Synthesis and rearrangements of 7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]- and 7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidines

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7*H*-Pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines were synthesized by the reactions of 2-ethoxymethyleneamino-1*H*-pyrrole-3-carbonitriles with acid hydrazides and by the reactions of aminoiminopyrimidines (prepared based on the above-mentioned carbonitriles) with acid chlorides.

Key words: 7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines, acid hydrazides, Dimroth rearrangement.

Triazolopyrimidines are of interest not only for the synthesis of heterocyclic systems but also as compounds having biological activity and exhibiting, in particular, hypotensive,[1] antiseptic,[2] antiarrhythmic,[3,4] and antiasthmatic[5] properties.

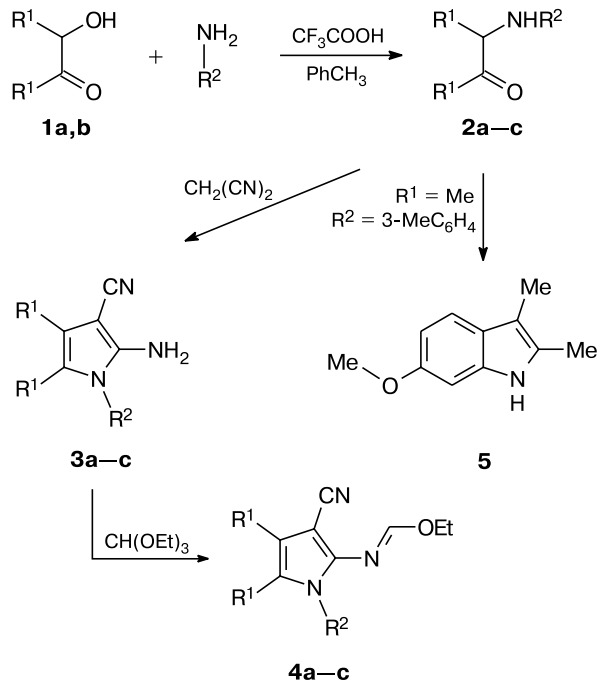
In the present study, we report a new preparative procedure for the synthesis of triazolo[1,5-*c*]pyrimidines (Scheme 1). The reactions of acyloins **1a,b** with amines afforded amino ketones **2a—c**, which were transformed into key starting 2-amino-3-cyanopyrroles **3a—c**. Based on the latter compounds, we developed a one-pot procedure for the synthesis of 7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines.

Acyloins **1a,b** are involved in the modified Voigt reaction with amines in the presence of trifluorocacetic acid as a catalyst. The resulting amino ketones **2a—c** are subjected to Knoevenagel condensation with malononitrile without isolation, and the resulting products undergo cyclization to form aminonitriles **3a—c**.

Aliphatic amines (except for *tert*-butylamine) and aromatic and heterocyclic amines (2- and 3-aminopyridines, 2-aminothiazoles, and aminobenzoxazole) can be involved in this reaction. The reactions of acyloins **1a,b** with *m*-anisidine (toluene, CF_3COOH) do not stop at the formation of amino ketones **2**, and the latter undergo cyclization to form 6-methoxy-2,3-dimethylindole **5** (the synthesis of such systems has been described in detail in the literature[6]).

Refluxing of aminonitriles **3a—c** with triethyl orthoformate over a short period of time affords imidic esters **4a—c** in nearly quantitative yields, and these esters are subjected to cascade heterocyclization with acid hydrazides (nucleophilic substitution of the ethoxy group to give compounds **6a—r** followed by the intramolecular nucleophilic addition at the carbon—nitrogen bond to form pyrrolopyrimidines **7a—r** and, finally, cyclization yielding pyrrolotriazolopyrimidines **8a—r**) (Scheme 2).

Scheme 1



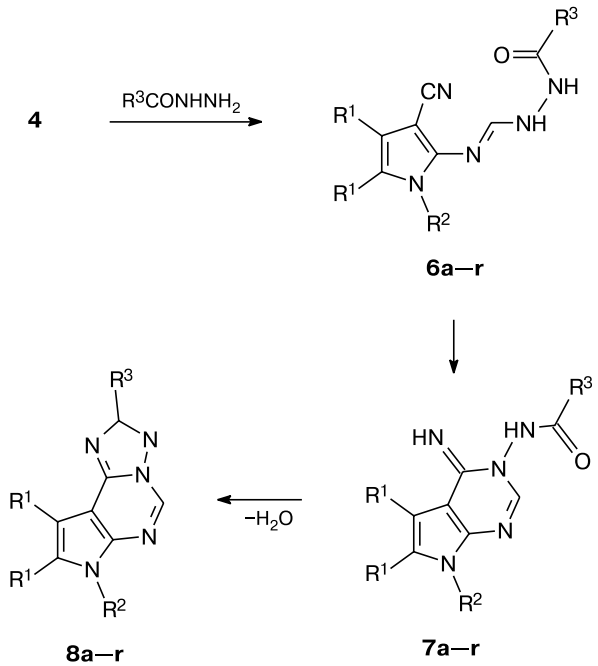
	R^1	R^2
a	Me	3-pyridyl
b	Ph	Bn
c	Me	2-furfuryl

The ease of bis-heterocyclization is attributed to the following fact. Being ambident, the starting hydrazides

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1438—1443, August, 2006.

1066-5285/06/5508-1492

Scheme 2



6—8	R^1	R^2	R^3
a	Me	3-pyridyl	4-$MeOC_6H_4CH_2$
b	Me	3-pyridyl	$PhOCH_2$
c	Me	3-pyridyl	2-HOC_6H_4
d	Me	3-pyridyl	4-pyridyl
e	Me	3-pyridyl	(2-benzoxazolylthio)methyl
f	Me	3-pyridyl	2-BrC_6H_4
g	Ph	Bn	4-$MeOC_6H_4CH_2$
h	Ph	Bn	$PhOCH_2$
i	Ph	Bn	2-HOC_6H_4
j	Ph	Bn	4-pyridyl
k	Ph	Bn	(2-benzoxazolylthio)methyl
l	Ph	Bn	2-BrC_6H_4
m	Me	2-furfuryl	4-$MeOC_6H_4CH_2$
n	Me	2-furfuryl	$PhOCH_2$
o	Me	2-furfuryl	2-HOC_6H_4
p	Me	2-furfuryl	4-pyridyl
q	Me	2-furfuryl	(2-benzoxazolylthio)methyl
r	Me	2-furfuryl	2-BrC_6H_4

contain the active highly nucleophilic amino group, which is favorable for condensation to form compounds **6a—r** followed by their cyclization to give iminopyrrolopyrimidines **7a—r**. In this case, the electrophilicity of the carbon atom of the CO group increases because the N atom of the hydrazide fragment is involved in the electron-withdrawing fragment of compounds **7a—r**. In addition, the presence of the azole N atom in intermediates **7a—r** adjacent to the imino group substantially increases the nucleophilicity of the latter, which facilitates cyclization of compounds **7a—r** to form pyrrolotriazolopyrimidines **8a—r**.

Acid hydrazides involved in the reaction can contain reactive groups (OH, NH_2, *etc.*), due to which compounds **8** can serve as the starting compounds for functionalization.

This transformation deserves attention because the formation of the pyrimidine and triazole rings occurs as a one-pot reaction and is, on the whole, a milder reaction compared to procedures for the synthesis of related compounds described earlier.[7,8] It should be noted that the pathway from acyloins **1a,b** to 2-substituted 7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines **8a—r** involves only three preparative steps because the synthesis of aminopyrroles **3** is performed without isolation of intermediate amino ketones **2**, and the reactions **4** → **8** proceed under reflux in chlorobenzene or acetic acid to give the target products in 35—90% yields. The procedure for the synthesis of 7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines **8** developed in the present study is much simpler than the widely used methods for the preparation of such tricyclic systems. For example, the most well-known multistep procedure for the synthesis (Scheme 3) involves the preparation of 3-amino-4-iminopyrimidines **9** followed by the reaction of the latter with carboxylic acids or their derivatives (anhydrides, acid chlorides, or esters).[9—11]

If desired acid hydrazides are preparatively inaccessible, the synthesis of target products **8** can be performed in two steps. The reaction of ester **4** with hydrazine hydrate produces 3-amino-4-iminopyrimidine **9** and acylation of the latter with the corresponding acid chloride affords compound **8** (see Scheme 3). Pyrimidine **9** can be transformed into hydrazinopyrimidine **10** by the Dimroth rearrangement and then into [1,2,4]triazolo[4,3-*c*]pyrimidines **11** in the same manner.

It should be emphasized that compounds **11** are generated only if R = H, Me, or Et. However, these compounds undergo the Dimroth rearrangement to give compounds **8** upon heating for several hours in an aqueous-ethanolic solution of an alkali. Under the reaction conditions, compounds **11** containing bulkier substituents R were rearranged into isomers **8**. The "steric pressure" of

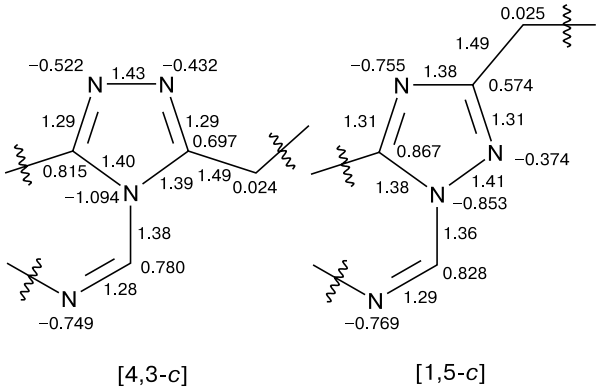
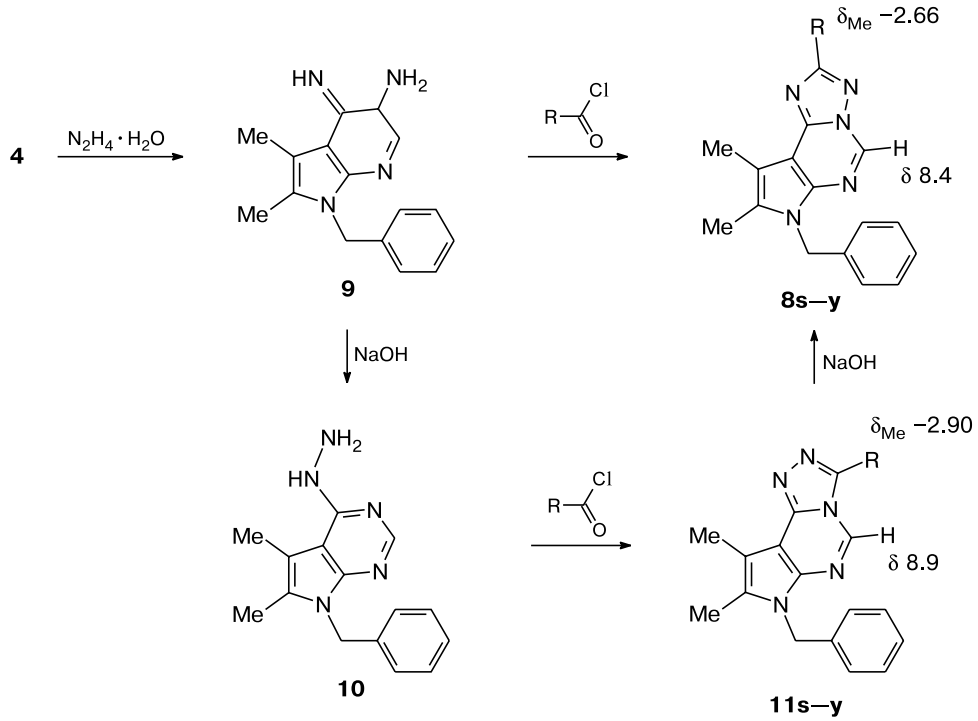


Fig. 1. Charges on atoms and interatomic distances in the [1,2,4]triazolo[1,5-*c*]- and [1,2,4]triazolo[4,3-*c*]pyrimidine fragments calculated by the B3LYP/6-31G** method.

Scheme 3



R = H (**s**),Me (**t**), Et (**u**), Pr (**v**), Bu (**w**), (4-methylphenoxy)methyl (**x**), 1,3(2*H*)-dioxo-1*H*-isoindol-2-ylmethyl (**y**)

bulky substituents is the main driving force for the rearrangement **11** → **8**.

The charges on atoms and interatomic distances in the [1,2,4]triazolo[1,5-*c*]- and [1,2,4]triazolo[4,3-*c*]pyrimidine fragments calculated by the B3LYP/6-31G** method (calculations were performed for compounds **8v** and **11v**) are presented in Fig. 1. In our opinion, a more uniform distribution of these parameters in the structure of **8** compared to **11** is the second factor responsible for higher thermodynamic stability of 7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines **8**.

Experimental

The ^{1}H NMR spectra were recorded on Bruker DPX-250 (250 MHz) and Varian Unity-300 (300 MHz) instruments in $CDCl_3$ with Me_4Si as the internal standard. The IR spectra were measured on a Specord IR-75 spectrometer in Nujol mulls. The electron-impact mass spectra were obtained on a Finigan Mat Incos 50 instrument at the ionizing voltage of 70 V using a direct inlet system. Chromatographic purification of the compounds was performed on aluminum oxide using chloroform as the eluent.

Acetone (Acros Organics), benzoin (Fluka), malononitrile (Alfa Alsar), benzylamine, 3-aminopyridine, and furfurylamine (Lancaster) were used in the synthesis.

Synthesis of compounds 3a—c (general procedure). A suspension of the corresponding amine (0.2 mol) and acyloin **1** (17.6 g, 0.2 mol) in toluene (100 mL) in the presence of 5 mol.% trichloroacetic acid was refluxed using a Dean—Stark trap until an equimolar amount of water was eliminated. The mixture was cooled to room temperature, and malononitrile (13.4 g, 0.2 mol) was added. Then the reaction mixture was refluxed with the use of a Dean—Stark trap until 0.2 mol of water was eliminated (the total times *t* of the first and second steps for particular compounds are given below). Toluene was distilled off. The precipitate was filtered off and washed with a small amount of Pr^iOH and diethyl ether. 2-Aminopyrrole-3-carbonitriles **3** are suitable for use without additional purification. Analytically pure samples were prepared by recrystallization from toluene.

2-Amino-4,5-dimethyl-1-(pyridin-3-yl)-1*H*-pyrrole-3-carbonitrile (3a), *t* = 4 h. The yield was 33 g (78%), colorless crystals, m.p. 190—193 °C. Found (%): C, 67.85; H, 5.69; N, 26.37. $C_{12}H_{12}N_4$. Calculated (%): C, 67.92; H, 5.66; N, 26.42. ^{1}H NMR, δ: 1.81 and 2.08 (both s, 3 H each, Me); 3.81 (s, 2 H, NH_2); 7.48 (t, 1 H, CH, J = 8.2 Hz); 7.64 (d, 1 H, CH, J = 8.5 Hz); 8.58 (s, 1 H, CH); 8.77 (d, 1 H, CH, J = 5.5 Hz).

2-Amino-1-benzyl-4,5-diphenyl-1*H*-pyrrole-3-carbonitrile (3b), *t* = 1.5 h. The yield was 1.71 g (49%), pale-yellow crystals, m.p. 120—121 °C. Found (%): C, 82.43; H, 5.49; N, 12.00. $C_{24}H_{19}N_3$. Calculated (%): C, 82.52; H, 5.44; N, 12.03. ^{1}H NMR, δ: 3.81 (s, 2 H, NH_2); 4.12 (m, 2 H, CH_2); 5.11 (s, 2 H, CH_2); 6.87—7.35 (m, 15 H, 15 CH).

2-Amino-1-(2-furfuryl)-4,5-dimethyl-1*H*-pyrrole-3-carbonitrile (3c), *t* = 1 h. The yield was 34.8 g (81%), colorless crystals, m.p. 108—110 °C. Found (%): C, 66.87; H, 6.12; N, 19.56. $C_{12}H_{13}N_3O$. Calculated (%): C, 66.98; H, 6.05; N, 19.53. ^{1}H NMR, δ: 2.06 and 2.16 (both s, 3 H each, Me); 3.85 (s, 2 H,

NH_2); 4.84 (s, 2 H, CH_2), 6.21 (d, 1 H, CH, J = 3.7 Hz); 6.31 (t, 1 H, CH, J = 3.2 Hz); 7.20 (s, 1 H, CH).

6-Methoxy-2,3-dimethyl-1*H*-indole (5). The yield was 13 g (75%), colorless crystals, m.p. 130 °C. Found (%): C, 75.34; H, 7.51; N, 8.73. $C_{11}H_{13}NO$. Calculated (%): C, 75.43; H, 7.43; N, 8.00. ^{1}H NMR, δ: 2.21, 2.35, and 3.85 (all s, 3 H each, Me); 6.74 (m, 2 H, CH_2); 7.33 (d, 1 H, CH, J = 8.8 Hz); 7.52 (s, 1 H, CH).

Synthesis of compounds 4a—c (general procedure). Compound **3** (0.1 mol) in triethyl formate (40 mL, 0.5 mol) containing 10 mol.% acetic acid was refluxed for 1.5 h, poured onto a Petri dish, and concentrated to dryness. The resulting imido esters are suitable for use without additional purification. Analytically pure samples were obtained by recrystallization from toluene.

2-Ethoxymethylideneamino-4,5-dimethyl-1-(pyridin-3-yl)pyrrole-3-carbonitrile (4a). The yield was 24.6 g (92%), colorless crystals, m.p. 68—71 °C. Found (%): C, 67.07; H, 6.03; N, 20.79. $C_{15}H_{16}N_4O$. Calculated (%): C, 67.16; H, 5.97; N, 20.90. ^{1}H NMR, δ: 1.81 and 2.08 (both s, 3 H each, Me); 2.43 (t, 3 H, Me, J = 7.8 Hz); 4.42 (m, 2 H, CH_2); 7.16 (t, 1 H, CH, J = 8.3 Hz); 7.42 (d, 1 H, CH, J = 8.6 Hz); 8.41 and 8.58 (both s, 1 H each, CH); 8.77 (d, 1 H, CH, J = 5.5 Hz).

1-Benzyl-2-ethoxymethylideneamino-4,5-diphenylpyrrole-3-carbonitrile (4b). The yield was 33 g (85%), colorless crystals, m.p. 111—113 °C. Found (%): C, 79.93; H, 5.75; N, 10.29. $C_{27}H_{23}N_3O$. Calculated (%): C, 80.00; H, 5.67; N, 10.37. ^{1}H NMR, δ: 1.35 (t, 3 H, Me, J = 7.2 Hz); 4.11 (m, 2 H, CH_2); 5.07 (s, 2 H, CH_2); 6.92—7.44 (m, 15 H, 15 CH); 8.55 (s, 1 H, CH).

2-Ethoxymethylideneamino-1-(2-furfuryl)-4,5-dimethylpyrrole-3-carbonitrile (4c). The yield was 23 g (85%), pale-yellow crystals, m.p. 124—125 °C. Found (%): C, 66.35; H, 6.36; N, 15.43. $C_{15}H_{17}N_3O_2$. Calculated (%): C, 66.42; H, 6.27; N, 15.49. ^{1}H NMR, δ: 2.42 (t, 3 H, Me, J = 7.8 Hz); 2.07 and 2.15 (both s, 3 H each, Me); 4.35 (m, 2 H, CH_2); 5.01 (s, 2 H, CH_2); 6.05 (d, 1 H, CH, J = 3.8 Hz); 6.28 (t, 1 H, CH, J = 4.0 Hz); 7.33 and 8.40 (both s, 1 H each, CH).

Synthesis of compounds 8a—r (general procedure). A suspension of imido ester **4** (0.01 mol) and the corresponding acid hydrazide (0.01 mol) was refluxed in chlorobenzene (30 mL) for 4 h. The mixture was cooled and chlorobenzene was distilled off. The reaction mixture was chromatographed ($CHCl_3/Al_2O_3$), filtered, and washed with ethyl ether.

2-(4-Methoxyphenyl)methyl-8,9-dimethyl-7-(pyridin-3-yl)-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8a). The yield was 2.95 g (77%), colorless crystals, m.p. 145—147 °C. Found (%): C, 68.54; H, 5.32; N, 21.82. $C_{22}H_{20}N_6O$. Calculated (%): C, 68.73; H, 5.24; N, 21.86. ^{1}H NMR, δ: 2.31, 2.62, and 3.78 (all s, 3 H each, Me); 4.27 (s, 2 H, CH_2); 6.88 (d, 2 H, CH, J = 9.0 Hz); 7.38 (d, 2 H, CH, J = 9.1 Hz); 7.55 (t, 2 H, CH, J = 8.6 Hz); 7.61 (t, 1 H, CH, J = 7.4 Hz); 7.81 (d, 1 H, CH, J = 8.4 Hz); 8.74 (s, 1 H, CH); 8.79 (d, 1 H, CH, J = 5.4 Hz); 8.9 (s, 1 H, CH).

8,9-Dimethyl-2-phenoxymethyl-7-(pyridin-3-yl)-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8b). The yield was 2.49 g (65%), colorless crystals, m.p. 170—172 °C. Found (%): C, 68.01; H, 4.95; N, 22.58. $C_{21}H_{18}N_6O$. Calculated (%): C, 68.09; H, 4.90; N, 22.69. ^{1}H NMR, δ: 2.31 and 2.58 (both s, 3 H each, Me); 5.43 (s, 2 H, CH_2); 7.01 (t, 1 H, CH, J = 7.5 Hz); 7.12 (d, 1 H, CH, J = 8.5 Hz); 7.32 (m, 3 H, CH); 7.64 (t, 1 H, CH, J = 7.9 Hz); 7.80 (d, 1 H, CH, J = 8.8 Hz); 8.71 (d, 1 H, CH, J = 3.0 Hz); 8.80 (d, 1 H, CH, J = 5.3 Hz); 9.0 (s, 1 H, CH).

2-(2-Hydroxyphenyl)-8,9-dimethyl-7-(pyridin-3-yl)-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8c). The yield was 2.53 g (71%), pale-yellow crystals, m.p. 250—252 °C. Found (%): C, 67.32; H, 4.56; N, 23.52. $C_{20}H_{16}N_6O$. Calculated (%): C, 67.40; H, 4.53; N, 23.58. ^{1}H NMR, δ: 2.33 and 2.65 (both s, 3 H each, Me); 7.01 (t, 1 H, CH, J = 7.9 Hz); 7.17 (d, 1 H, CH, J = 8.5 Hz); 7.40 (t, 1 H, CH, J = 8.2 Hz); 7.57 (t, 1 H, CH, J = 8.7 Hz); 7.79 (d, 1 H, CH, J = 8.7 Hz); 8.21 (d, 1 H, CH, J = 7.6 Hz); 8.77 (d, 1 H, CH, J = 3.0 Hz); 8.81 (d, 1 H, CH, J = 5.0 Hz); 9.0 (s, 1 H, CH); 11.6 (s, 1 H, OH).

8,9-Dimethyl-2,7-di(pyridin-3-yl)-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8d). The yield was 2.53 g (66%), colorless crystals, m.p. 230—231 °C. Found (%): C, 66.77; H, 4.50; N, 28.75. $C_{19}H_{15}N_7$. Calculated (%): C, 66.85; H, 4.43; N, 28.72. ^{1}H NMR, δ: 2.32 and 2.65 (both s, 3 H each, Me); 7.58 (t, 1 H, CH, J = 8.7 Hz); 7.81 (d, 1 H, CH, J = 8.4 Hz); 8.24 (d, 1 H, CH, J = 6.4 Hz); 8.30 (d, 1 H, CH, J = 7.9 Hz); 8.81 (m, 4 H, 4 CH); 9.00 (s, 1 H, CH).

2-(2-Benzoxazolylthio)methyl-8,9-dimethyl-7-(pyridin-3-yl)-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8e). The yield was 2.47 g (58%), colorless crystals, m.p. 178—181 °C. Found (%): C, 61.78; H, 4.12; N, 22.88; S, 7.52. $C_{22}H_{17}N_7OS$. Calculated (%): C, 61.81; H, 4.01; N, 22.94; S, 7.50. ^{1}H NMR, δ: 2.29 and 2.61 (both s, 3 H each, Me); 4.88 (s, 2 H, CH_2); 7.25 (m, 2 H, 2 CH); 7.46 (d, 1 H, CH, J = 8.2 Hz); 7.60 (t, 1 H, CH, J = 8.0 Hz); 7.67 (d, 1 H, CH, J = 8.2 Hz); 7.81 (d, 1 H, CH, J = 8.3 Hz); 8.70 (d, 1 H, CH, J = 3.2 Hz); 8.79 (d, 1 H, CH, J = 5.2 Hz); 9.00 (s, 1 H, CH).

2-(2-Bromophenyl)-8,9-dimethyl-7-(pyridin-3-yl)-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8f). The yield was 2.77 g (66%), colorless crystals, m.p. 193—195 °C. Found (%): C, 57.17; H, 3.61; Br, 19.06; N, 20.04. $C_{20}H_{15}BrN_6$. Calculated (%): C, 57.29; H, 3.61; Br, 19.06; N, 20.04. ^{1}H NMR, δ: 2.35 and 2.61 (both s, 3 H each, Me); 7.32 (t, 1 H, CH, J = 7.5 Hz); 7.41 (t, 1 H, CH, J = 8.0 Hz); 7.58 (t, 1 H, CH, J = 7.4 Hz); 7.80 (m, 2 H, 2 CH); 8.01 (d, 1 H, CH, J = 8.3 Hz); 8.75 (d, 1 H, CH, J = 3.3 Hz); 8.82 (d, 1 H, CH, J = 6.1 Hz); 9.04 (s, 1 H, CH).

7-Benzyl-2-(4-methoxyphenyl)methyl-8,9-diphenyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8g). The yield was 3.75 g (72%), colorless crystals, m.p. 145—146 °C. Found (%): C, 78.17; H, 5.29; N, 13.37. $C_{34}H_{27}N_5O$. Calculated (%): C, 78.29; H, 5.22; N, 13.43. ^{1}H NMR, δ: 3.78 (s, 3 H, Me); 5.49 (s, 2 H, CH_2); 6.81 (d, 4 H, CH, J = 8.9 Hz); 7.11—7.43 (m, 13 H, CH); 7.62 (d, 2 H, CH, J = 9.9 Hz); 9.00 (s, 1 H, CH).

7-Benzyl-2-phenoxymethyl-8,9-diphenyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8h). The yield was 3.54 g (68%), pale-yellow crystals, m.p. 141—143 °C. Found (%): C, 77.95; H, 4.98; N, 13.76. $C_{33}H_{25}N_5O$. Calculated (%): C, 78.09; H, 4.96; N, 13.80. ^{1}H NMR, δ: 5.38 and 5.50 (both s, 2 H each, CH_2); 6.9 (m, 2 H, 2 CH); 7.10—7.44 (m, 17 H, 17 CH); 7.51 (d, 1 H, CH, J = 9.9 Hz); 9.11 (s, 1 H, CH).

7-Benzyl-2-(2-hydroxyphenyl)-8,9-diphenyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8i). The yield was 4.14 g (84%), colorless crystals, m.p. 205—207 °C. Found (%): C, 77.78; H, 4.76; N, 14.06. $C_{32}H_{23}N_5O$. Calculated (%): C, 77.87; H, 4.70; N, 14.19. ^{1}H NMR, δ: 5.61 (s, 2 H, CH_2);

6.90 (m, 4 H, CH_2); 7.22—7.48 (m, 14 H, CH); 8.11 (d, 1 H, CH, J = 7.47 Hz); 9.49 (s, 1 H, CH); 11.45 (s, 1 H, OH).

7-Benzyl-8,9-diphenyl-2-(pyridin-4-yl)-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8j). The yield was 3.25 g (68%), pale-yellow crystals, m.p. 207—209 °C. Found (%): C, 77.71; H, 4.72; N, 17.49. $C_{31}H_{22}N_6$. Calculated (%): C, 77.80; H, 4.63; N, 17.56. ^{1}H NMR, δ: 5.51 (s, 2 H, CH_2); 6.92 (m, 2 H, CH); 7.14—7.40 (m, 11 H, 11 CH); 7.62 (d, 2 H, CH, J = 7.8 Hz); 8.03 (d, 2 H, CH, J = 6.1 Hz); 8.75 (d, 2 H, CH, J = 6.8 Hz); 9.16 (s, 1 H, CH).

2-(2-Benzoxazolylthio)methyl-7-benzyl-8,9-diphenyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8k). The yield was 4.34 g (77%), colorless crystals, m.p. 165—167 °C. Found (%): C, 72.26; H, 4.35; N, 14.79. $C_{34}H_{24}N_6OS$. Calculated (%): C, 72.32; H, 4.28; N, 14.88. ^{1}H NMR, δ: 4.92 and 5.53 (both s, 2 H each, CH_2); 6.90 (d, 2 H, CH, J = 8.7 Hz); 7.12—7.50 (m, 17 H, CH); 9.11 (s, 1 H).

7-Benzyl-2-(2-bromophenyl)-8,9-diphenyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8l). The yield was 4.61 g (83%), colorless crystals, m.p. 187—191 °C. Found (%): C, 69.06; H, 4.06. Br, 14.39; N, 12.52. $C_{32}H_{22}BrN_5$. Calculated (%): C, 69.07; H, 3.98; Br, 14.36; N, 12.59. ^{1}H NMR, δ: 5.51 (s, 2 H, CH_2); 6.89 (m, 4 H, CH); 7.24—7.46 (m, 13 H, CH); 7.61 (d, 2 H, CH, J = 8.7 Hz); 7.72 (d, 1 H, CH, J = 8.0 Hz); 8.00 (d, 1 H, CH, J = 7.7 Hz); 9.20 (s, 1 H, CH).

7-(2-Furfuryl)-2-(4-methoxyphenyl)methyl-8,9-dimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8m). The yield was 2.67 g (69%), pale-yellow crystals, m.p. 123—125 °C. Found (%): C, 68.13; H, 5.52; N, 17.93. $C_{22}H_{21}N_5O_2$. Calculated (%): C, 68.20; H, 5.46; N, 18.08. ^{1}H NMR, δ: 2.41, 2.55, and 3.79 (all s, 3 H each, Me); 4.25 and 5.42 (both s, 2 H each, CH_2); 6.21 (d, 1 H, CH, J = 4.1 Hz); 6.32 (t, 1 H, CH, J = 6.2 Hz); 6.86 (d, 2 H, 2 CH, J = 9.1 Hz); 7.21—7.38 (m, 3 H, 3 CH); 8.95 (s, 1 H, CH).

7-(2-Furfuryl)-8,9-dimethyl-2-phenoxymethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8n). The yield was 3.06 g (82%), colorless crystals, m.p. 157—160 °C. Found (%): C, 67.46; H, 5.19; N, 18.67. $C_{21}H_{19}N_5O_2$. Calculated (%): C, 67.55; H, 5.13; N, 18.76. ^{1}H NMR, δ: 2.41 and 2.48 (both s, 3 H each, Me); 5.42 and 5.51 (both s, 2 H each, CH_2); 6.20 (d, 1 H, CH, J = 3.7 Hz); 6.33 (t, 1 H, CH, J = 3.3 Hz); 6.95 (t, 2 H, 2 CH, J = 7.5 Hz); 7.15 (d, 2 H, 2 CH, J = 8.7 Hz); 7.32 (m, 3 H, 3 CH); 9.00 (s, 1 H, CH).

7-(2-Furfuryl)-2-(2-hydroxyphenyl)-8,9-dimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8o). The yield was 2.66 g (74%), pale-yellow crystals, m.p. 178—180 °C. Found (%): C, 66.77; H, 4.84; N, 19.41. $C_{20}H_{17}N_5O_2$. Calculated (%): C, 66.84; H, 4.77; N, 19.49. ^{1}H NMR, δ: 2.44 and 2.53 (both s, 3 H each, Me); 5.49 (s, 2 H, CH_2); 6.22 (d, 1 H, CH, J = 7.3 Hz); 6.30 (t, 1 H, CH, J = 7.0 Hz); 6.95 (t, 1 H, CH, J = 8.5 Hz); 7.11 (d, 2 H, 2 CH, J = 9.0 Hz); 7.41 (m, 2 H, 2 CH); 8.22 (d, 1 H, CH, J = 9.0 Hz); 9.04 (s, 1 H, CH); 11.74 (s, 1 H, OH).

7-(2-Furfuryl)-8,9-dimethyl-2-(pyridin-4-yl)-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8p). The yield was 2.68 g (78%), colorless crystals, m.p. 195—198 °C. Found (%): C, 66.20; H, 4.75; N, 24.33. $C_{19}H_{16}N_6O$. Calculated (%): C, 66.27; H, 4.68; N, 24.40. ^{1}H NMR, δ: 2.47 and 2.57 (both s, 3 H each, Me); 5.49 (s, 2 H, CH_2); 6.25 (d, 1 H, CH, J = 4.3 Hz); 6.30 (t, 1 H, CH, J = 5.1 Hz); 7.35 (d, 1 H, CH, J = 3.2 Hz); 8.21 (d, 2 H, 2 CH, J = 6.5 Hz); 8.79 (d, 2 H, 2 CH, J = 6.7 Hz); 9.02 (s, 1 H, CH).

2-(2-Benzoxazolylthio)methyl-7-(2-furfuryl)-8,9-dimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8q). The yield was 2.58 g (75%), colorless crystals, m.p. 172—175 °C. Found (%): C, 61.27; H, 4.27; N, 19.44; S, 7.49. $C_{22}H_{18}N_6O_2S$. Calculated (%): C, 61.38; H, 4.21; N, 19.52; S, 7.45. ^{1}H NMR, δ: 2.41 and 2.48 (both s, 3 H each, Me); 4.88 and 5.47 (both s, 2 H each, CH_2); 6.20 (d, 1 H, CH, J = 4.1 Hz); 6.28 (t, 1 H, CH, J = 5.0 Hz); 7.25—7.33 (m, 3 H, 3 CH); 7.45 (d, 1 H, CH, J = 8.1 Hz); 7.65 (d, 1 H, CH, J = 7.7 Hz); 8.98 (s, 1 H, CH).

2-(2-Bromophenyl)-7-(2-furfuryl)-8,9-dimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8r). The yield was 3.50 g (83%), pale-yellow crystals, m.p. 159—161 °C. Found (%): C, 56.81; H, 3.89; Br, 18.97; N, 16.47. $C_{20}H_{16}BrN_5O$. Calculated (%): C, 56.89; H, 3.82; Br, 18.92; N, 16.58. ^{1}H NMR, δ: 2.42 and 2.49 (both s, 3 H each, Me); 5.53 (s, 2 H, CH_2); 6.21 (d, 1 H, J = 8.4 Hz); 6.30 (t, 1 H, CH); 7.28 (m, 3 H, 3 CH); 7.53 and 8.00 (both d, 1 H each, CH, J = 7.8 Hz); 9.03 (s, 1 H, CH).

7-Benzyl-4-imino-5,6-dimethyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidine-3-amine (9). A suspension of imido ester (0.1 mol) and hydrazine hydrate (6 mL, 0.12 mol) in benzene was refluxed for 1 h. Then sodium methoxide (20 mg) was added and the mixture was refluxed for 2 h. Then benzene was evaporated. The resulting solution was washed with a small amount of Pr^iOH and ethyl ether and recrystallized from toluene. The yield was 21.6 g (81%), pale-yellow crystals, m.p. 145—147 °C. Found (%): C, 67.34; H, 6.32; N, 26.19. $C_{15}H_{17}N_5$. Calculated (%): C, 67.41; H, 6.37; N, 26.22. ^{1}H NMR, δ: 2.13 and 2.37 (both s, 3 H each, Me); 4.79 (s, 2 H, CH_2); 5.25 (s, 2 H, NH_2); 6.20—6.80 (br.s, 1 H, NH); 7.02 (d, 2 H, CH, J = 8.5 Hz); 7.27 (m, 3 H, CH); 7.88 (s, 1 H, CH).

7-Benzyl-4-hydrazino-5,6-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (10). Amino imine **9** (22 g, 0.1 mol) was refluxed in an aqueous-ethanolic solution (75 mL of water and 75 mL of ethanol) in the presence of NaOH (20 mg) for 48 h. The reaction mixture was concentrated to dryness, and ethanol (25 mL) was added. After 12 h, the precipitate was filtered off and washed with petroleum ether. The yield was 15.75 g (59%), colorless crystals, m.p. 145—147 °C. Found (%): C, 67.28; H, 6.35; N, 26.31. $C_{15}H_{17}N_5$. Calculated (%): C, 67.41; H, 6.37; N, 26.22. ^{1}H NMR, δ: 2.14 and 2.29 (both s, 3 H each, Me); 4.22—4.48 (br.d, 2 H, NH_2, J = 16.8 Hz); 5.34 (s, 2 H, CH_2); 7.01 (d, 2 H, CH, J = 8.6 Hz); 7.22 (m, 3 H, CH); 7.61 (br.d, 1 H, NH, J = 16.2 Hz); 8.07 (s, 1 H, CH).

Synthesis of compounds 8s and 11s (general procedure). A solution of 4-imino-3*H*-pyrrolo[2,3-*d*]pyrimidine-3-amine **9** or hydrazine **10** (0.01 mol) in orthoformic ester (4 mL, 0.05 mol) containing 10 mol.% acetic acid was refluxed for 2 h and purified by column chromatography ($CHCl_3/Al_2O_3$). Product **8s** or **11s** was recrystallized from ethanol, filtered off, and washed with ethanol.

7-Benzyl-8,9-dimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8s). The yield was 2.24 g (81%), colorless crystals, m.p. 145—147 °C. Found (%): C, 69.24; H, 5.37; N, 27.36. $C_{16}H_{15}N_5$. Calculated (%): C, 69.31; H, 5.42; N, 27.27. ^{1}H NMR, δ: 2.27 and 2.60 (both s, 3 H each, Me); 5.52 (s, 2 H, CH_2), 7.04 (d, 2 H, 2 CH, J = 8.5 Hz); 7.29 (m, 3 H, CH); 8.37 and 9.0 (both s, 1 H each, CH).

7-Benzyl-8,9-dimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (11s). The yield was 1.88 g (68%), colorless crystals, m.p. 145—147 °C. Found (%): C, 69.26; H, 5.36; N, 27.32. $C_{16}H_{15}N_5$. Calculated (%): C, 69.31; H, 5.42; N, 27.27. ^{1}H NMR, δ: 2.28 and 2.58 (both s, 3 H each, Me); 5.51 (s, 2 H, CH_2); 7.05 (d, 2 H, 2 CH, J = 8.5 Hz); 7.27 (m, 3 H, CH); 8.61 and 8.86 (both s, 1 H each, CH).

Synthesis of compounds 8t—y and 11t,u (general procedure). A suspension of the starting acid (0.01 mol) in chlorobenzene (20 mL) and $SOCl_2$ (0.72 mL, 0.01 mol) in the presence of 10 mol.% DMF was refluxed until elimination of HCl ceased. Then amino imine **9** (method *A*) or hydrazine **10** (method *B*) was added. The reaction mixture was refluxed for 4 h, extracted three times with chloroform (20 mL) and an aqueous ammonia solution (15% solution, 20 mL), purified by column chromatography ($CHCl_3/Al_2O_3$), recrystallized from ethanol, filtered off, and washed with ethanol.

7-Benzyl-2,8,9-trimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8t). The yield was 1.42 g (49%), colorless crystals, m.p. 138—141 °C. Found (%): C, 70.10; H, 5.84; N, 24.05. $C_{17}H_{17}N_5$. Calculated (%): C, 70.10; H, 5.84; N, 24.05. ^{1}H NMR, δ: 2.29, 2.50, and 2.66 (all s, 3 H each, Me); 5.51 (s, 2 H, CH_2); 7.0 (d, 2 H, 2 CH, J = 8.5 Hz); 7.30 (m, 3 H, CH); 8.90 (s, 1 H, CH).

7-Benzyl-2-ethyl-8,9-dimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8u). The yield was 2.07 g (68%), colorless crystals, m.p. 125—128 °C. Found (%): C, 70.67; H, 6.26; N, 22.85. $C_{18}H_{19}N_5$. Calculated (%): C, 70.82; H, 6.23; N, 22.95. ^{1}H NMR, δ: 1.43 (t, 3 H, Me, J = 7.6 Hz); 2.28 and 2.54 (both s, 3 H each, Me); 3.01 (m, 2 H, CH_2); 5.51 (s, 2 H, CH_2); 7.00 (d, 2 H, 2 CH, J = 8.6 Hz); 7.26 (m, 3 H, CH); 8.92 (s, 1 H, CH).

8,9-Dimethyl-2-propyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8v). The yield was 1.75 g (55%) (method *A*), 1.85 g (58%) (method *B*), colorless crystals, m.p. 99—101 °C. Found (%): C, 71.36; H, 6.62; N, 21.88. $C_{19}H_{21}N_5$. Calculated (%): C, 71.47; H, 6.58; N, 21.95. ^{1}H NMR, δ: 1.22 (t, 3 H, Me, J = 7.6 Hz); 1.90 (m, 2 H, CH_2); 2.32 and 2.51 (both s, 3 H each, Me); 3.00 (t, 2 H, CH_2, J = 8.1 Hz); 5.49 (s, 2 H, CH_2); 7.03 (d, 2 H, 2 CH, J = 8.5 Hz); 7.25 (m, 3 H, CH); 8.91 (s, 1 H, CH).

7-Benzyl-2-butyl-8,9-dimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8w). The yield was 1.63 g (49%) (method *A*), 1.43 g (43%) (method *B*), pale-yellow crystals, m.p. 85—87 °C. Found (%): C, 71.89; H, 6.87; N, 21.00. $C_{20}H_{23}N_5$. Calculated (%): C, 72.07; H, 6.91; N, 21.02. ^{1}H NMR, δ: 1.01 (t, 3 H, Me, J = 7.5 Hz); 1.48 and 1.87 (both m, 2 H each, CH_2); 2.27 and 2.52 (both s, 3 H each, Me); 2.95 (t, 2 H, CH_2, J = 8.2 Hz); 5.50 (s, 2 H, CH_2); 7.02 (d, 2 H, 2 CH, J = 7.7 Hz); 7.27 (m, 3 H, CH); 8.91 (s, 1 H, CH).

7-Benzyl-8,9-dimethyl-2-(4-methylphenoxy)methyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8x). The yield was 2.86 g (72%) (method *A*), 2.46 g (62%) (method *B*), colorless crystals, m.p. 162—163 °C. Found (%): C, 72.44; H, 6.87; N, 17.56. $C_{24}H_{23}N_5O$. Calculated (%): C, 72.59; H, 6.80; N, 17.60. ^{1}H NMR, δ: 2.27 and 2.59 (both s, 3 H each, Me); 5.39 and 5.52 (both s, 2 H each, CH_2); 7.02 (m, 6 H, 6 CH); 7.30 (m, 3 H, CH); 8.98 (s, 1 H, CH).

7-Benzyl-8,9-dimethyl-2-[1,3(2*H*)-dioxo-1*H*-isoindol-2-ylmethyl]-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (8y). The yield was 1.93 g (43%) (method *A*), 1.88 g (42%) (method *B*), colorless crystals, m.p. 202—205 °C. Found (%): C, 69.24; H, 5.49; N, 27.19. $C_{25}H_{20}N_6O_2$. Calculated (%): C, 69.31; H, 5.42; N, 27.27. ^{1}H NMR, δ: 2.28 and 2.51 (both s, 3 H each, Me); 5.25 and 5.51 (both s, 2 H each, CH_2); 6.97 (d, 2 H, 2 CH, J = 8.5 Hz); 7.26 (m, 3 H, CH); 7.82 and 7.95 (both m, 2 H each, 2 CH each); 8.84 (s, 1 H, CH).

7-Benzyl-3,8,9-trimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (11t). The yield was 1.92 g (66%) (method *B*), pale-yellow crystals, m.p. 189—191 °C. Found (%): C, 70.01; H, 5.90; N, 23.98. $C_{17}H_{17}N_5$. Calculated (%): C, 70.10; H, 5.84; N, 24.05. ^{1}H NMR, δ: 2.30, 2.48, and 2.87 (all s, 3 H each, Me); 5.51 (s, 2 H, CH_2); 7.01 (d, 2 H, 2 CH, J = 8.5 Hz); 7.25 (m, 3 H, CH); 8.38 (s, 1 H, CH).

7-Benzyl-3-ethyl-8,9-dimethyl-7*H*-pyrrolo[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (11u). The yield was 2.17 g (71%) (method *B*), colorless crystals, m.p. 170—173 °C. Found (%): C, 70.76; H, 6.30; N, 22.94. $C_{18}H_{19}N_5$. Calculated (%): C, 70.82; H, 6.23; N, 22.95. ^{1}H NMR, δ: 1.56 (t, 3 H, Me, J = 7.7 Hz); 2.29 and 2.58 (both s, 3 H each, Me); 3.21 (m, 2 H, CH_2); 5.51 (s, 2 H, CH_2); 7.0 (d, 2 H, 2 CH, J = 8.5 Hz); 7.25 (m, 3 H, CH); 8.40 (s, 1 H, CH).

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Received April 25, 2006;
in revised form July 28, 2006