Nitrogen Bridgehead Compounds. Part 88 [1]. Synthesis of 3*H*,7*H*-[1,4]Diazepino[3,4-*b*]quinazoline-3,7-diones

Mónika Szabó, József Kökösi*, and László Örfi

Institute for Pharmaceutical Chemistry, Semmelweis University of Medicine, Högyes E.u. 9, H-1092 Budapest, Hungary

Attila Kovács

Institute for General and Analytical Chemistry, Technical University, Gellért tér 4, H-1114 Budapest, Hungary

István Hermecz

CHINOIN Pharmaceutical and Chemical Works Ltd., P. O. Box 110, H-1325, Budapest, Hungary

Received May 29, 1996

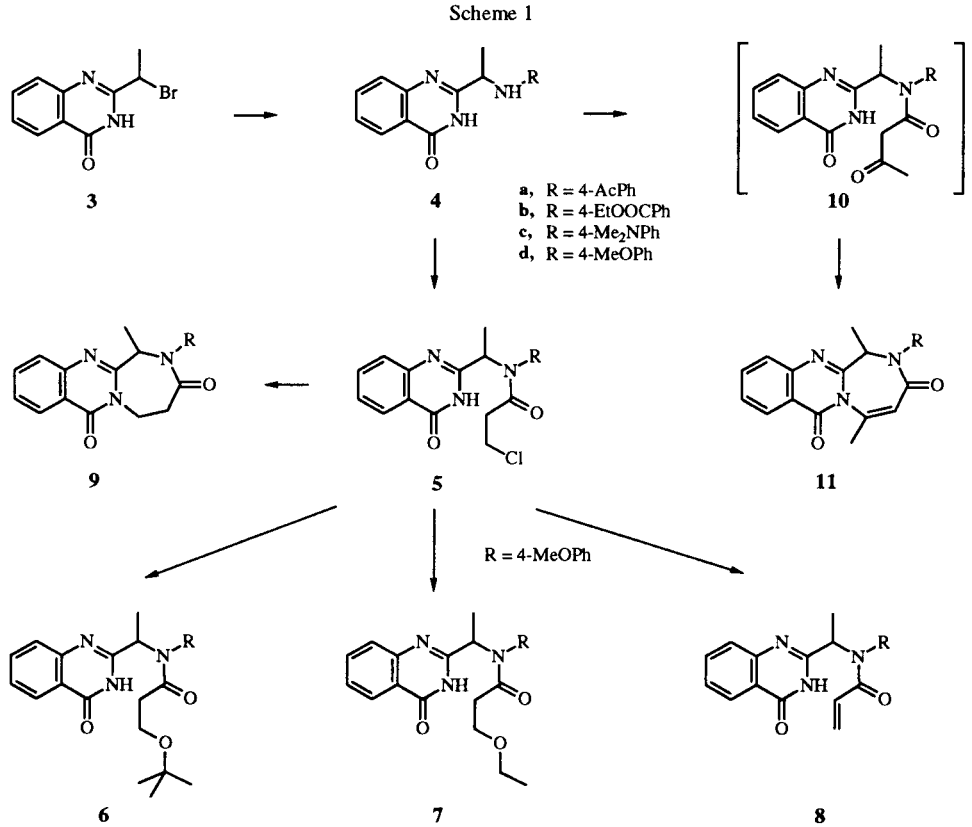
3*H*,7*H*-[1,4]Diazepino[3,4-*b*]quinazolone-3,7-diones **9**, **11** were synthesized starting from 2-(1-bromoethyl)quinazolin-4(3*H*)-ones **3** and **17** *via* 2-[1-(4-methoxyphenylamino)ethyl]quinazolin-4(3*H*)-ones **4** and **18**. Cyclization of 3-[2-(1-bromoethyl)-4-oxo-3,4-dihydroquinazolin-3-yl)propionic acid **14** by the action of triethylamine provided the first representative of the tricyclic 7*H*-[1,4]oxazepino[3,4-*b*]quinazoline-3,7-dione system, compound **15**. The new tricyclic derivatives **9**, **11** and **15** are characterized by uv, ir and ^{1}H nmr spectroscopy.

J. Heterocyclic Chem., **34**, 21 (1997).

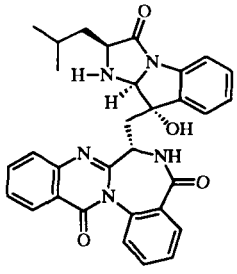
Introduction.

The investigation of cholecystokinins has attracted considerable interest due to their neurotransmitter and neuromodulator effects [2,3]. These studies opened new possibilities for the development of new cholecystokinin agonists and antagonists as new therapeutic agents in analgesic [4], schizophrenic [5-7] and gastric therapy [8,9]. One of the most important cholecystokinin receptor antagonists is

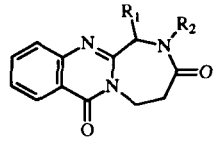
Scheme 1



asperlicin **1**, the first natural nonpeptide compound, extracted from microbial source, *Aspergillus alliaceus* [10,11]. The synthesis of asperlicin [12] and it's partial structural derivatives [12] has considerably provided to the understanding of the function and structure of cholecystokinin receptors. The synthesis of benzodiazepine fragment of asperlicin **1** contributed to the development of cholecystokinin selective pharmacone families [13,14].



1



2

In this paper we report a new synthetic method for derivatives [1,4]diazepino[3,4-*b*]quinazoline-3,7-diones **2** fragment of asperlicin **1**, starting from 2-(1-bromoethyl)quinazolin-4(3*H*)-ones **3**. *Until now only a few 2-substituted* 1,2,4,5-tetrahydro-3*H*,7*H*-[1,4]diazepino[3,4-*b*]quinazolin-7-ones have been prepared by cyclocondensation of *anthranilic acid and 4-substituted 2-methylthio*-4,5,6,7-tetrahydro-3*H*-1,4-diazepines [15].

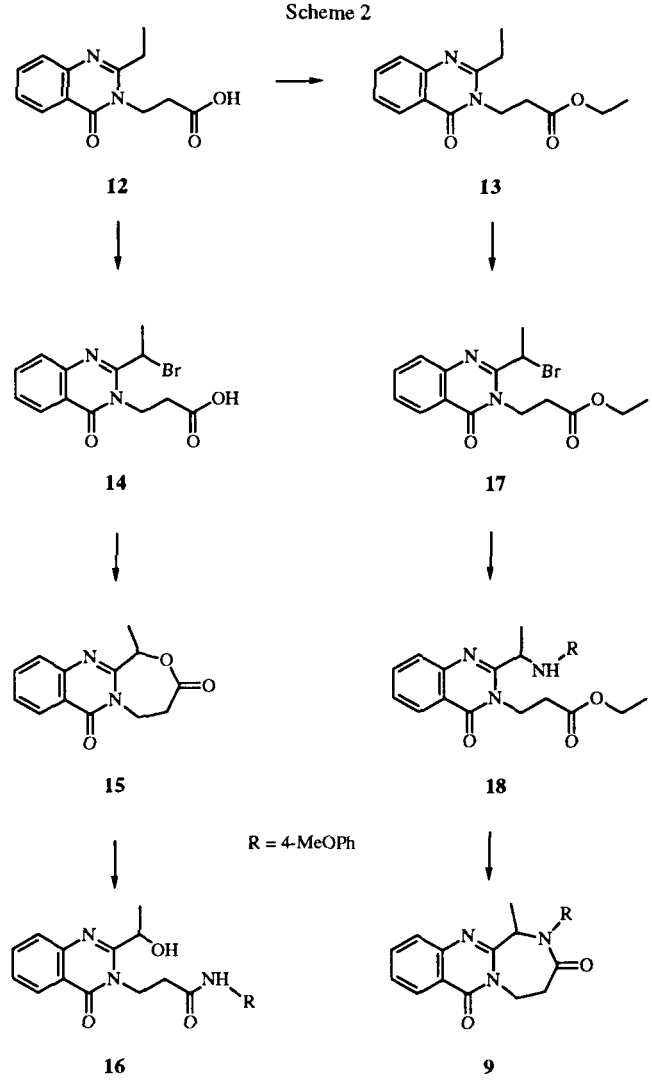
Synthesis.

The active methylene group reactivity of the 2-alkyl moiety of 2-alkylquinazolin-4(3*H*)-ones was applied for the functionalization of the quinazolone ring system in electrophilic substitution reactions [16,17].

2-(1-Bromoethyl)quinazolin-4(3*H*)-ones **3**, **14**, **17** were obtained from 2-ethylquinazolin-(3*H*)-one [17] and its 3-propionic acid derivatives **12** and **13** with molar equivalents of bromine in glacial acetic acid in the presence of sodium acetate. 2-[1-(Arylamino)ethyl)quinazolin-4(3*H*)-ones 4 were prepared from 2-(1-bromoethyl) derivative **3** with anilines in *N*,*N*-dimethylformamide at 100°. *4-Dimethylaminophenyl derivative* **4c** *was prepared under* nitrogen atmosphere. The amino group of compound **4d** was acylated with 3-chloropropionyl chloride in good yield. Instead of cyclization 2-{1-[*N*-(3-chloropropionyl)-*N*-(4-methoxyphenyl)amino]ethyl} derivative **5** gave either substituted **6** and **7** or elimination product **8**, when it was reacted with potassium *tert*-butoxide and sodium ethylate in tetrahydrofuran (Scheme 1).

The desired [1,4]diazepino[3,4-*b*]quinazoline-3,7-dione **9** was obtained under phase-transfer condition in 39% yield when compound **5** was heated under reflux in a mixture of 20% sodium hydroxide solution and dichloromethane in the presence of benzyltriethylammonium chloride. A better yield (57%) could be achived when ethyl 3-{2-[1-(4-methoxyphenylamino)ethyl]4-oxo-3,4-dihydroquinazolin-3-yl}propionate **18**, prepared from 2-(1-bromoethyl) derivative **17** with 4-methoxyaniline, was treated with sodium hydride in tetrahydrofuran (Scheme 2).

Scheme 2



12 **13** **14** **17** **15** **18** **16** **9**

First representative of 1,3,4,5-tetrahydro-7*H*-[1,4]oxazepino[3,4-*b*]quinazoline-3,7-dione ring system, compound **15**, was obtained in good yield by the cyclization of 3-[2-(1-bromoethyl)-4-oxo-3,4-dihydroquinazolin-3-yl}propionic acid **14** in the presence of triethylamine in chloroform at ambient temperature for 12 hours. When the [1,4]oxazepino[3,4-*b*]quinazoline-3,7-dione **15** was treated with 4-methoxyaniline in boiling ethanol, a ring-opened product **16** was obtained, instead of 3*H*,7*H*-[1,4]diazepino[3,4-*b*]quinazoline-3,7-dione **9**.

1,5-Dimethyl-2-(4-methoxyphenyl-1,2-dihydro-3*H*,7*H*-[1,4]diazepino[3,4-*b*]quinazoline-3,7-dione **11** was pre-

pared in 58% yield when compound **4d** was first reacted with ethyl acetoacetate at 190° for 5 hours, then the condensation product **10** was treated with polyphosphoric acid at 120° for 3 hours (Scheme 1).

EXPERIMENTAL

Melting points were determined on a Boetius apparatus and are uncorrected. Yields were not maximized. The uv spectra were recorded in ethanol with a Unicam SP-800 spectrometer, and the ir spectra were recorded with a Pye Unicam SP-1100 IR apparatus in potassium bromide disk. The ^{1}H nmr spectra were obtained in deuteriochloroform on a JEOL FX-100 (100 MHz) and Bruker AC-250 (250 MHz) equipment (TMS was used as internal standard). Elemental analyses (C, H, N) were performed with Perkin Elmer 2400 CHN Analyzer.

2-(1-Aminoethyl)quinazolin-4(3*H*)-ones **4a-d**.

General Procedure.

A mixture of 2-(bromoethyl)quinazolin-4-(3*H*)-one **3** (253 mg, 1 mmole) [17], the appropriate aniline (2.5 mmoles) and *N,N*-dimethylformamide (5 ml) was stirred for 2.5 hours at 100°. The reaction mixture was poured into ice water and the precipitated solid part was filtered off, and washed with water. The dried product **4** was crystallized from ethanol.

2-[1-(4-Acetylphenylamino)ethyl]quinazolin-4(3*H*)-one (**4a**).

This compound was obtained in a yield of 55%, mp 205-209°; uv: 319 (log ε 2.50), 350 (3.52), 275 (3.90), 270 (3.92), 228 nm (4.35); ir: ν_{CO} 1685 cm^{-1}.

Anal. Calcd. for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.33; H, 5.58; N, 13.57.

2-[1-(4-Ethoxycarbonylphenylamino)ethyl]quinazolin-4(3*H*)-one (**4b**).

This compound was obtained in a yield of 48%, mp 174-178°; uv: 310 (log ε 2.50), 300 (3.53), 278 (3.90), 270 (3.91), 224 nm (4.35); ir: ν_{CO} 1685 cm^{-1}.

Anal. Calcd. for $C_{19}H_{19}N_3O_3$: C, 67.64; H, 5.68; N, 12.45. Found: C, 67.65; H, 5.73; N, 12.57.

2-[1-(4-Dimethylphenylamino)ethyl]quinazolin-4(3*H*)-one (**4c**).

The reaction was carried out under a nitrogen atmosphere, and this compound was obtained in a yield of 83%, mp 152-154°; uv: 414 (log ε 3.18), 320 (3.50), 305 (3.57), 275 (3.90), 259 (3.91), 225 nm (4.35); ir: ν_{CO} 1685 cm^{-1}.

Anal. Calcd. for $C_{18}H_{20}N_4O$: C, 70.11; H, 6.54; N, 18.17. Found: C, 70.13; H, 6.48; N, 18.22.

2-[1-(4-Methoxyphenylamino)ethyl]quinazolin-(3*H*)-one (**4d**).

This compound was obtained in a yield of 67% yield, mp 191-195°; uv: 320 (log ε 2.48), 350 (3.51), 278 (3.88), 277 (3.92), 227 nm (4.32); ir: ν_{CO} 1685 cm^{-1}.

Anal. Calcd. for $C_{17}H_{17}N_3O_2$: C, 69.14; H, 5.80, N, 14.63. Found: C, 69.17; H, 5.84, N, 14.20.

2-{1-[*N*-(3-Chloropropionyl)-*N*-(4-methoxyphenyl)amino]-ethyl}quinazolin-4(3*H*)-one (**5**).

To a solution of compound **4d** (295 mg, 1 mmole) in *N,N*-dimethylformamide (5 ml), 3-chloropropionyl chloride (159 mg, 1.25 mmoles) was dropwise added under cooling. The reaction mixture was stirred for 1 hour, then it was poured into ice water. The precipitated crystals were filtered off and recrystallized from 2-propanol. Compound **5** was obtained in 87% yield, mp 186-187°; ^{1}H nmr: (100 MHz) 1.67 δ (d, CH-C*H*$_3$, 3H), 3.87 (s, OC*H*$_3$, 3H), 3.55 (t, CO-CH$_2$, 2H), 4.55 (t, CH$_2$Cl, 2H), 5.75 (q, C*H*-CH$_3$, 1H), 6.82-7.86 (m, C$_6$H$_4$, 6-H, 7-H, 8-H, 7H), 8.38 (d, 5-H, 1H), 10.54 (br s, NH, 1H).

Anal. Calcd. for $C_{20}H_{20}N_3O_3Cl$: C, 62.26; H, 5.22, N, 10.89; Cl, 9.19. Found: C, 62.30; H, 5.26, N, 10.81; Cl, 9.25.

2-{1-[*N*-(3-*tert*-Butoxypropionyl)-*N*-(4-methoxyphenyl)-amino]ethyl}quinazolin-4(3*H*)-one (**6**).

A mixture of compound **5** (386 mg, 1 mmole), potassium *tert*-butoxide (112 mg, 1 mmole) and tetrahydrofuran (5 ml) was heated under reflux for 2 hours. The reaction mixture was evaporated *in vacuo* to dryness. The residue was suspended in water (10 ml) and the *p*H was adjusted to 7 with 5% acetic acid solution. The solid part was filtered off and was recrystallised from 2-propanol to give compound **6** in 75% yield, mp 132-135°; uv: 322 (log ε 3.54), 307 (3.56), 278 (3.91), 270 (3.93), 232 nm (4.28); ir: ν_{CO} 1685 and 1678 cm^{-1}.

Anal. Calcd. for $C_{24}H_{29}N_3O_4$: C, 68.07; H, 6.90; N, 9.92. Found: C, 68.02; H, 6.96; N, 9.91.

2-{1-[*N*-(3-Ethoxypropionyl)-*N*-(4-methoxyphenyl)amino]-ethyl}quinazolin-4(3*H*)-one (**7**).

A mixture of compound **5** (386 mg, 1 mmole), sodium ethoxide (136 mg, 2 mmole) and tetrahydrofuran (5 ml) was stirred for 1 hour at ambient temperature. The reaction mixture was evaporated *in vacuo* to dryness and the residue was treated with water (10 ml) and the *p*H of the reaction mixture was adjusted to 7 with 5% acetic acid solution. The reaction mixture was extracted with chloroform (3 x 15 ml). The combined and dried organic phase was evaporated *in vacuo* to dryness and the residue was recrystallized from diethyl ether to give compound **7** in 82% yield, mp 126-129°; uv: 318 (log ε 3.52), 306 (3.54), 273 (3.90), 271 (3.92), 240 nm (4.28); ir: ν_{CO} 1685 and 1675 cm^{-1}; ^{1}H nmr: (100 MHz) 1.17 δ (t, CH$_2$-CH$_3$, 3H), 1.43 (d, CH-C*H*$_3$, 3H), 2.40 (t, CO-CH$_2$, 2H), 3.52 (c, 2H, OC*H*$_2$-CH$_3$, 2H), 3.67 (t, 2H, CH$_2$-C*H*$_2$O, 2H), 3.82 (s, OCH$_3$, 3H), 5.87 (q, C*H*-CH$_3$, 1H), 6.81-7.83 (m, C$_6$H$_4$, 6-H, 7-H, 8-H, 7H), 8.39 (d, 5-H, 1H), 10.30 (br s, NH).

Anal. Calcd. for $C_{22}H_{25}N_3O_4$: C, 66.82; H, 6.37; N, 10.63. Found: C, 66.87; H, 6.35; N, 10.76.

2{1-[*N*-Acryloyl-*N*-(4-methoxyphenyl)amino]ethyl}quinazolin-4(3*H*)-one (**8**).

A mixture of compound **5** (386 mg, 1 mmole), sodium ethoxide (136 mg, 2 mmoles) and ethanol (5 ml) was refluxed for 2 hours. The reaction mixture was evaporated *in vacuo* to dryness. The residue was treated with water (10 ml) and the *p*H was adjusted to 7 with 5% acetic acid solution. The reaction mixture was extracted with chloroform (3 x 15 ml) and the combined and dried organic phase was evaporated *in vacuo* to dryness. The residue was recrystallized from diethyl ether to give compound **8** in 79% yield, mp 163-167°; uv: 318 (log ε 3.53), 308 (3.56), 276 (3.98), 272 (3.91), 235 nm (4.26); ir: ν_{CO} 1687 and 1675 cm^{-1}; ^{1}H nmr: (100 MHz) 1.44 δ (d, CH-C*H*$_3$, 3H), 3.67 (s, OCH$_3$, 3H), 5.76 (q, C*H*-CH$_3$, 1H), 6.15 (m, CH=C*H*$_2$, 2H),

6.58 (dd, J = 16.2 Hz, C*H*=CH_2, 1H), 6.82-7.82 (m, 7H, C_6H_4, 6-H, 7-H, 8-H, 7H), 8.40 (d, 5-H, 1H), 11.10 (br s, NH, 1H).

Anal. Calcd. for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.77; H, 5.56; N, 12.05.

3-(2-Ethyl-4-oxo-3,4-dihydroquinazolin-3-yl)propionic Acid (**12**).

A mixture of 2-ethyl[3,1]benzoxazin-4-one [18] (175 mg, 1 mmole), β-alanine (178 mg, 2 mmoles) and glacial acetic acid (5 ml) was refluxed for 3 hours. After cooling to room temperature the reaction mixture was poured into ice water and the white crystals were filtred off and recrystallized from water to give compound **12** in 58% yield, mp 191-193°.

Anal. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.42; H, 5.78; N, 11.41.

Ethyl 3-[2-Ethyl-4-oxo-3,4-dihydroquinazolin-3-yl]propionate (**13**).

A mixture of compound **12** (246 mg, 1 mmole) and ethanol (5 ml) was heated under reflux in the presence of concentrated hydrogen chloride solution (0.1 ml) for 9 hours. The reaction mixture was evaporated *in vacuo* to dryness, and residue was dissolved in diethyl ether (5 ml). The organic phase was extracted with saturated 10% sodium carbonate solution (3 x 5 ml). Then the dried organic phase was evaporated *in vacuo* to dryness. The residue was recrystallized from diethyl ether. This way compound **13** was obtained in 65% yield, mp 191-193°; uv: 324 (log ε 3.54), 304 (3.55), 271 (4.00), 227 nm (4.32).

Anal. Calcd. for $C_{15}H_{10}N_2O_3$: C, 65.68; H, 6.61, N, 10.21. Found: C, 65.72; H, 6.63, N, 10.24.

Ethyl 3-[2-(1-Bromoethyl)-4-oxo-3,4-dihydroquinazolin-3-yl]propionate (**17**).

To a mixture of compound **13** (274 mg, 1 mmole), sodium acetate (98 mg, 1.2 mmoles) and glacial acetic acid (5 ml) bromine (160 mg, 1 mmole) in glacial acetic acid (1 ml) was added dropwise at 40-50° and the reaction mixture was stirred at ambient temperature for 3 hours. The reaction mixture was left to stand in a refrigerator overnight and the precipitated crystals were filtered off, washed with water. The dried crystals were recrystallized from ethanol to give compound **17** in 73% yield, mp 166-169°; uv: 324 (log ε 3.53), 309 (3.55), 386 (3.98), 230 nm (4.32); ir: ν_{CO} 1728 and 1695 cm^{-1}.

Anal. Calcd. for $C_{15}H_{17}N_2BrO_3$: C, 51.01; H, 4.85; N, 7.93; Br, 22.62. Found: C, 51.00; H, 4.88; N, 7.90; Br, 22.65.

Ethyl 3-{2-[1-(4-Methoxyphenylamino)ethyl]-4-oxo-3,4-dihydroquinazolin-3-yl}propionate (**18**).

A mixture of compound **17** (353 mg, 1 mmole) 4-methoxyaniline (246 mg, 2 mmoles) and ethanol (5 ml) was heated under reflux for 6 hours, then the reaction mixture was evaporated *in vacuo* to dryness. The residue was dissolved in chloroform (10 ml) and the solution was extracted with saturated 10% sodium carbonate solution (3 x 15 ml). The dried organic phase was evaporated *in vacuo* to dryness. The residue was recrystallized from 2-propanol to give compound **18** in 66% yield, mp 132-134°. ^1H nmr: (100 MHz) 1.16 (t, O-CH_2CH_3, 3H), 1.60 δ (d, CH-CH_3, 3H), 2.63 (t, $COCH_2$, 2H), 3.65 (s, OCH_3, 2H), 4.02 (q, O-CH_2CH_3, 2H), 4.18 (t, N-CH_2, 2H), 4.93 (q, C*H*-CH_3, 1H), 7.26 (s br, NH, 1H), 7.76-7.24 (m, 6-H, 7-H, 8-H, 1H), 8.26 (d, 5-H, 1H).

Anal. Calcd. for $C_{22}H_{25}N_3O_4$: C, 66.82; H, 6.37; N, 10.63. Found: C, 66.88; H, 6.45; N, 10.91.

3-[2-(1-Bromoethyl)-4-oxo-3,4-dihydroquinazolin-3-yl]propionic Acid (**14**).

To a mixture of compound **12** (246 mg, 1 mmole), sodium acetate (82 mg, 1 mmole) and glacial acetic acid (5 ml) bromine (160 mg, 1 mmole) in glacial acetic acid (1 ml) was added dropwise at 40-50° and the reaction mixture was stirred for 3 hours. The reaction mixture left to stand in a refrigerator overnight. The crystals were filtered off, washed with water and recrystallized from 2-propanol to give compound **14** in 73% yield, mp 166-169°; uv: 318 (log ε 3.50), 307 (3.52), 300 (3.95), 234 nm (4.32); ir: ν_{CO} 1710 and 1680 cm^{-1}; ^1H nmr: (100 MHz) 2.19 δ (t, CH-CH_3, 3H), 2.91 (t, $COCH_2$, 2H), 4.48 (d, N-CH_2, 2H), 5.50 (q, CM-Br, 1 H), 7.48-7.82 (m, 6-H, 7-H, 8-H, 3H), 8.26 (d, 5-H, 1H), 9.00 (s, OH, 1H).

Anal. Calcd. for $C_{13}H_{13}N_2O_3Br$: C, 48.02; H, 4.03; N, 8.62; Br, 24.57. Found: C, 48.13; H, 4.06; N, 8.65; Br, 24.52.

1-Methyl-1,3,4,5-tetrahydro-7*H*-[1,4]oxazepino[3,4-*b*]quinazoline-3,7-dione (**15**).

A mixture of compound **14** (325 mg, 1 mmole), triethylamine (202 mg, 2 mmoles) and chloroform (5 ml) was stirred at room temperature for 12 hours. The reaction mixture was extracted with 5% acetic acid (3 x 5 ml), then with water (3 x 5 ml). The dried organic phase was evaporated *in vacuo* to dryness and the residue was recrystallized from diethyl ether to give tricyclic compound **15** in 75% yield, mp 199-201°; uv: 320 (log ε 3.56), 307 (3.60), 283 (3.92), 272 (3.95), 232 nm (4.29); ir: ν_{CO} 1738 and 1680 cm^{-1}; ^1H nmr: (250 MHz) 1.90 δ (d, 1-CH_3, 3H), 3.22 (m, 4-H_2, 2H), 4.00 (t, J = 14.6, and 6.5 Hz, 5-H_{ax}, 1H), 5.17 (t, J = 14.6, and 6.5 Hz, 5-H_{eq}, 1H), 5.55 (q, 1-H, 1H), 7.68-7.42 (m, 9-H, 10-H, 11-H, 3H), 8.10 (d, 8-H, 1H).

Anal. Calcd. for $C_{13}H_{12}N_2O_3$: C, 63.04; H, 5.73; N, 11.38. Found: C, 63.56; H, 5.85; N, 11.45.

N-(4-Methoxyphenyl)-3-[2-(1-hydroxyethyl)-4-oxo-3,4-dihydroquinazolin-3-yl]propionamide (**16**).

A mixture of compound **15** (325 mg, 1 mmole) 4-methoxyaniline (246 mg, 2 mmoles) and ethanol (5 ml) was heated under reflux for 5 hours. The reaction mixture was evaporated *in vacuo* to dryness and residue was treated with 5% hydrogen chloride solution (5 ml) and it was mixed with chlorofom (3 x 5 ml). The dried and combined organic phase was evaporated *in vacuo* to dryness and the residue was recrystallized from a mixture of 2-propanol and diethyl ether to give compound **16** in 66% yield, mp 137-141°. ^1H nmr: (250 MHz) 1.67 δ (d, CH-CH_3, 3H), 2.95 (t, $COCH_2$, 2H), 3.55 (s, OH, 1H), 3.72 (s, OCH_3, 3H), 4.32 (dt, J = 17.7, and 7.3 Hz, N-CH_{ax}, 1H), 4.55 (dt, J = 17.7, and 7.3 Hz, N-CH_{eq}, 1H), 5.22 (q, C*H*-CH_3, 1H), 7.76-7.04 (m, 6-H, 7-H, 8-H, 3H), 7.94 (s, NH, 1H), 8.22 (d, 5-H, 1H).

Anal. Calcd. for $C_{20}H_{21}N_3O_4$: C, 65.38; H, 5.76; N, 11.44. Found: C, 65.41; H, 5.81; N, 11.57.

1-Methyl-2-(4-methoxyphenyl)-1,2,4,5-tetrahydro-3*H*,7*H*-[1,4]diazepino[3,4-*b*]quinazoline-3,7-dione (**9**).

Method A.

A mixture of compound **5** (386 mg, 1 mmole), benzyltriethylammonium chloride (114 mg, 0.5 mmole), 20% sodium hydroxide solution (5 ml) and dichloromethane (5 ml) was heated under reflux for 5 hours. After cooling the separeted organic phase was extracted with water (3 x 5 ml). The dried organic phase was

evaporated *in vacuo* to dryness and the residue was recrystallized from 2-propanol to give tricyclic compound **9** in 39% yield, mp 147-148°; uv: 312 (log ε 3.67), 302 (3.71), 268 (3.88), 225 nm (4.12); ir: ν_{CO} 1687 and 1678 cm^{-1}; ^1H nmr: (250 MHz) 1.96 δ (d, 1-CH_3, 3H), 2.94 (t, 4-H_2, 2H), 3.67 (s, OCH_3, 3H), 4.45 (dt, J = 14.3, and 6.5 Hz, 5-H_{ax}, 1H), 5.08 (dt, J = 14.3, and 6.5 Hz, 5-H_{eq}, 1H), 5.56 (q, 1-H, 1H), 6.81-7.83 (m, C_6H_4, 9-H, 10-H, 11-H, 7H), 8.21 (d, 7-H, 1H).

Anal. Calcd. for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.75; H, 5.45; N, 12.07.

Method B.

A mixture of compound **18** (395 mg, 1 mmole), sodium hydride (120 mg, 5 mmoles) and tetrahydrofuran (5 ml) was stirred at room temperature for 2 hours, then it was heated under reflux for 3 hours. To the cooled reaction mixture some drops of glacial acetic acid were added, and the reaction mixture was evaporated *in vacuo* to dryness. The residue was treated chloroform (5 ml) and the organic phase was extracted first with 10% sodium carbonate solution (2 x 5 ml), then with water (2 x 5 ml). The dried organic phase was evaporated *in vacuo* to dryness and the residue was recrystallized from ethyl acetate to give compound **9** in 57% yield, mp 147-148°, and it did not give melting point depression with a sample prepared according to method A.

1,5-Dimethyl-2-(4-methoxyphenyl)-1,2-dihydro-3*H*,7*H*-[1,4]diazepino[3,4-*b*]quinazolin-3,7-dione (**11**).

A mixture of compound **4d** (295 mg, 1 mmole) and ethyl acetoacetate, (1.3 g, 10 mmoles) was heated under reflux for 5 hours. The reaction mixture was evaporated *in vacuo* to dryness, and the residue **10** was heated in polyphosphoric acid (3.3 g, Fluka) at 120° for 3 hours. After cooling the reaction mixture was treated with water (10 ml), and the reaction mixture was extracted with chloroform (3 x 15 ml). The combined organic phase was washed with 5% sodium carbonate solution (2 x 20 ml) and the dried organic phase was evaporated *in vacuo* to dryness. The oily residue was crystallized from ethyl acetate to give tricyclic compound **11** in 58% yield, mp 181-183°; uv: 325 (log ε 3.45), 312 (3.51), 278 (3.96), 238 nm (4.23); ir: ν_{CO} 1680 and 1665 cm^{-1}; ^1H nmr: (100 MHz) 1.57 δ (d, 1-CH_3, 3H), 2.34 (s, 5-CH_3, 3H), 3.87 (s, OCH_3, 3H), 4.93 (q, 1-H, 1H), 5.88 (s, 4-H, 1H), 6.82-7.83 (m, C_6H_4, 9-H, 10-H, 11-H, 7H), 8.14 (d, 8-H, 1H).

Anal. Calcd. for $C_{21}H_{19}N_3O_3$: C, 69.79; H, 5.30; N, 11.63. Found: C, 69.75; H, 5.37; N, 11.61.

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