 and 9), 127.6 (C-8), 128.6 (C-7), 130.1 (C-5a), 131.2 (C-9a), 131.8 (C-3b), 135.7 (C-10a), 141.8 (C-9b), 157.1 (C-3a), 173.5 (C-2).

*Anal.* Calcd. for $C_{14}H_{10}N_2S$ (MW 238.31): C, 70.56; H, 4.23; N, 11.75; S, 13.45. Found: C, 70.65; H, 4.45; N, 11.60; S, 13.42.

2-(4-Methylbenzalamino)-10*H*-thiazolo[5,4-*b*]benz[*e*]indene (**7**).

To a solution of 2.4 g (0.01 mole) of 2-amino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **5** (R = H) in 60 ml of methanol, 0.05 g of *p*-toluenesulfonic acid and a solution of 1.42 g (0.012 mole) of 4-methylbenzaldehyde (Aldrich) in 5 ml of dimethylformamide were added and the mixture refluxed for 2 days. After cooling the crystals that precipitated were filtered off and washed with methanol to yield 1.67 g (49%) of 2-(4-methylbenzalamino)-10*H*-thiazolo[5,4-*b*]benz[*e*]indene (**7**) that after recrystallisation form 2-butanone melted at 187-188°; ir: ν C=N = 1598 and 1565 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 2.40 (s, 3H, $CH_3$), 4.04 (s, 2H, $CH_2$-10), 7.25 [dd (J = 7.7 and 1.0), 2H, PhH-3' and 5'], 7.38 [dt (J = 7.9 and 0.9 Hz), 1H, CH-8], 7.42 [dt (J = 8.3 and 1.0 Hz), 1H, CH-7], 7.84-7.96 (m, 6H, CH-4, 5, 6, 9 and PhH-2' and 6'), 8.98 (s, 1H, CH); cmr (deuteriochloroform): δ, ppm 21.7 ($CH_3$), 32.0 (C-10), 118.5 (C-4), 122.9*, 125.0*, 126.6* (C-5, 6, and 9), 128.2 (C-8), 129.2 (C-7), 129.7*, 129.9* (PhC-2', 3', 5, and 6'), 130.7 (C-5a), 132.2 (C-9a), 132.9 (C-3b), 133.7 (PhC-1'), 135.2 (C-10a), 141.6 (C-9b), 143.4 (PhC-4'), 160.5*, 161.9* (C-3a and benzal CH), 176.4 (C-2).

*Anal.* Calcd. for $C_{22}H_{16}N_2S$ (MW 340.45): C, 77.61; 4.75; N, 8.23; S, 9.42. Found: C, 77.66; H, 5.01; N, 8.44; S, 9.31.

2-Methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene 5 (R = methyl).

To a solution of 14.7 g (0.056 mole) of 2,3-dihydro-2-bromo-1*H*-thiazolo[5,4-*b*]benz[*e*]inden-3-one (**2**) in 600 ml of hot methanol a solution of 5.52 g (0.061 mole) of *N*-methylthiourea (Fluka) in 100 ml of methanol was added and refluxed with stirring for 1.5 hours. After cooling, the product that precipitated was filtered off to yield 12.8 g (69%) of 2-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene hydrobromide that was dissolved in 500 ml of water and made alkaline with concentrated ammonium hydroxide. The crystals that precipitated were filtered off and washed with water end acetone to yield 9.46 g (67%) of 2-methylamino10*H*-thiazolo[5,4-*b*]benz[*e*]indene **5** (R = methyl), mp 228-230° (*n*-butanol); ir: ν C=N = 1596, 1558 and 1525 $cm^{-1}$; pmr (DMSO-$d_6$): δ, ppm 2.93 [d (J = 4.7 Hz), 3H, $NCH_3$), 4.04 (s, 2H, $CH_2$-10), 7.39 [dt (J = 8.0 and 1.0 Hz), 1H, CH-8], 7.51 [dt (J = 8.2 and 1.0 Hz), 1H, CH-7], 7.68 [d (J = 8.0 Hz), 1H, CH-9], 7.70 [q (J = 4.7 Hz), 1H, NH), 7.87 (d (J = 8.2 Hz), 1H, CH-6), 7.90-7.98 (m, 2H, CH-4 and 5); cmr (DMSO-$d_6$): δ, ppm 30.9 ($NCH_3$), 31.1 ($CH_2$-10), 117.6 (C-4), 121.4*, 123.0* and 124.4* (C-5, 6 and 9), 126.4 (C-8), 127.4 (C-7), 128.8 (C-5a), 130.2 (C-9a), 130.8 (C-3b), 135.4 (C-10a), 141.4 (C-9b), 157.0 (C-3a), 174.2 (C-2).

*Anal.* Calcd. for $C_{15}H_{12}N_2S$(MW 252.34): C, 71.40; H, 4.79; N, 11.10; S, 12.71. Found: C, 71.23; H, 4.88; N, 11.31; S, 12.68.

2-Methylamino-10*H*-thiazolo[5,4-*b*]benz[e]indene **5** (R = methyl) from **4**.

A solution of 0.27 g (0.001 mole) of *N*-methyl-*S*-(2,3-dihydro-1*H*-benz[*e*]inden-3-on-2-yl)isothiourea (**4**) in 2 ml of *n*-butanol was refluxed for 5 minutes. After cooling the crystals that precipitated were filtered off and washed with ether to yield 0.12 g (48%) of **5** (R = methyl), mp 227-229°. The product was identical (mixed mp, ir) with that obtained above.

2-Acetyl-2-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **9** ($R^1$ = methyl).

To a solution of 0.57 g (0.002 mole) of 2-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **5** (R = methyl) in a mixture of 10 ml of pyridine and 5 ml of dimethylformamide 0.74 g (0.68 ml, 0.0096 mole) of acetyl chloride **8** ($R^1$ = methyl) was added dropwise with ice cooling. After standing overnight at room temperature the reaction mixture was poured into cracked ice, the crystals that precipitated were filtered off and washed with water to yield 0.34 g (58%) of 2-acetyl-2-methylamino-10*H*-thiazolo[5,4-*b*]benz[e]indene **9** ($R^1$ = methyl), mp 252-254° (dimethylformamide); ir: ν C=O = 1664 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 2.43 (s, 3H, $COCH_3$), 3.83 (s, 3H, $NCH_3$), 4.10 (s, 2H, $CH_2$), 7.41 [dt (J = 8.0 and 1.3 Hz), 1H, CH-8], 7.51 [dt (J = 8.3 and 1.3 Hz), 1H, CH-7], 7.83-8.04 (m, 4H, CH-4, 5, 6 and 9]; cmr (DMSO-$d_6$ + deuteriochloroform): δ, ppm 23.0 ($COCH_3$), 31.2 (C-10), 35.8 ($NCH_3$), 117.6 (C-4), 122.8*, 124.6*, 126.4* (C-5, 6 and 9), 127.5 (C-8), 128.7 (C-7), 129.0 (C-5a), 130.3 (C-9a), 131.2 (C-3b), 134.8 (C- 10a), 141.9 (C-9b), 155.2 (C-3a), 158.4 (C-2), 169.8 (C=O).

*Anal.* Calcd. for $C_{17}H_{14}N_2OS$ (MW 294.38): C, 69.36; 4.79; N, 9.52; S, 10.89. Found: C, 69.44; H, 4.90; N, 9.45; S, 10.71.

2-Chloroacetyl-2-methylamino-10*H*-thiazolo[5,4-*b*]benz-[*e*]indene **9** ($R^1$ = chloromethyl).

To a solution of 18.6 g (0.0737 mole) of 2-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **5** (R = methyl) in a mixture of 45 ml of pyridine and 280 ml of *n*-butanol 10.73 g (7.57 ml, 0.095 mole) of chloroacetyl chloride **8** ($R^1$ = chloromethyl) was added dropwise with ice cooling below 5°. After standing for two days at room temperature the reaction mixture was poured into cracked ice, the crystals that precipitated were filtered off and washed with water and ethanol to yield 20.95 g (86%) of 2-chloroacetyl-2-methylamino-10*H*-thiazolo[5,4-*b*]benz-[*e*]indene **9** ($R^1$ = chloromethyl), mp 225-230° dec; ir: ν C=O = 1661 $cm^{-1}$; pmr (DMSO-$d_6$): δ, ppm 3.79 (s, 3H, $NCH_3$), 4.25 (s, 2H, $CH_2$-10), 4.89 (s, 2H, $CH_2Cl$), 7.46 [dt (J = 6.8 and 1.3 Hz), 1H, CH-8], 7.56 [dt (J = 6.8 and 1.2 Hz), 1H, CH-7], 7.82 [d (J = 6.8 Hz), 1H, CH-9], 7.94 [d (J = 6.8 Hz), 1H, CH-6], 8.01 [t (J = 7.0 Hz), 2H, CH-4 and 5]; cmr (DMSO-$d_6$): δ, ppm 31.2 (C-10), 34.7 ($NCH_3$), 42.9 $CH_2Cl$), 117.5 (C-4), 123.1*, 124.9*, 126.6* (C-5, 6 and 9), 127.7 (C-8), 128.7 (C-7), 130.3 (C-5a), 131.4 (C-9a), 131.9 (C-3b), 134.4 (C-10a), 142.2 (C-9b), 155.2 (C-3a), 158.2 (C-2), 166.2 (C=O).

*Anal.* Calcd. for $C_{17}H_{13}ClN_2OS$ (MW 328.82): C, 62.10; H, 3.99; N, 8.52; S, 9.75; Cl, 10.78. Found: C, 62.28; H, 4.20; N, 8.55; S, 9.62; Cl, 10.80.

2-Furoyl-2-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **9** ($R^1$ = furan-2-yl).

To a stirred solution of 9.3 g (0.0369 mole) of 2-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **5** (R = methyl) in 48 ml of a 1:1 mixture of butanol and pyridine 6.58 g (0.05 mole) of furane-2-carboxychloride **8** ($R^1$ = furan-2-yl) (Aldrich) was added dropwise below 5°. The reaction mixture was stirred for 30 minutes at 5°, allowed to warm to room temperature and left to stand overnight. The next day it was poured into 150 ml of cracked ice, the crystals that precipitated were filtered off and washed with ethanol to yield 9.0 g (70%) of 2-furoyl-2-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **9** ($R^1$ = furan-2-yl), mp 216-218° (acetonitrile); ir: ν C=O = 1635 $cm^{-1}$; pmr

(deuteriochloroform): δ, ppm 4.06 (s, 5H, $NCH_3$ and $CH_2$-10), 6.56 [dd (J = 3.5 and 1.8 Hz), 1H, furan H-4'], 7.24 [dd (J = 3.5 and 0.6 Hz), 1H, furan H-3'], 7.38 [dt (J = 6.8 and 1.3 Hz), 1H, CH-8], 7.47 [dt (J = 6.8 and 1.4 Hz), 1H, CH-7], 7.62 [dd (J = 2.4 and 1.0 Hz), 1H, furan H-5'), 7.82-7.93 (m, 4H, CH-4, 5, 6 and 9); cmr (DMSO-$d_6$): δ, ppm 31.3 (C-10), 35.2 ($NCH_3$), 111.9 (furan C-4'), 117.4 (furan C-3'), 118.8 (C-4), 123.0*, 124.8* and 126.5* (C-5, 6 and 9), 127.6 (C-8), 128.6 (C-7), 130.1 (C-5a), 131.2 (C-9a), 131.8 (C-3b), 134.3 (C-10a), 142.1 (C-9b), 155.2 (C-3a), 158.1 (C-2), 163.7 (C=O).

*Anal.* Calcd. for $C_{20}H_{14}N_2O_2S$ (MW 346.41): C, 69.35; H, 4.07; N, 8.09; S, 9.26. Found: C, 69.30; H, 3.82; N, 7.97; S, 9.00.

General Method for the Synthesis of Derivatives **12**.

A solution of 2.52 g (0.01 mole) of 2-chloroacetyl-2-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene [**9** ($R^1$ = chloromethyl] and 0.022 mole of the appropriate amine **11** in 10 ml of dimethylformamide was stirred at room temperature for 1 hour. Acetone (5 ml) was added to the reaction mixture, the crystals that precipitated were filtered off, thoroughly washed with water and acetone and recrystallised from an appropriate solvent.

2-(*N*-Pyrrolidinoacetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene **12/1** ($NR^2R^3$ = pyrrolidino).

The yield was 70%, mp 180-181° (90% ethanol); ir: ν C=O = 1658 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 1.84 (m, 4H, pyrr $CH_2$-3' and 4'), 2.70 [t (J = 5.3 Hz), 4H, pyrr $CH_2$-2' and 5'], 3.62 (s, 2H, $COCH_2$), 3.85 (s, 3H, $NCH_3$), 4.09 (s, 2H, $CH_2$-10), 7.40 [dt (J = 8.5 and 1.3 Hz), 1H, CH-8], 7.50 [dt (J = 8.1 and 1.3 Hz), 1H, CH-7], 7.87-7.93 (m, 4H, CH-4, 5, 6 and 9); cmr (deuteriochloroform): δ, ppm 23.9 (pyrr C-3' and 4'), 31.3 (C-10), 34.9 ($NCH_3$), 54.1 (pyrr C-2' and 5'), 58.9 ($COCH_2$), 118.1 (C-4), 122.8*, 124.6* and 126.4* (C-5, 6 and 9), 127.7 (C-8), 129.0 (C-7), 130.7 (C-5a), 131.4 (C-9a), 131.8 (C-3b), 135.4 (C-10a), 142.0 (C-9b), 156.1 (C-3a), 163.8 (C-2), 169.4 (C=O).

*Anal.* Calcd. for $C_{21}H_{21}N_3OS$ (MW 363.49): C, 69.39; H, 5.82; N, 11.56; S, 8.82. Found: C, 69.43; H, 5.98; N, 11.52; S, 8.89.

Maleate **12/1**.

To a hot solution of 1.8 g (0.005 mole) of 2-(*N*-pyrrolidinoacetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene (**12/1**, $NR^2R^3$ = pyrrolidino) in 310 ml of 95% ethanol a solution of 0.58 g (0.005 mole) of maleic acid in 10 ml of hot ethanol was added. The solution was filtered and allowed to crystallise. After cooling, the crystals that precipitated were filtered off and washed with ethanol to yield 1.44 g (89%) of 2-(*N*-pyrrolidinoacetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene maleate (**12/1** maleate), mp 215° dec.

*Anal.* Calcd. for $C_{25}H_{25}N_3O_5S$ (MW 479.57): C, 62.61; H, 5.25; N, 8.76; S, 6.69. Found: C, 62.45; H, 5.38; N, 8.57; S, 6.54.

2-(*N*-Piperidinoacetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene (**12/2**, $NR^2R^3$ = piperidino).

This compound was obtained in 94% yield, mp 208-210° (acetonitrile); ir: ν C=O = 1657 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 1.46 (m, 2H, pip $CH_2$-4'), 1.62 (m, 4H, pip $CH_2$-3' and 5'], 2.53 [t, 4H, pip $NCH_2$], 3.42 (s, 2H, $COCH_2$), 3.89 (s, 3H, $NCH_3$), 4.09 (s, 2H, $CH_2$-10), 7.40 [dt (J = 8.5 and 1.3 Hz), 1H, CH-8], 7.50 [dt (J = 8.0 and 1.4 Hz), 1H, CH-7], 7.87-7.96 (m, 4H, CH-4, 5, 6 and 9); cmr (deuteriochloroform): δ, ppm 24.0 (pip C-4'), 26.0 (pip C-3' and 5'), 31.4 (C-10), 35.3 ($NCH_3$), 54.7 (pip C-2' and 6'), 62.8 ($COCH_2$), 118.2 (C-4), 122.9*, 124.7* and 126.4* (C-5, 6 and 9), 127.8 (C-8), 129.0 (C-7), 130.8 (C-5a), 131.5 (C-9a), 131.9 (C-3b), 135.4 (C-10a), 142.0 (C-9b), 156.2 (C-3a), 164.1 (C-2), 169.4 (C=O).

*Anal.* Calcd. for $C_{22}H_{23}N_3OS$ (MW 377.51): C, 70.00; H, 6.14; N, 11.13; S, 8.49. Found: C, 69.83; H, 6.35; N, 11.08; S, 8.54.

Maleate **12/2**.

To a hot suspension of 9.0 g (0.024 mole) of 2-(*N*-piperidinoacetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene (**12/2**, $NR^2R^3$ = piperidino) in 950 ml of ethanol a solution of 2.78 g (0.024 mole) of maleic acid in 50 ml of hot ethanol was added. The solution was filtered and allowed to crystallise. After cooling the crystals that precipitated were filtered off and washed with ethanol to yield 8.29 g (70%) of 2-(*N*-piperidinoacetyl)-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene maleate (**12/2** maleate), mp 204-205° dec.

*Anal.* Calcd. for $C_{26}H_{27}N_3O_5S$ (MW 493.60): C, 63.27; H, 5.51; N, 8.51; S, 6.50. Found: C, 63.00; H, 5.44; N, 8.49; S, 6.50.

2-(*N*-Morpholinoacetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene (**12/3**, $NR^2R^3$ = morpholino).

This compound was obtained in 82% yield, mp 192-194° (ethanol); ir: ν C=O = 1657 $cm^{-1}$, ν COC = 1117 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 2.60 [t (J = 4.5 Hz), 4H, $NCH_2$], 3.42 (s, 2H, $COCH_2$), 3.75 [t (J = 4.5 Hz), 4H, $OCH_2$], 3.82 (s, 3H, $NCH_3$), 4.05 (s, 2H, $CH_2$-10), 7.39 [dt (J = 8.3 and 1.3 Hz), 1H, CH-8], 7.48 [dt (J = 6.8 and 1.2 Hz), 1H, CH-7], 7.85-7.93 (m, 4H, CH-4, 5, 6 and 9); cmr (deuteriochloroform): δ, ppm 31.4 (C-10), 35.2 ($NCH_3$), 53.7 ($NCH_2$), 61.9 ($COCH_2$), 66.9 ($OCH_2$), 118.4 (C-4), 122.9*, 124.8* and 126.5* (C-5, 6 and 9), 127.9 (C-8), 129.1(C-7), 130.8 (C-5a), 131.6 (C-9a), 131.9 (C-3b), 135.3 (C-10a), 142.0 (C-9b), 156.3 (C-3a), 163.9 (C-2), 168.5 (C=O).

*Anal.* Calcd. for $C_{21}H_{21}N_3O_2S$ (MW 379.48): C, 66.47; H, 5.58; N, 11.07; S, 8.45. Found: C, 66.32; H, 5.48; N, 11.21; S, 8.33.

Maleate **12/3**.

To a hot solution of 4.94 g (0.013 mole) of 2-(*N*-morpholinoacetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene (**12/3**, $NR^2R^3$ = morpholino) in 900 ml of ethanol a solution of 1.51 g (0.013 mole) of maleic acid in 50 ml of hot ethanol was added. The solution was treated with charcoal, filtered and allowed to crystallise. After cooling, the crystals that precipitated were filtered off and washed with dioxane to yield 5.73 g (89%) of 2-(*N*-morpholinoacetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz-[*e*]indene maleate (**12/3** maleate), mp 210-212° dec.

*Anal.* Calcd. for $C_{25}H_{25}N_3O_6S$ (MW 495.57): C, 60.59; H, 5.09; N, 8.48; S, 6.47. Found: C, 60.76; H, 4.89; N, 8.48; S, 6.41.

2-[*N*-(4-Methylpiperazin-1-yl-acetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene (**12/4**, $NR^2R^3$ = 4-methylpiperazine-1-yl).

This compound was obtained in 93% yield, mp 205-208° (ethanol); ir ν C=O = 1680 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 2.30 (s, 3H , pip $NCH_3$), 2.51 (m, 4H, pip $CH_2$-3' and 5'], 2.65 [t, 4H, pip $CH_2$-2' and 6'], 3.48 (s, 2H, $COCH_2$), 3.88 (bs, 3H, $NCH_3$), 4.02 (s, 2H, $CH_2$-10), 7.40 [dt (J = 8.5 and 1.3 Hz),

1H, CH-8], 7.51 [dt (J = 8.3 and 1.3 Hz), 1H, CH-7], 7.87-7.97 (m, 4H, CH-4, 5, 6 and 9); cmr (deuteriochloroform): δ, ppm 31.3 (C-10), 35.1 ($NCH_3$), 45.9 (pip $NCH_3$), 53.3 (pip C-3' and 5'), 55.0 (pip C-2' and 6'), 61.7 ($COCH_2$), 118.1 (C-4), 122.8*, 124.6* and 126.4* (C-5, 6 and 9), 127.8 (C-8), 129.0 (C-7), 130.7 (C-5a), 131.5 (C-9a), 131.8 (C-3b), 135.3 (C-10a), 142.0 (C-9b), 156.1 (C-3a), 163.8 (C-2), 168.8 (C=O).

*Anal.* Calcd. for $C_{22}H_{24}N_4OS$ (MW 392.53): C, 67.32; H, 6.16; N, 14.27; S, 8.17. Found: C, 67.44; H, 6.35; N, 14.22; S, 8.21.

Semifumarate **12/4**.

To a hot suspension of 8.6 g (0.0219 mole) of 2-[*N*-(4-methylpiperazin-1-yl-acetyl)methylamino-10*H*-thiazolo[5,4-*b*]-benz[*e*]indene (**12/4**, $NR^2R^3$ = 4-methylpiperazin-1-yl) in 1250 ml of ethanol a solution of 2.54 g (0.0219 mole) of fumaric acid in 100 ml of hot ethanol was added. A clear solution was obtained that shortly began to crystallise while hot. After cooling the crystals that precipitated were filtered off and washed with ethanol to yield 9.24 g (94%) of 2-(*N*-piperidinoacetyl)methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene semifumarate (**12/4** semifumarate), mp 222-223° dec. (50% ethanol).

*Anal.* Calcd. for $C_{22}H_{24}N_4OS \cdot 1/2C_4H_4O_4$ (MW 450.57): C, 63.97; H, 5.82; N, 12.44; S, 7.12. Found: C, 64.20; H, 5.73; N, 12.30; S, 7.10.

2-{*N*-[4-(2-Hydroxyethyl)piperazine-1-yl-acetyl]}methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene [**12/5**, $NR^2R^3$ = 4-(2-hydroxyethyl)piperazin-1-yl].

This compound was obtained in 76% yield, mp 190-191° (acetonitrile); ir: ν C=O = 1675 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 2.53-2.66 (m, 10H, $NCH_2$), 3.47 (s, 2H, $COCH_2$), 3.62 [t (J = 5.3 Hz), 2H, $OCH_2$), 3.85 (bs, 3H, $NCH_3$), 4.09 (s, 2H, $CH_2$-10), 7.41 [dt (J = 7 and 1.5 Hz), 1H, CH-8], 7.49 [dt (J = 8.2 and 1.5 Hz), 1H, CH-7], 7.86-7.95 (m, 4H, CH-4, 5, 6 and 9); cmr (deuteriochloroform): δ, ppm 31.5 (C-10), 35.3 ($NCH_3$), 52.9 and 53.4 (pip $NCH_2$), 58.0 ($NCH_2$), 59.4 ($OCH_2$), 61.6 ($COCH_2$), 118.2 (C-4), 122.9*, 124.8* and 126.5* (C-5, 6 and 9), 127.9 (C-8), 129.1 (C-7), 130.8 (C-5a), 131.6 (C-9a), 132.0 (C-3b), 135.4 (C-10a), 142.1 (C-9b), 156.4 (C-3a), 164.0 (C-2), 168.9 (C=O).

*Anal.* Calcd. for $C_{23}H_{26}N_4O_2S$ (MW 422.55): C, 65.38; H, 6.20; N, 13.26; S, 7.59. Found: C, 65.45; H, 6.48; N, 13.18; S, 7.66.

Maleate **12/5**.

To a hot solution of 5.25 g (0.0124 mole) of 2-{*N*-[4-(2-hydroxyethyl)piperazin-1-ylacetyl]}methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]inden [**12/5**, $NR^2R^3$ = 4-(2-hydroxyethyl)-piperazin-1-yl] in 520 ml of ethanol a hot solution of 1.4 g (0.012 mole) of maleic acid in 10 ml of hot ethanol was added. The solution obtained was treated with charcoal, filtered, and allowed to crystallise. After cooling, the crystals that precipitated were filtered off and washed with ethanol to yield 5.13 g (64%) of 2-{*N*-[4-(2-hydroxyethyl)piperazine-1-ylacetyl]}-methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene maleate (**12/5** maleate), mp 187-190° dec.

*Anal.* Calcd. for $C_{27}H_{30}N_4O_6S$ (MW 538.64): C, 60.21; H, 5.61; N, 10.40; S, 5.95. Found: C, 59.99; H, 5.69; N, 10.27; S, 6.02.

2-{*N*-[4-(3-Chlorophenyl)piperazin-1-ylacetyl]}methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene [**12/6**, $NR^2R^3$ = 4-(3-chlorophenyl)piperazin-1-yl].

This compound was obtained in 83% yield, mp 203-205° (ethanol); ir: ν C=O = 1667 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 2.75 [t (J = 4.7 Hz), 4H, pip $CH_2$-2' and 6'], 3.24 [t (J = 4.7 Hz), 4H, pip $CH_2$-3' and 5'], 3.50 (s, 2H, $COCH_2$), 3.86 (bs, 3H, $NCH_3$), 4.08 (s, 2H, $CH_2$-10), 6.79-6.87 (m, 3H, PhH-2, 4 and 6), 7.15 [t (J = 8 Hz), 1H, PhH-5], 7.40 [dt (J = 7 and 1.3 Hz), 1H, CH-8], 7.49 [dt (J = 7 and 1.3 Hz), 1H, CH-7], 7.86-7.95 (m, 4H, CH-4, 5, 6 and 9); cmr (deuteriochloroform): δ, ppm 31.0 (C-10), 34.6 ($NCH_3$), 46.5 (pip C-3' and 5'), 51.9 (pip C-2' and 6'), 58.7 ($COCH_2$), 113.5 (PhC-2"), 114.6 (PhC-6"), 117.2 (PhC-4"), 118.2 (C-4), 122.7*, 124.5*, 126.3* (C-5, 6 and 9), 127.4 (C-7), 128.4 (C-8), 130.0 (PhC-5"), 131.1*, 131.2* (C-5a and 9a), 131.6 (PhC-3"), 133.7 (C-3b), 134.2 (C-10a), 141.8 (C-9b), 151.4 (C-3a), 163.1 (C-2), 166.2 (PhC-1"), 167.4 (C=O).

*Anal.* Calcd. for $C_{27}H_{25}ClN_4OS$ (MW 489.04): C, 66.31; H, 5.15; N, 11.46; S, 6.56; Cl, 7.25. Found: C, 66.42; H, 5.34; N, 11.36; S, 6.43; Cl, 7.28.

Maleate **12/6**.

To a hot solution of 6.61 g (0.0135 mole) of 2-{*N*-[4-(3-chlorophenyl)piperazin-1-ylacetyl]}methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene [**12/6**, $NR^2R^3$ = 4-(3-chlorophenyl)-piperazin-1-yl] in 300 ml of dioxane a hot solution of 1.57 g (0.0135 mole) of maleic acid in 15 ml of hot ethanol was added. The hot solution was treated with charcoal, filtered, and allowed to crystallise. After cooling, the crystals that precipitated were filtered off and washed with ethanol to yield 5.4 g (66%) of 2-{*N*-[4-(3-chlorophenyl)piperazin-1-ylacetyl]}methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene maleate (**12/6** maleate), mp 210-212° dec. (dioxane).

*Anal.* Calcd. for $C_{31}H_{29}ClN_4O_5S$ (MW 605.13): C, 61.53; H, 4.83; N, 9.26; S, 5.30, Cl, 5.86. Found: C, 61.58; H, 5.02; N, 9.13; S, 5.25; Cl, 5.93.

Hydrochloride Monohydrate **12/6**.

To a stirred solution of 6.3 g (0.0128 mole) of 2-{*N*-[4-(3-chlorophenyl)piperazin-1-ylacetyl]}methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene [**12/6**, $NR^2R^3$ = 4-(3-chlorophenyl)-piperazin-1-yl] in 500 ml of dimethylformamide 15 ml of concentrated hydrochloric acid was added dropwise below 40°. After cooling, the crystals that precipitated were filtered off and washed with ethanol to yield 4.4 g (63%) of 2-{*N*-[4-(3-chlorophenyl)piperazin-1-ylacetyl]}methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene hydrochloride monohydrate [**12/6**•HCl•$H_2O$], mp >255° (95% ethanol).

*Anal.* Calcd. for $C_{27}H_{28}Cl_2N_4O_2S$ (MW 543.53): C, 59.66; H, 5.19; N, 10.31; S, 5.90; Cl, 13.05. Found: C, 59.67; H, 5.27; N, 10.38; S, 5.83; Cl, 12.88.

2-{*N*-[4-(Pyrimidin-2-yl)piperazin-1-ylacetyl]}methylamino-10*H*-thiazolo[5,4-*b*]benz[*e*]indene [**12/7**, $NR^2R^3$ = 4-(pyrimidin-2-yl)piperazin-1-yl].

This compound was obtained in 91% yield, mp 244-246° (ethanol); ir: ν C=O = 1663 $cm^{-1}$; pmr (deuteriochloroform): δ, ppm 2.68 [t (J = 4.9 Hz), 4H, pip $CH_2$-2, and 6'], 3.52 (s, 2H, $COCH_2$), 3.90 (b, 7H, $NCH_3$ and pip $CH_2$-3' and 5'), 4.10 (s, 2H, $CH_2$-10), 6.48 [t (J = 4.8 Hz), 1H, pyrim 4'], 7.40 [dt (J = 7 and 1.3 Hz), 1H, CH-8], 7.49 [dt (J = 7 and 1.3 Hz), 1H, CH-7], 7.86-7.95 (m, 4H, CH-4, 5, 6 and 9), 8.30 [d (J = 4.8 Hz), 2H, pyrim 3' and 5'].

*Anal.* Calcd. for $C_{25}H_{24}N_6OS$ (MW 456.57): C, 65.77; H, 5.30; N, 18.41; S, 7.02. Found: C, 65.86; H, 5.42; N, 18.36; S, 6.98.

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