2428 Russian Chemical Bulletin, International Edition, Vol. 50, No. 12, pp. 2428—2432, December, 2001

Reactions of cyclic enaminoketones with benzylidenemalononitriles. Synthesis of new fused heterocyclic systems containing the 1,4-dihydropyridine fragment

B. V. Lichitsky, S. N. Ivanov, A. A. Dudinov, S. A. Woznesensky, and M. M. Krayushkin★

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (095) 135 5328. E-mail: mkray@ioc.ac.ru

The reactions of cyclic enaminoketones with benzylidenemalononitriles were examined and a new procedure was developed for the synthesis of fused heterocyclic systems containing the 1,4-dihydropyridine ring, *viz.*, thienopyrimidoquinolines and furopyrimidoquinolines. The characteristic features of the reactions and the structures of the resulting compounds were investigated.

Key words: cyclic enaminoketones, benzylidenemalononitriles, fused 1,4-dihydropyridines, thienopyrimidoquinolines, furopyrimidoquinolines, Michael reaction.

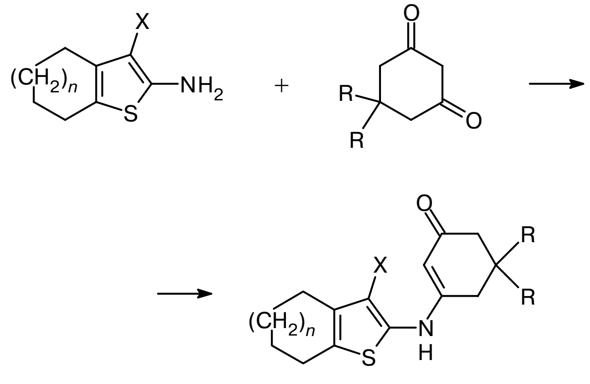
1,4-Dihydropyridines and their fused derivatives have attracted considerable recent attention due to their high biological activities.[1—4] As a continuation of our studies on the synthesis of 1,4-dihydropyridine-containing systems,[5,6] we examined the reactions of *N*-hetaryl-substituted enaminoketones with benzylidenemalononitriles giving rise to new heterocyclic structures in which the dihydropyridine ring is annelated with the thienopyrimidine or furopyrimidine fragment.

Cyclic enaminoketones have promise as the starting compounds for the synthesis of the above-mentioned compounds. The use of these compounds allows one to prepare fused 1,4-dihydropyridines containig substituents at the ring nitrogen atom introduced in a stage of the synthesis of enaminoketones. For example, the reactions of 3-anilino-5,5-dimethylcyclohexen-2-one with benzylidenemalononitriles in the presence of a base afford substituted hexahydroquinolines.[7] The use of functionally substituted heterocyclic amines in these reactions makes it possible to substantially extend the range of new 1,4-dihydropyridine-containing systems.

The starting enaminoketones **1** and **2** were prepared by the reactions of aminothiophenes with cyclic β-diketones (Scheme 1).

Enaminones **1** readily react with benzylidenemalononitriles. Depending on the reaction conditions, two different types of products can be obtained. Thus heating of the reactants in ethanol over a short period (15—20 min) in the presence of a catalytic amount of piperidine afforded hexahydroquinolines **3**, the reactions proceeding readily even in the case of deactivated benzylidene derivatives to give products in rather high yields (85—95%) (Scheme 2).

Scheme 1



1a—c, 2a—c

	1			2		
	R	*n*	X	R	*n*	X
a	Me	1	CN	Me	1	CO_2Et
b	H	1	CN	H	1	CO_2Et
c	Me	2	CN	Me	2	CO_2Et

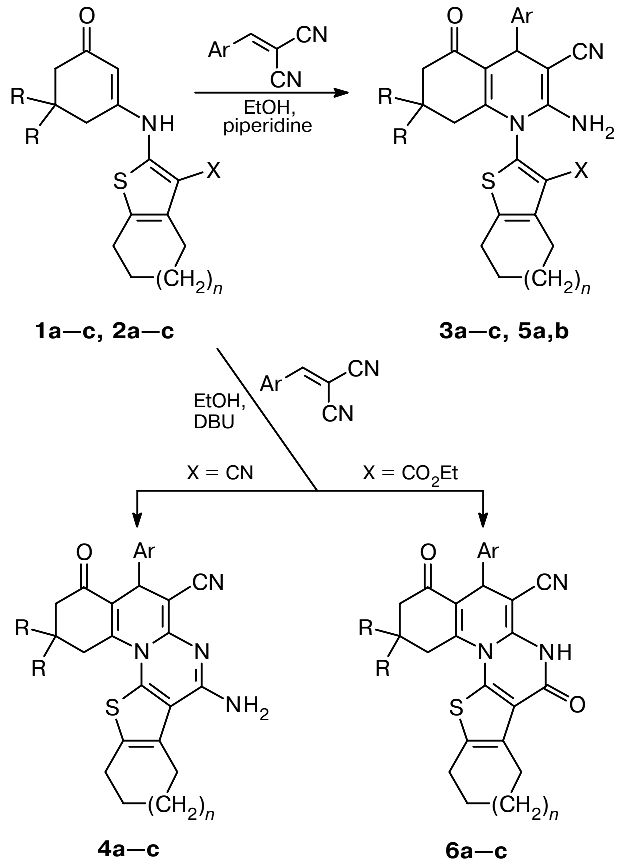
When a mixture of enaminoketones **1** and benzylidenemalononitriles was refluxed for 4—5 h in the presence of DBU as a catalyst, the reaction was not terminated at the stage of formation of hexahydroquinolines **3** and was completed with intramolecular cyclization to form fused thienopyrimidoquinolines **4**.

It should be noted that compounds **4** can also be obtained as minor products along with products **3** using piperidine as a catalyst and upon prolonged refluxing (24 h).

Presumably, the formation of thienopyrimidoquinolines **4** involves the generation of the enaminoketone anion under the action of a base, the Michael

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2319—2323, December, 2001.

Scheme 2



1a—c, 2a—c **3a—c, 5a,b** **4a—c** **6a—c**

3, 4	R	*n*	Ar	X = CN
a	Me	1	Ph	
b	H	1	C_6H_4Cl-4	
c	Me	2	C_6H_4OMe-4	
5	R	*n*	Ar	X = CO_2Et
a	Me	1	C_6H_4Cl-4	
b	H	1	$C_6H_4NO_2$-3	

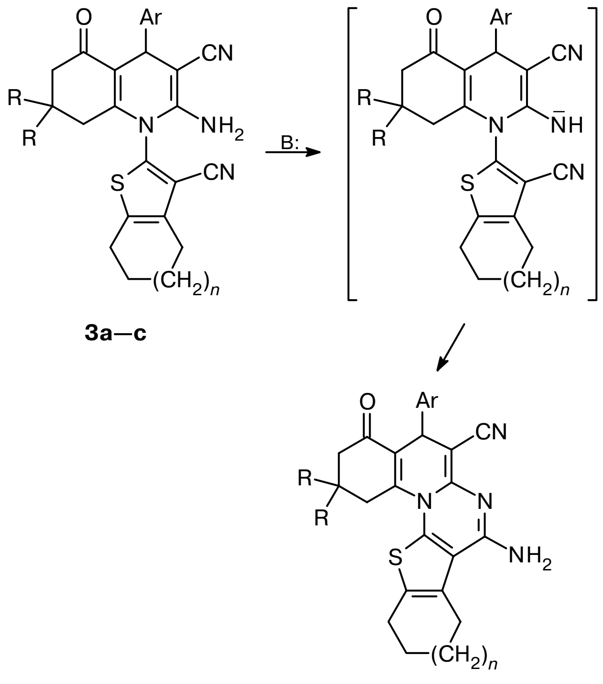
6	R	*n*	Ar
a	Me	1	C_6H_4Cl-4
b	H	1	Ph
c	Me	2	C_6H_4OMe-4

addition of the anion to benzylidenemalononitrile, intramolecular cyclization to form intermediate hexahydroquinolines **3**, and the final base-catalyzed cyclization involving the cyano group (Scheme 3).

Compounds **4a—c** were generated not only in the direct reactions of enaminoketones **1a—c** with benzylidenemalonodinitriles, but also from intermediate hexahydroquinolines **3a—c**, which have been prepared according to a standard procedure with the use of piperidine. However, the transformations of products **3a—c** into thienopyrimidoquinolines **4a—c** upon refluxing in ethanol in the presence of a catalytic amount of DBU proceeded slowly (8—10 h). This is probably associated with poor solubilities of both the starting compounds **3a—c** and the final products **4a—c** in ethanol, *i.e.*, with the heterogeneity of the reaction mixture.

The reactions of enaminoketones **2a—c** with benzylidenemalononitriles also afforded two types of products.

Scheme 3



3a—c **4a—c**

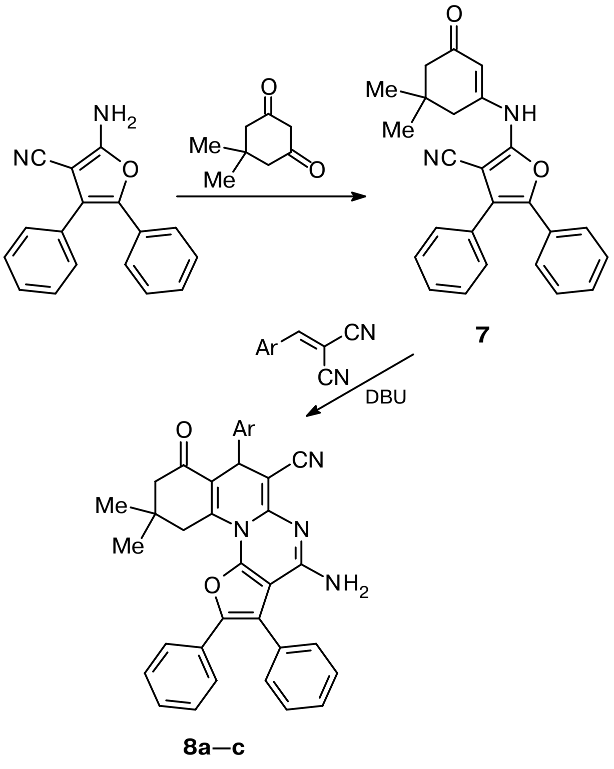
Thus refluxing of the reactants in EtOH over a short period (15—20 min) in the presence of a catalytic amount of piperidine yielded hexahydroquinolines **5a,b**, whereas fused thienopyrimidoquinolines **6a—c**, which are analogs of compounds **4a—c**, were the major reaction products upon prolonged refluxing (2—3 h).

Compounds **6a—c** were also obtained upon heating of the reactants in EtOH over a short period (25—30 min) in the presence of DBU or upon refluxing of hexahydroquinolines **5a,b** in EtOH with piperidine or DBU. Apparently, the scheme of the synthesis of thienopyrimidoquinolines **6a—c** is analogous to that considered above for compounds **4a—c**. However, it should be noted that the last stage in the latter case proceeded more readily than in the case of nitrile analogs **2a—c**. Intermediate hexahydroquinolines **5a,b** can be isolated in the pure form only with the use of benzylidenemalonodinitriles containing electron-withdrawing substituents in the aromatic ring. In the other cases, exclusively the final reaction products **6a—c** were obtained.

Thienopyrimidoquinolines **4a—c** and **6a—c** are high-melting (m.p. > 300 °C) yellow crystalline compounds poorly soluble in organic solvents.

The reaction under consideration is common to heterocyclic amines containing the cyano or ester group in the position 4 with respect to the amino group. Thus the use of readily accessible cyclic enaminoketones **7** generated from substituted aminofurans made it possible to synthesize fused furopyrimidoquinolines **8a—c** (Scheme 4).

Scheme 4



Ar = Ph (**a**), C_6H_4Cl-4 (**b**), C_6H_4OMe-4 (**c**)

To summarize, the examination of the characteristic features of the reactions of *N*-hetaryl-substituted enaminoketones with benzylidenemalononitriles allowed us to develop a simple regioselective procedure for the synthesis of functionally substituted fused heterocycles **4a—c**, **6a—c**, and **8a—c** containing the 1,4-dihydropyridine fragments.

Experimental

The ^{1}H NMR spectra were recorded on Bruker AM-300 (300.13 MHz) and Bruker WM-250 (250.13 MHz) instruments in DMSO-d_6. The melting points were measured on a Boetius heating stage and were not corrected. The reaction mixtures were analyzed and the purities of the products were monitored by TLC on Silufol UV-254 plates in a 3 : 1 EtOAc—hexane solvent system.

2-[(5,5-Dimethyl-3-oxocyclohexen-1-yl)amino]-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carbonitrile (1a). A solution of dimedone (4.20 g, 0.03 mol), 2-amino-3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene^8 (5.34 g, 0.03 mol), and TsOH (0.2 g, 0.0011 mol) in benzene (70 mL) was refluxed using a Dean—Stark trap for 5 h. The reaction mixture was cooled, and the precipitate of the product that formed was filtered off and washed on a filter with a small amount of benzene. Enaminoketone **1a** was obtained in a yield of 8.35 g (93%), m.p. 227—228 °C. Found (%): C, 68.13; H, 6.58; N, 9.17; S, 10.93. $C_{17}H_{20}N_2OS$. Calculated (%): C, 67.97; H, 6.71; N, 9.32; S, 10.67. ^{1}H NMR, δ: 1.05 (s, 6 H, 2 Me); 1.75 (m, 4 H, 2 CH_2); 2.10 and 2.40 (both s, 2 H each, CH_2); 2.60—2.80 (m, 4 H, 2 CH_2); 5.15 (s, 1 H, CH); 9.20 (br.s, 1 H, NH).

2-[(3-Oxocyclohexen-1-yl)amino]-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carbonitrile (1b) was prepared analogously from cyclohexane-1,3-dione (3.36 g, 0.03 mol) and 2-amino-3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene^8 (5.34 g, 0.03 mol) in a yield of 6.94 g (85%), m.p. 165—166 °C. Found (%): C, 65.91; H, 6.07; N, 10.47; S, 11.61. $C_{15}H_{16}N_2OS$. Calculated (%): C, 66.15; H, 5.92; N, 10.28; S, 11.77. ^{1}H NMR, δ: 1.75 (m, 4 H, 2 CH_2); 1.95, 2.20, and 2.55 (all m, 2 H each, CH_2); 2.60—2.75 (m, 4 H, 2 CH_2); 5.20 (s, 1 H, CH); 9.25 (br.s, 1 H, NH).

2-[(5,5-Dimethyl-3-oxocyclohexen-1-yl)amino]-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophene-3-carbonitrile (1c) was prepared analogously from dimedone (4.20 g, 0.03 mol) and 2-amino-3-cyano-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophene^8 (5.76 g, 0.03 mol) in a yield of 8.29 g (88%), m.p. 195—197 °C. Found (%): C, 68.94; H, 6.88; N, 9.12; S, 10.03. $C_{18}H_{22}N_2OS$. Calculated (%): C, 68.75; H, 7.05; N, 8.91; S, 10.20. ^{1}H NMR, δ: 1.05 (s, 6 H, 2 Me); 1.60 (m, 4 H, 2 CH_2); 1.85, 2.15, and 2.40 (all s, 2 H each, CH_2); 2.60—2.80 (m, 4 H, 2 CH_2); 5.20 (s, 1 H, CH); 9.25 (br.s, 1 H, NH).

2-Amino-1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)-7,7-dimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (3a). Several drops of piperidine were added to a solution of enaminoketone **1a** (0.60 g, 0.002 mol) and benzylidenemalonodinitrile (0.31 g, 0.002 mol) in EtOH (7 mL). The reaction mixture was refluxed for 20 min and then cooled. The precipitate that formed was filtered off and washed on a filter with a small amount of EtOH. Hexahydroquinoline **3a** was obtained in a yield of 0.83 g (91%), m.p. 275—276 °C. Found (%): C, 71.47; H, 5.69; N, 12.57; S, 6.88. $C_{27}H_{26}N_4OS$. Calculated (%): C, 71.34; H, 5.76; N, 12.32; S, 7.05. ^{1}H NMR, δ: 0.80 and 1.00 (both s, 3 H each, Me); 1.75—2.45 (m, 8 H, 4 CH_2); 2.65—2.90 (m, 4 H, 2 CH_2); 4.45 (s, 1 H, CH); 6.05 (br.s, 2 H, NH_2); 7.10—7.35 (m, 5 H, H arom.).

2-Amino-4-(4-chlorophenyl)-1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (3b) was obtained analogously from enaminoketone **1b** (0.54 g, 0.002 mol) and 4-chlorobenzylidenemalonodinitrile (0.38 g, 0.002 mol) in a yield of 0.87 g (95%), m.p. 288—290 °C. Found (%): C, 65.39; H, 4.73; Cl, 7.41; N, 12.31; S, 7.18. $C_{25}H_{21}ClN_4OS$. Calculated (%): C, 65.14; H, 4.59; Cl, 7.69; N, 12.15; S, 6.96. ^{1}H NMR, δ: 1.50—2.45 (m, 10 H, 5 CH_2); 2.70—2.95 (m, 4 H, 2 CH_2); 4.50 (s, 1 H, CH); 6.10 (br.s, 2 H, NH_2); 7.20 and 7.35 (both d, 2 H each, H arom., *J* = 8 Hz).

2-Amino-1-(3-cyano-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thien-2-yl)-4-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (3c) was prepared analogously from enaminoketone **1c** (0.63 g, 0.002 mol) and 4-methoxybenzylidenemalonodinitrile (0.37 g, 0.002 mol) in a yield of 0.85 g (85%), m.p. 281—283 °C. Found (%): C, 70.04; H, 5.90; N, 10.97; S, 6.68. $C_{29}H_{30}N_4O_2S$. Calculated (%): C, 69.85; H, 6.06; N, 11.24; S, 6.43. ^{1}H NMR, δ: 0.80 and 0.95 (both s, 3 H each, Me); 1.75—2.45 (m, 10 H, 5 CH_2); 2.65—2.90 (m, 4 H, 2 CH_2); 3.75 (s, 3 H, OMe); 4.35 (s, 1 H, CH); 5.90 (br.s, 2 H, NH_2); 6.80 and 7.15 (both d, 2 H each, H arom., *J* = 8 Hz).

8-Amino-2,2-dimethyl-4-oxo-5-phenyl-1,3,4,5,9,10,11,12-octahydro-2*H*-benzo[4′,5′]thieno[3′,2′:5,6]pyrimido[1,2-*a*]quinoline-6-carbonitrile (4a). Several drops of DBU were added to a solution of enaminoketone **1a** (0.60 g, 0.002 mol) and benzylidenemalonodinitrile (0.31 g, 0.002 mol) in EtOH (7 mL). The reaction mixture was refluxed for 5 h and then cooled. The precipitate that formed was filtered off and washed on a filter with a small amount of EtOH. Thienopyrimidoquinoline **4a** was obtained in a yield of 0.86 g (94%), m.p. > 320 °C. Found (%): C, 71.58; H, 5.85; N, 12.09; S, 7.18. $C_{27}H_{26}N_4OS$. Calculated (%): C, 71.34; H, 5.76; N, 12.32; S, 7.05. ^{1}H NMR, δ: 0.95 and 1.15 (both s, 3 H each, Me); 1.60—1.95 (m, 4 H, 2 CH_2); 2.20 (d, 1 H, CH_2, *J* = 18 Hz); 2.55—2.90 (m, 7 H, CH_2); 4.65 (s, 1 H, CH); 7.05—7.35 (m, 7 H, NH_2 + H arom.).

8-Amino-5-(4-chlorophenyl)-4-oxo-1,3,4,5,9,10,11,12-octahydro-2*H*-benzo[4′,5′]thieno[3′,2′:5,6]pyrimido[1,2-*a*]quinoline-6-carbonitrile (4b) was prepared analogously from enaminoketone **1b** (0.54 g, 0.002 mol) and 4-chlorobenzylidenemalonodinitrile (0.38 g, 0.002 mol) in a yield of 0.86 g (93%), m.p. > 320 °C. Found (%): C, 65.31; H, 4.45; Cl, 7.95; N, 11.92; S, 7.18. $C_{25}H_{21}ClN_4OS$. Calculated (%): C, 65.14; H, 4.59; Cl, 7.69; N, 12.15; S, 6.96. ^{1}H NMR, δ: 1.50—2.45 (m, 8 H, 5 CH_2); 2.70—2.95 (m, 6 H, 2 CH_2); 4.70 (s, 1 H, CH); 7.15 (d, 2 H, H arom., *J* = 8 Hz); 7.35 (m, 4 H, NH_2 + H arom.).

8-Amino-5-(4-methoxyphenyl)-2,2-dimethyl-4-oxo-1,3,4,5,10,11,12,13-octahydro-2*H*,9*H*-cyclohepta[4′,5′]thieno[3′,2′:5,6]pyrimido[1,2-*a*]quinoline-6-carbonitrile (4c) was prepared analogously from enaminoketone **1c** (0.63 g, 0.002 mol) and 4-methoxybenzylidenemalonodinitrile 0.37 g (0.002 mol) in a yield of 0.96 g (96%), m.p. > 320 °C. Found (%): C, 69.57; H, 6.21; N, 11.42; S, 6.28. $C_{29}H_{30}N_4O_2S$. Calculated (%): C, 69.85; H, 6.06; N, 11.24; S, 6.43. ^{1}H NMR, δ: 0.90 and 1.15 (both s, 3 H each, Me); 1.60—1.95 (m, 6 H, 3 CH_2); 2.20 (d, 1 H, CH_2, *J* = 18 Hz); 2.55—3.05 (m, 7 H, CH_2); 3.70 (s, 3 H, OMe); 4.60 (s, 1 H, CH); 6.80 and 6.95 (both d, 2 H each, H arom., *J* = 8 Hz); 7.25 (br.s, 2 H, NH_2).

Transformation of hexahydroquinoline 3a into thienopyrimidoquinoline 4a. Several drops of DBU were added to a suspension of hexahydroquinoline **3a** (0.45 g, 0.001 mol) in boiling EtOH (8 mL). The reaction mixture was refluxed for 8 h and then cooled. The precipitate that formed was filtered off and washed on a filter with a small amount of EtOH. Thienopyrimidoquinoline **4a** was obtained in a yield of 0.41 g (91%), m.p. > 320 °C. According to the ^{1}H NMR spectroscopic data, thienopyrimidoquinoline **4a** was identical with that prepared according to a procedure described above.

Ethyl 2-[(5,5-dimethyl-3-oxocyclohexen-1-yl)amino]-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (2a). A solution of dimedone (4.20 g, 0.03 mol), ethyl 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate[8] (6.75 g, 0.03 mol), and TsOH (0.2 g, 0.0011 mol) in benzene (70 mL) was refluxed using a Dean—Stark trap for 10 h. Then the reaction mixture was cooled, the solvent was evaporated, and the residue was recrystallized from an ethyl acetate—heptane mixture. Enaminoketone **2a** was obtained in a yield of 7.52 g (72%), m.p. 155—156 °C. Found (%): C, 65.89; H, 7.11; N, 3.85; S, 9.01. $C_{19}H_{25}NO_3S$. Calculated (%): C, 65.68; H, 7.25; N, 4.03; S, 9.23. ^{1}H NMR, δ: 1.05 (s, 6 H, 2 Me); 1.35 (t, 3 H, $\underline{\text{Me}}\text{CH}_2$, *J* = 7 Hz); 1.75 (m, 4 H, 2 CH_2); 2.05 and 2.45 (both s, 2 H each, CH_2); 2.60—2.80 (m, 4 H, 2 CH_2); 4.25 (q, 2 H, $\text{Me}\underline{\text{CH}_2}$, *J* = 7 Hz); 5.60 (s, 1 H, CH); 9.85 (s, 1 H, NH).

Ethyl 2-[(3-oxocyclohexen-1-yl)amino]-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (2b) was prepared analogously from cyclohexane-1,3-dione (3.36 g, 0.03 mol) and ethyl 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate[8] (6.75 g, 0.03 mol) in a yield of 6.51 g (68%), m.p. 136—137 °C. Found (%): C, 64.21; H, 6.78; N, 4.12; S, 9.82. $C_{17}H_{21}NO_3S$. Calculated (%): C, 63.92; H, 6.63; N, 4.38; S, 10.04. ^{1}H NMR, δ: 1.35 (t, 3 H, $\underline{\text{Me}}\text{CH}_2$, *J* = 7 Hz); 1.75 (m, 4 H, 2 CH_2); 1.95, 2.20, and 2.55 (all m, 2 H each, CH_2); 2.60—2.80 (m, 4 H, 2 CH_2); 4.25 (q, 2 H, $\text{MeC}\underline{\text{H}_2}$, *J* = 7 Hz); 5.55 (s, 1 H, CH); 9.80 (s, 1 H, NH).

Ethyl 2-[(5,5-dimethyl-3-oxocyclohexen-1-yl)amino]-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophene-3-carboxylate (2c) was prepared analogously from dimedone (4.20 g, 0.03 mol) and ethyl 2-amino-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophene-3-carboxylate[8] (7.17 g, 0.03 mol) in a yield of 6.73 g (62%), m.p. 124—126 °C. Found (%): C, 66.70; H, 7.41; N, 3.72; S, 9.08. $C_{20}H_{27}NO_3S$. Calculated (%): C, 66.45; H, 7.53; N, 3.87; S, 8.87. ^{1}H NMR, δ: 1.05 (s, 6 H, 2 Me); 1.35 (t, 3 H, $\underline{\text{Me}}\text{CH}_2$, *J* = 7 Hz); 1.65 (m, 4 H, 2 CH_2); 1.80 (m, 2 H, CH_2); 2.05 and 2.45 (both s, 2 H each, CH_2); 2.60—2.80 (m, 4 H, 2 CH_2); 4.25 (q, 2 H, $\text{MeC}\underline{\text{H}_2}$, *J* = 7 Hz); 5.60 (s, 1 H, CH); 9.80 (s, 1 H, NH).

Ethyl 2-[2-amino-4-(4-chlorophenyl)-3-cyano-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydro-1-quinolinyl]-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (5a). Several drops of piperidine were added to a solution of enaminoketone **2a** (0.69 g, 0.002 mol) and 4-chlorobenzylidenemalonodinitrile (0.38 g, 0.002 mol) in EtOH (5 mL). The reaction mixture was refluxed for 15 min and then cooled. The precipitate that formed was filtered off and washed on a filter with a small amount of EtOH. Hexahydroquinoline **5a** was obtained in a yield of 0.81 g (76%), m.p. 245—246 °C. Found (%): C, 65.15; H, 5.78; Cl, 6.48; N, 7.71; S, 6.17. $C_{29}H_{30}ClN_3O_3S$. Calculated (%): C, 64.97; H, 5.64; Cl, 6.61; N, 7.84; S, 5.98. ^{1}H NMR, δ: 0.80 (s, 3 H, Me); 1.00 (s, 1 H, Me); 1.25 (t, 3 H, $\underline{\text{Me}}\text{CH}_2$, *J* = 7 Hz); 1.75—2.35 (m, 8 H, 4 CH_2); 2.70—2.85 (m, 4 H, 2 CH_2); 4.25 (q, 2 H, $\text{Me}\underline{\text{CH}_2}$, *J* = 7 Hz); 4.45 (s, 1 H, CH); 5.55 (s, 2 H, NH_2); 7.15—7.40 (m, 4 H, H arom.).

Ethyl 2-[2-amino-3-cyano-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydro-1-quinolinyl]-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (5b) was prepared analogously from enaminoketone **2b** (0.64 g, 0.002 mol) and 3-nitrobenzylidenemalonodinitrile (0.40 g, 0.002 mol) in a yield of 0.86 g (83%), m.p. 268—269 °C. Found (%): C, 62.38; H, 4.98; N, 10.98; S, 6.34. $C_{27}H_{26}N_4O_5S$. Calculated (%): C, 62.53; H, 5.05; N, 10.80; S, 6.18. ^{1}H NMR, δ: 1.25 (t, 3 H, $\underline{\text{Me}}\text{CH}_2$, *J* = 7 Hz); 1.50—2.45 (m, 10 H, 5 CH_2); 2.70—2.85 (m, 4 H, 2 CH_2); 4.25 (q, 2 H, $\text{Me}\underline{\text{CH}_2}$, *J* = 7 Hz); 4.55 (s, 1 H, CH); 5.60 (s, 2 H, NH_2); 7.50—8.20 (m, 4 H, H arom.).

2,2-Dimethyl-5-(4-chlorophenyl)-4,8-dioxo-1,3,4,5,7,8,9,10,11,12-decahydro-2*H*-benzo[4′,5′]thieno[3′,2′:5,6]pyrimido[1,2-*a*]quinoline-6-carbonitrile (6a). Several drops of DBU were added to a solution of enaminoketone **2a** (0.69 g, 0.002 mol) and 4-chlorobenzylidenemalonodinitrile (0.38 g, 0.002 mol) in EtOH (8 mL). The reaction mixture was refluxed for 30 min and then cooled. The precipitate that formed was filtered off and washed on a filter with a small amount of EtOH. Thienopyrimidoquinoline **6a** was obtained in a yield of 0.91 g (93%), m.p. > 320 °C. Found (%): C, 66.35; H, 5.09; Cl, 7.17; N, 8.72; S, 6.43. $C_{27}H_{24}ClN_3O_2S$. Calculated (%): C, 66.18; H, 4.94; Cl, 7.32; N, 8.58; S, 6.54. ^{1}H NMR, δ: 1.00 (s, 3 H, Me); 1.15 (s, 1 H, Me); 1.70—1.85 (m, 4 H, 2 CH_2); 2.15 (d, 1 H, CH_2, *J* = 18 Hz); 2.55—2.95 (m, 7 H, CH_2); 4.70 (s, 1 H, CH); 7.10 and 7.35 (both d, 2 H each, H arom., *J* = 8 Hz); 11.15 (s, 1 H, NH).

4,8-Dioxo-5-phenyl-1,3,4,5,7,8,9,10,11,12-decahydro-2*H*-benzo[4′,5′]thieno[3′,2′:5,6]pyrimido[1,2-*a*]quinoline-6-carbonitrile (6b) was prepared analogously from enaminoketone **2b** (0.64 g, 0.002 mol) and benzylidenemalonodinitrile (0.31 g, 0.002 mol) in a yield of 0.77 g (90%), m.p. > 320 °C. Found (%): C, 70.05; H, 5.02; N, 9.66; S, 7.71. $C_{25}H_{21}N_3O_2S$. Calculated (%): C, 70.24; H, 4.95; N, 9.83; S, 7.50. ^{1}H NMR, δ: 1.50—2.45 (m, 10 H, 5 CH_2); 2.60—2.85 (m, 4 H, CH_2);

4.65 (s, 1 H, CH); 7.10—7.30 (m, 5 H, H arom.); 11.10 (s, 1 H, NH).

5-(4-Methoxyphenyl)-2,2-dimethyl-4,8-dioxo-1,3,4,5,7,8,10,11,12,13-decahydro-2*H*,9*H*-cyclohepta[4′,5′]thieno[3′,2′:5,6]pyrimido[1,2-*a*]quinoline-6-carbonitrile (6c) was prepared analogously from enaminoketone **2c** (0.72 g, 0.002 mol) and 4-methoxybenzylidenemalonodinitrile (0.37 g, 0.002 mol) in a yield of 0.86 g (86%), m.p. > 320 °C. Found (%): C, 69.49; H, 5.97; N, 8.65; S, 6.54. $C_{29}H_{29}N_3O_3S$. Calculated (%): C, 69.72; H, 5.85; N, 8.41; S, 6.42. ^{1}H NMR, δ: 1.00 (s, 3 H, Me); 1.15 (s, 1 H, Me); 1.60—1.85 (m, 6 H, 3 CH_2); 2.15 (d, 1 H, CH_2, J = 18 Hz); 2.55—3.00 (m, 7 H, CH_2); 3.75 (s, 3 H, OCH_3); 4.55 (s, 1 H, CH); 6.80 and 7.00 (both d, 2 H each, H arom., J = 8 Hz); 11.10 (s, 1 H, NH).

Transformation of hexahydroquinoline 5a into thienopyrimidoquinoline 6a. Several drops of DBU were added to a solution of hexahydroquinoline **5a** (0.54 g, 0.001 mol) in boiling EtOH (8 mL). The reaction mixture was refluxed for 2 h and then cooled. The precipitate that formed was filtered off and washed on a filter with a small amount of EtOH. Thienopyrimidoquinoline **6a** was obtained in a yield of 0.47 g (96%), m.p. > 320 °C. According to the ^{1}H NMR spectroscopic data, the product was identical with thienopyrimidoquinoline **6a**, which was prepared as described above.

2-[(5,5-Dimethyl-3-oxocyclohexen-1-yl)amino]-4,5-diphenylfuran-3-carbonitrile (7). A solution of dimedone (0.42 g, 0.003 mol), 2-amino-3-cyano-4,5-diphenylfuran[9] (0.78 g, 0.003 mol), and TsOH (0.02 g, 0.0001 mol) in benzene (10 mL) was refluxed using a Dean—Stark trap for 5 h and then cooled. The precipitate that formed was filtered off and washed on a filter with a small amount of benzene. Enaminoketone **7** was obtained in a yield of 0.95 g (83%), m.p. 182—183 °C. Found (%): C, 78.32; H, 5.75; N, 7.17. $C_{25}H_{22}N_2O_2$. Calculated (%): C, 78.51; H, 5.80; N, 7.32. ^{1}H NMR, δ: 1.05 (s, 6 H, 2 Me); 2.15 and 2.55 (both s, 2 H each, CH_2); 5.80 (s, 1 H, CH); 7.25—7.55 (m, 10 H, H arom.); 10.45 (s, 1 H, NH).

4-Amino-10,10-dimethyl-8-oxo-2,3,7-triphenyl-8,9,10,11-tetrahydro-7*H*-furo[3′,2′:5,6]pyrimido[1,2-*a*]quinoline-6-carbonitrile (8a). Several drops of DBU were added to a solution of enaminoketone **7** (0.25 g, 0.65 mmol) and benzylidenemalonodinitrile (0.10 g, 0.65 mmol) in EtOH (4 mL). The reaction mixture was refluxed for 4 h and then cooled. The precipitate that formed was filtered off and washed on a filter with a small amount of EtOH. Furopyrimidoquinoline **8a** was obtained in a yield of 0.24 g (68%), m.p. 295—296 °C. Found (%): C, 78.21; H, 5.31; N, 10.72. $C_{35}H_{28}N_4O_2$. Calculated (%): C, 78.34; H, 5.26; N, 10.44. ^{1}H NMR, δ: 1.00 and 1.20 (both s, 3 H each, Me); 2.20, 2.55, 2.85, and 3.50 (all d, 1 H each, CH_2, J = 18 Hz); 4.70 (s, 1 H, CH); 4.85 (br.s, 1 H, NH); 7.10—7.65 (m, 15 H, H arom.); 8.05 (br.s, 1 H, NH).

4-Amino-7-(4-chlorophenyl)-10,10-dimethyl-2,3-diphenyl-8-oxo-8,9,10,11-tetrahydro-7*H*-furo[3′,2′:5,6]pyrimido[1,2-*a*]quinoline-6-carbonitrile (8b) was prepared analogously from enaminoketone **7** (0.38 g, 0.001 mol) and 4-chlorobenzylidenemalonodinitrile (0.19 g, 0.001 mol) in a yield of 0.32 g (56%), m.p. 334—335 °C. Found (%): C, 73.45; H, 7.89; Cl, 6.54; N, 9.97. $C_{35}H_{27}ClN_4O_2$. Calculated (%): C, 73.61; H, 7.77; Cl, 6.21; N, 9.81. ^{1}H NMR, δ: 1.00 and 1.20 (both s, 3 H each, Me); 2.20, 2.55, 2.85, and 3.50 (all d, 1 H each, CH_2, J = 18 Hz); 4.70 (s, 1 H, CH); 4.85 (br.s, 1 H, NH); 7.20—7.75 (m, 14 H, H arom.); 8.10 (br.s, 1 H, NH).

4-Amino-7-(4-methoxyphenyl)-10,10-dimethyl-2,3-diphenyl-8-oxo-8,9,10,11-tetrahydro-7*H*-furo[3′,2′:5,6]pyrimido[1,2-*a*]quinoline-6-carbonitrile (8c) was prepared analogously from enaminoketone **7** (0.25 g, 0.65 mmol) and 4-methoxybenzylidenemalonodinitrile (0.12 g, 0.65 mol) in a yield of 0.20 g (55%), m.p. 298—299 °C. Found (%): C, 76.22; H, 5.41; N, 9.62. $C_{36}H_{30}N_4O_3$. Calculated (%): C, 76.31; H, 5.34; N, 9.89. ^{1}H NMR, δ: 1.00 and 1.15 (both s, 3 H each, Me); 2.20, 2.55, 2.80, and 3.50 (all d, 1 H each, CH_2, J = 18 Hz); 3.70 (s, 3 H, OCH_3); 4.60 (s, 1 H, CH); 4.80 (br.s, 1 H, NH); 6.80 and 7.10 (both d, 2 H each, H arom., J = 8 Hz); 7.20—7.65 (m, 10 H, H arom.); 8.00 (br.s, 1 H, NH).

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Received March 13, 2001;
in revised form June 20, 2001