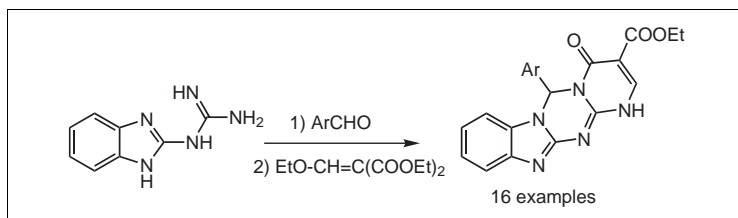


Anton V. Dolzhenko, Wai-Keung Chui* and Anna V. Dolzhenko

Department of Pharmacy, Faculty of Science, National University of Singapore, 18 Science Drive 4, Singapore
117543, Singapore. E-mail: phaewk@nus.edu.sg

Received December 29, 2005



The synthesis of ethyl 6-aryl-4-oxo-4,6-dihydro-1(12)(13)*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazole-3-carboxylates (**4a-p**) was described *via* pyrimidine ring annulation to 4-aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines (**2a-p**) which were obtained from 2-guanidino-benzimidazole (**1**). Tautomerism in the prepared compounds was investigated using nmr spectroscopy. Compounds **2a-p** were found to be present in dimethyl sulfoxide solution predominantly as 3,4-dihydro tautomeric form. Compounds **4a-p** existed in dynamic equilibrium of 1-, 12- and 13*H*- forms. It was found that methylation of **4a-d** led to 13-methyl substituted derivatives **9a-d** exclusively.

J. Heterocyclic Chem., **43**, 1513 (2006).

Heterocyclic compounds with 1,3,5-triazino[1,2-*a*]benzimidazole nucleus have been reported to possess a variety of biological effects [2-13]. Our laboratory has been working on the synthesis and biological evaluation of new fused 1,3,5-triazines with a particular interest in 1,3,5-triazino[1,2-*a*]benzimidazoles because of their potential antifolate activity [1-3]. In this report we describe the synthesis of a new fused four-ring heterocyclic compounds bearing the 1,3,5-triazino[1,2-*a*]benzimidazole nucleus.

The reported methods for the synthesis of such fused four-ring system can be broadly divided into 2 groups. The first group uses benzimidazole that is substituted with another heterocyclic ring as the starting material. [5+1] Cyclization of the benzimidazole using a one carbon atom inserting reagent that ring closes to give 1,3,5-triazine which results in the formation of the four-ring nucleus [14-19]. The formation of the fused 1,3,5-triazine ring depends on the strategic location of the amino group in the starting benzimidazole derivative. Only a limited number of reports [20-22] have discussed the second group of methods which is based on the annulation of a fourth heterocyclic ring to an existing 1,3,5-triazino[1,2-*a*]benzimidazole skeleton. The synthesis that we report herein falls into this second group of methods and employs 4-aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines (**2a-p**) as amidine-type synthons.

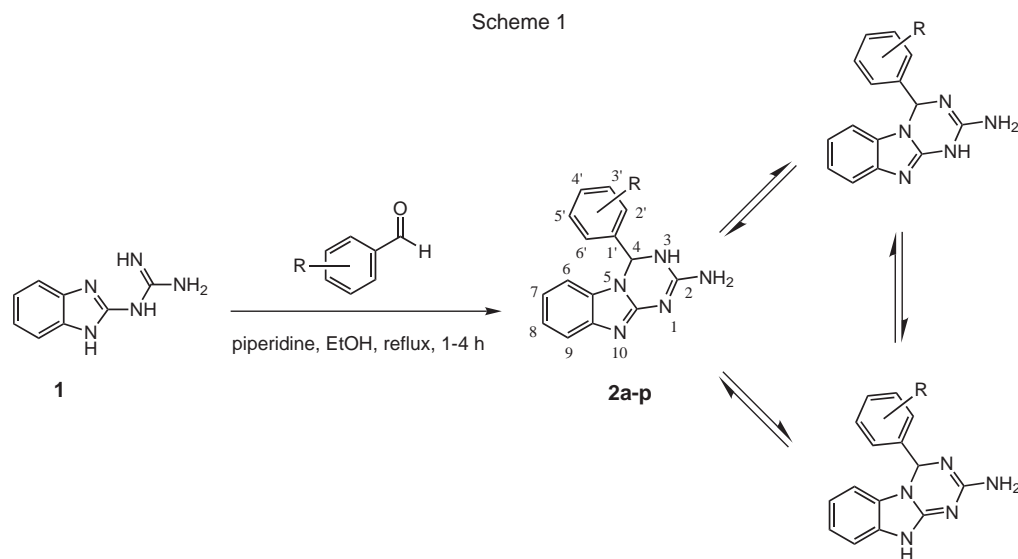
The synthesis of 3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines through a base catalyzed cyclization of 2-guanidinobenzimidazole (**1**) with benzaldehyde was first reported by Nagarajan *et al* in

1970 [23]. Using **1**, a variety of aromatic aldehydes and piperidine as a catalyst, we have prepared a library of 4-aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines (**2a-p**) (Scheme 1).

The formation of the dihydro-1,3,5-triazine ring with a sp^3 hybridized C-4 was confirmed by spectral data, particularly, the signals of C-4 at 61.0-65.9 ppm in ^{13}C nmr spectra. The signals of the other two sp^2 carbon atoms of the formed 1,3,5-triazine ring (C-2 and C-10a), surrounded by three nitrogen atoms each, were located at 154.9-155.5 and 153.2-153.9 ppm, respectively.

Evidence indicating that the 4-aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines (**2a-p**) could exist in 3,4-dihydro, 1,4-dihydro and 4,10-dihydro tautomeric forms was observed (Scheme 1). The prototropic interconversion between these tautomeric forms led to the broadening of the signals of C-2, C-4 and C-10a atoms in the ^{13}C nmr spectra of **2a-p**. In NOESY 2D experiments the pair of strong cross-peaks was observed for the signal of N-H proton and the signal of H-4. The close spatial relationship of H-4 and proton at the annular nitrogen atom corresponded to the 3,4-dihydro tautomeric form. The absence of cross-peaks between H-9 and NH indicated the predominance of 3,4-dihydro tautomeric form in dimethyl sulfoxide solution.

The reaction of the prepared 4-aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines (**2a-p**) with diethyl ethoxymethylenemalonate afforded the formation of ethyl 6-aryl-4-oxo-4,6-dihydro-1(12)(13)*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazole-3-carboxylates (**4a-p**) (Scheme 2).

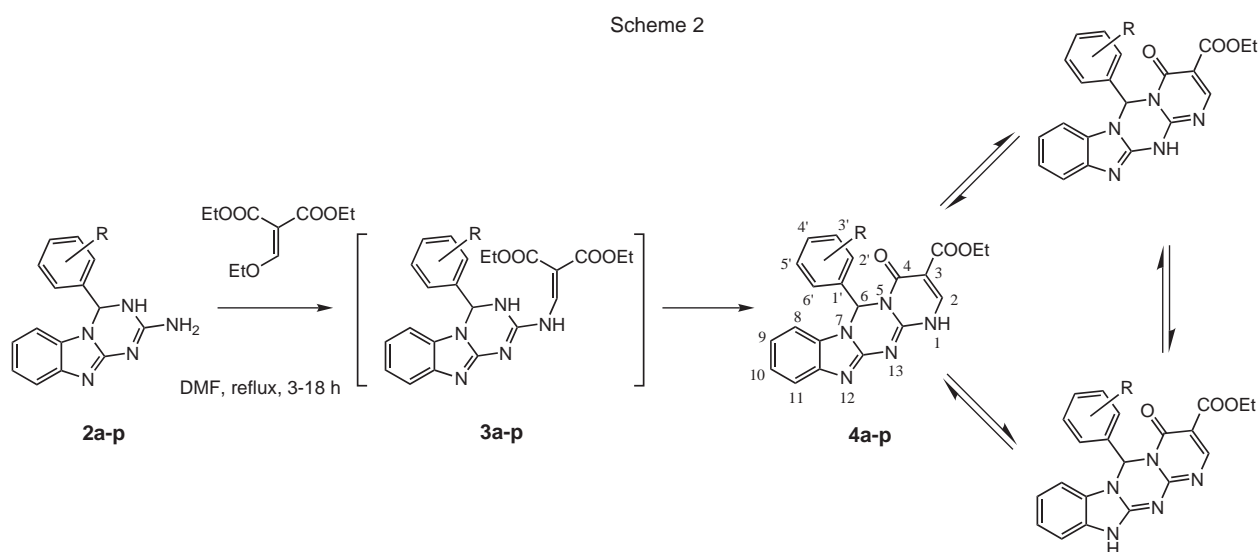


The ring closure was found to be regioselective and led to the intramolecular acylation to N-3 of the intermediates **3a-p**. Structures of the compounds **4a-p** were deduced from the spectral data. The possible formation of the compounds **5-7** (Figure) was investigated. Structure **6** might have formed from the same presumable intermediate **3** by ring closure to N-1. Structures **5** and **7** might have been derived from **2a-p** if the triazine ring nitrogens N-3 or N-1 instead of exocyclic nitrogen were involved in the initial adducts formation that was followed by intramolecular acylation of the amino group. Inasmuch as no cross peak was found for the singlets of the triazine and pyrimidine ring protons in NOESY 2D spectra, the structure **5** was ruled out. Only two pairs of annular tautomeric forms with N-H proton located at pyrimidine or triazine ring are possible for structures **6** and **7**. Therefore, the broadening of some signals of

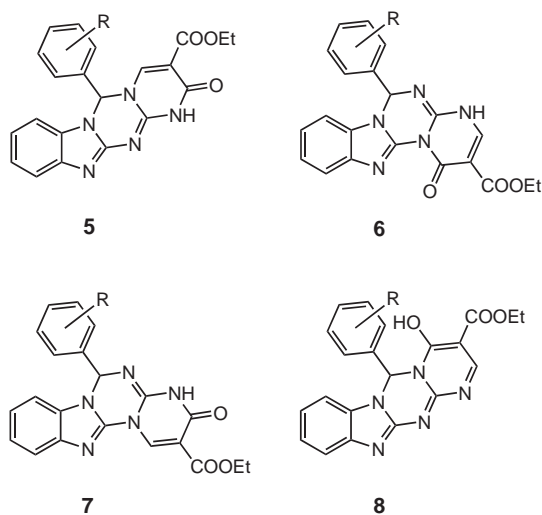
benzimidazole nucleus in ^{13}C nmr spectra (*vide infra*) made it possible to exclude the formation of the structures **6** and **7**. The significant (~ 1 ppm) downfield shift of the signal of triazine C-H proton in the ^1H nmr spectra of compounds **4a-p** was attributed to the anisotropic effect of the spatially close carbonyl group oxygen. This fact proved the formation of the assigned structure **4a-p**.

The tolerance of the method to the variety of substituents was observed in the course of the reactions. However, 18 h were required to convert compound **2e**, with 2'-methoxy group, to **4e** instead of 3-5 h for the synthesis of the other compounds in the series.

It should be noted that compounds **4a-p** could exist at least in three tautomeric forms with proton at N-1, N-12 or N-13 (Scheme 2). The prototropic interconversion between these tautomeric forms was postulated based on the broadening of the signals of 4,6-dihydro-1(12)(13)*H*-pyrimido[2',1':4,5]-



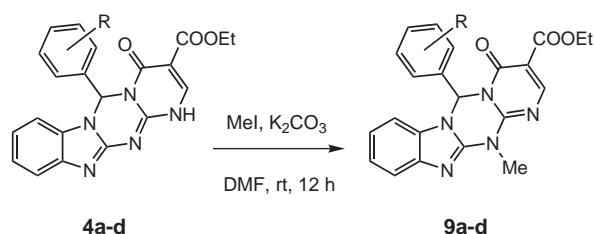
[1,3,5]triazino[1,2-*a*]benzimidazole heterocyclic system in the ^{13}C nmr spectra of the compounds **4a-p**, particularly, the signals of C-2, C-11, C-12a, 13a and especially C-11a. These atoms are located in close proximity with the nitrogen atoms that are involved in the annular tautomerism. The discrete and sharp signal of carbonyl group (C-4) in the ^{13}C nmr spectra indicates that the presence of theoretically possible 4-hydroxy tautomeric form **8** (Figure) in the proton transfer equilibrium is unlikely.



Figure

The methylation of **4a-d** with methyl iodide was attempted (Scheme 3). For elucidation of the structure of the isolated compounds NOESY 2D experiment was used. No cross-peaks for the introduced methyl group were observed in the spectra that signified the structure of 13-methyl substituted derivatives **9a-d**.

Scheme 3



In summary, 4-aryl substituted 3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines (**2a-p**) were prepared. The compounds **2a-p** were found to be useful synthons for the preparation of the hitherto unknown 4,6-dihydro-1(12)(13)*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazoles. The methylation of **4a-d** was found to furnish 13-methyl substituted derivatives **9a-d** exclusively. The tautomerism of the compounds **2a-p** and **3a-p** was discussed.

Table 1

4-Aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines

Compound*	R	Yield %	Mp (°C)	Molecular Formula	Analysis %, Calcd./Found		
					C	H	N
2b	2-Me	85	286-287	C ₁₆ H ₁₅ N ₅	69.30	5.45	25.25
					69.18	5.62	25.02
2c	3-Me	81	268-270	C ₁₆ H ₁₅ N ₅	69.30	5.45	25.25
					69.12	5.78	24.97
2d	4-Me	84	278-279	C ₁₆ H ₁₅ N ₅	69.30	5.45	25.25
					69.15	5.63	25.08
2e	2-MeO	86	268-269	C ₁₆ H ₁₅ N ₅ O	65.52	5.15	23.88
					65.44	5.27	23.72
2f	3-MeO	82	269-270	C ₁₆ H ₁₅ N ₅ O	65.52	5.15	23.88
					65.39	5.32	23.70
2g	4-MeO	70	247-248	C ₁₆ H ₁₅ N ₅ O	65.52	5.15	23.88
					65.43	5.28	23.72
2k	2-Cl	78	281-282	C ₁₅ H ₁₂ ClN ₅	60.51	4.06	23.52
					60.42	4.20	23.43
2l	3-Cl	62	253-254	C ₁₅ H ₁₂ ClN ₅	60.51	4.06	23.52
					60.38	4.25	23.39
2m	4-Cl	68	247-248	C ₁₅ H ₁₂ ClN ₅	60.51	4.06	23.52
					60.48	4.12	23.48
2n	2-Br	77	281-282	C ₁₅ H ₁₂ BrN ₅	52.65	3.53	20.47
					52.53	3.62	20.35
2o	3-Br	65	258-260	C ₁₅ H ₁₂ BrN ₅	52.65	3.53	20.47
					52.56	3.63	20.38
2p	4-Br	74	254-255	C ₁₅ H ₁₂ BrN ₅	52.65	3.53	20.47
					52.48	3.67	20.32

* - **2a**, **2h-j** were described in our previous reports [2,3].

Table 2

Spectral Data of 4-Aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines

Compound	¹ H nmr (300 MHz), dimethyl sulfoxide- <i>d</i> ₆ /TMS, δ (ppm)	¹³ C nmr (75 MHz), dimethyl sulfoxide- <i>d</i> ₆ /TMS, δ (ppm)
2b	2.35 (s, 3H, Me), 6.32 (s, 2H, NH ₂), 6.41 (d, 1H, H-9, <i>J</i> = 7.9 Hz), 6.71 (t, 1H, H-8, <i>J</i> = 7.5 Hz), 6.90 (t, 1H, H-7, <i>J</i> = 7.7 Hz), 6.90 (s, 1H, H-4), 7.05 (d, 1H, H-6, <i>J</i> = 7.5 Hz), 7.15-7.26 (m, 4H, H-3', -4', -5' and -6'), 7.97 (s, 1H, NH)	18.1 (Me), 64.7 (C-4), 107.9 (C-6), 115.9 (C-9), 118.7 (C-8), 120.6 (C-7), 126.4 (C-5'), 127.2 (C-6'), 129.1 (C-4'), 131.3 (C-5a), 131.3 (C-3'), 135.7 (C-2'), 137.0 (C-1'), 143.4 (C-9a), 153.9 (C-10a), 155.2 (C-2)
2c	2.26 (s, 3H, Me), 6.70-6.76 (m, 4H, NH ₂ , H-4 and -9), 6.80 (td, 1H, H-8, <i>J</i> = 7.5, 1.1 Hz), 6.94 (td, 1H, H-7, <i>J</i> = 7.5, 1.5 Hz), 7.13-7.24 (m, 4H, H-6, -2', -4' and -6'), 7.27 (t, 1H, H-5', <i>J</i> = 7.5 Hz), 8.35 (br s, 1H, NH)	20.9 (Me), 65.9 (C-4), 108.2 (C-6), 115.7 (C-9), 118.9 (C-8), 120.8 (C-7), 123.4 (C-6'), 126.6 (C-2'), 128.7 (C-5'), 129.8 (C-4'), 131.1 (C-5a), 138.1 (C-3'), 140.3 (C-1'), 142.8 (C-9a), 153.3 (C-10a), 155.3 (C-2)
2d	2.27 (s, 3H, Me), 6.41 (s, 2H, NH ₂), 6.70 (s, 1H, H-4), 6.71 (d, 1H, H-9, <i>J</i> = 7.9 Hz), 6.78 (td, 1H, H-8, <i>J</i> = 7.5, 1.1 Hz), 6.92 (td, 1H, H-7, <i>J</i> = 7.5, 1.1 Hz), 7.19 (d, 2H, H-3' and -5', <i>J</i> = 8.2 Hz), 7.22 (d, 1H, H-6, <i>J</i> = 7.9 Hz), 7.25 (d, 2H, H-2' and -6', <i>J</i> = 8.2 Hz), 8.00 (s, 1H, NH)	20.6 (Me), 65.7 (C-4), 108.2 (C-6), 115.8 (C-9), 118.9 (C-8), 120.7 (C-7), 126.1 (C-2' and -6'), 129.3 (C-3' and -5'), 131.1 (C-5a), 137.5* (C-1'), 138.6* (C-4'), 143.1 (C-9a), 153.5 (C-10a), 155.4 (C-2)
2e	3.86 (s, 3H, OMe), 6.68 (s, 2H, NH ₂), 6.74 (d, 1H, H-9, <i>J</i> = 7.5 Hz), 6.75-6.82 (m, 2H, H-8 and -3'), 6.85 (t, 1H, H-5', <i>J</i> = 7.5 Hz), 6.94 (t, 1H, H-7, <i>J</i> = 7.2 Hz), 7.03 (s, 1H, H-4), 7.10 (d, 1H, H-6', <i>J</i> = 8.3 Hz), 7.22 (d, 1H, H-6, <i>J</i> = 7.9 Hz), 7.31 (t, 1H, H-4', <i>J</i> = 7.7 Hz), 8.08 (s, 1H, NH)	55.7 (OMe), 61.0 (C-4), 107.7 (C-6), 111.7 (C-3'), 115.8 (C-9), 118.8 (C-8), 120.5 (C-5'), 120.7 (C-7), 126.3 (C-1'), 127.4 (C-6'), 130.3 (C-4'), 131.2 (C-5a), 143.2 (C-9a), 153.8 (C-10a), 155.5 (C-2), 156.2 (C-2')
2f	3.70 (s, 3H, OMe), 6.80 (s, 1H, H-4), 6.81-7.01 (m, 8H, NH ₂ , H-7, -8, -9, -2', -4' and -6'), 7.23 (d, 1H, H-6, <i>J</i> = 7.5 Hz), 7.29 (t, 1H, H-5', <i>J</i> = 7.9 Hz), 8.49 (s, 1H, NH)	55.0 (OMe), 65.5 (C-4), 108.2 (C-6), 112.2 (C-2'), 114.0 (C-4'), 115.8 (C-9), 118.0 (C-6'), 119.0 (C-8), 120.8 (C-7), 130.1 (C-5'), 131.1 (C-5a), 142.0 (C-1'), 143.0 (C-9a), 153.5 (C-10a), 155.4 (C-2), 159.4 (C-3')
2g	3.72 (s, 3H, OMe), 6.72 (d, 1H, H-9, <i>J</i> = 7.5 Hz), 6.76 (s, 1H, H-4), 6.79 (t, 1H, H-8, <i>J</i> = 7.5 Hz), 6.93 (t, 1H, H-7, <i>J</i> = 7.7 Hz), 6.93 (s, 2H, NH ₂), 6.94 (d, 2H, H-3' and -5', <i>J</i> = 8.7 Hz), 7.18 (d, 1H, H-6, <i>J</i> = 7.9 Hz), 7.34 (d, 2H, H-2' and -6', <i>J</i> = 8.7 Hz), 8.42 (s, 1H, NH)	55.1 (OMe), 65.5 (C-4), 108.3 (C-6), 114.1 (C-3' and -5'), 115.7 (C-9), 118.8 (C-8), 120.7 (C-7), 127.7 (C-2' and -6'), 131.2 (C-5a), 132.4 (C-1'), 143.1 (C-9a), 153.5 (C-10a), 155.5 (C-2), 159.7 (C-4')
2k	6.44 (s, 2H, NH ₂), 6.61 (d, 1H, H-9, <i>J</i> = 7.5 Hz), 6.78 (t, 1H, H-8, <i>J</i> = 7.5 Hz), 6.95 (t, 1H, H-7, <i>J</i> = 7.7 Hz), 7.08 (d, 1H, H-6', <i>J</i> = 7.5 Hz), 7.09 (s, 1H, H-4), 7.25 (d, 1H, H-6, <i>J</i> = 7.5 Hz), 7.33 (t, 1H, H-5', <i>J</i> = 7.2 Hz), 7.40 (t, 1H, H-4', <i>J</i> = 7.2 Hz), 7.54 (d, 1H, H-3', <i>J</i> = 7.5 Hz), 8.10 (s, 1H, NH)	63.4 (C-4), 107.5 (C-6), 116.0 (C-9), 118.9 (C-8), 120.9 (C-7), 128.0* (C-6'), 128.4* (C-5'), 130.1 (C-3'), 130.9 (C-4'), 131.0 (C-2), 131.3 (C-5a), 136.5 (C-1'), 143.3 (C-9a), 153.5 (C-10a), 155.0 (C-2)
2l	6.86 (t, 1H, H-8, <i>J</i> = 7.4 Hz), 6.90 (d, 1H, H-9, <i>J</i> = 7.6 Hz), 6.91 (s, 1H, H-4), 6.98 (td, 1H, H-7, <i>J</i> = 7.2, 1.9 Hz), 7.08 (br s, 2H, NH ₂), 7.24-7.32 (m, 2H, H-6 and -6'), 7.37-7.45 (m, 2H, H-4' and -5'), 7.49 (s, 1H, H-2'), 8.66 (s, 1H, NH)	64.9 (C-4), 108.2 (C-6), 116.0 (C-9), 119.2 (C-8), 121.0 (C-7), 124.6 (C-6'), 126.1 (C-2'), 129.0 (C-5'), 131.0 (C-4'), 131.0 (C-5), 133.4 (C-3'), 142.8* (C-1'), 142.9* (C-9a), 153.3 (C-10a), 155.3 (C-2)
2m	6.62 (s, 2H, NH ₂), 6.79 (d, 1H, H-9, <i>J</i> = 7.0 Hz), 6.82 (t, 1H, H-8, <i>J</i> = 7.5 Hz), 6.82 (s, 1H, H-4), 6.94 (td, 1H, H-7, <i>J</i> = 7.2, 2.3 Hz), 7.23 (d, 1H, H-6, <i>J</i> = 7.9 Hz), 7.38 (d, 2H, H-2' and -6', <i>J</i> = 8.5 Hz), 7.47 (d, 2H, H-3' and -5', <i>J</i> = 8.5 Hz), 8.22 (s, 1H, NH)	65.0 (C-4), 108.0 (C-6), 116.0 (C-9), 118.9 (C-8), 120.8 (C-7), 128.0* (C-2' and -6'), 128.9* (C-3' and -5'), 131.0 (C-5a), 133.6 (C-4'), 139.4 (C-1'), 143.3 (C-9a), 153.3 (C-10a), 155.2 (C-2)
2n	6.44 (s, 2H, NH ₂), 6.57 (d, 1H, H-9, <i>J</i> = 7.9 Hz), 6.78 (t, 1H, H-8, <i>J</i> = 7.5 Hz), 6.95 (t, 1H, H-7, <i>J</i> = 7.5 Hz), 7.04 (s, 1H, H-4), 7.07 (dd, 1H, H-6', <i>J</i> = 7.2, 1.5 Hz), 7.25 (d, 1H, H-6, <i>J</i> = 7.9 Hz), 7.32 (td, 1H, H-4', <i>J</i> = 7.2, 1.5 Hz), 7.38 (td, 1H, H-5', <i>J</i> = 7.2, 1.1 Hz), 7.71 (dd, 1H, H-3', <i>J</i> = 7.5, 1.1 Hz), 8.10 (s, 1H, NH)	65.8 (C-4), 107.6 (C-6), 116.0 (C-9), 119.0 (C-8), 120.9 (C-7), 121.1 (C-2), 128.6* (C-6'), 128.7* (C-5'), 131.0 (C-4'), 131.2 (C-5a), 133.3 (C-3'), 137.9 (C-1'), 143.4 (C-9a), 153.5 (C-10a), 154.9 (C-2)
2o	6.82-6.91 (m, 3H, H-8, -9 and -4), 6.98 (td, 1H, H-7, <i>J</i> = 7.0, 2.3 Hz), 6.99 (br s, 2H, NH ₂), 7.26 (d, 1H, H-6, <i>J</i> = 7.9 Hz), 7.29-7.38 (m, 2H, H-5' and -6'), 7.55 (dt, 1H, H-4', <i>J</i> = 7.0, 2.0 Hz), 7.62 (s, 1H, H-2'), 8.59 (s, 1H, NH)	64.9 (C-4), 108.1 (C-6), 116.0 (C-9), 119.2 (C-8), 121.0 (C-7), 122.0 (C-3'), 125.0 (C-6'), 128.9 (C-2'), 131.0 (C-5), 131.2 (C-5'), 131.9 (C-4'), 143.0 (C-1'), 143.0 (C-9a), 153.3 (C-10a), 155.3 (C-2)
2p	6.70 (s, 2H, NH ₂), 6.79 (d, 1H, H-9, <i>J</i> = 7.5 Hz), 6.82 (s, 1H, H-4), 6.82 (t, 1H, H-8, <i>J</i> = 7.0 Hz), 6.95 (td, 1H, H-7, <i>J</i> = 7.0, 2.3 Hz), 7.23 (d, 1H, H-6, <i>J</i> = 7.9 Hz), 7.31 (d, 2H, H-2' and -6', <i>J</i> = 8.3 Hz), 7.60 (d, 2H, H-3' and -5', <i>J</i> = 8.3 Hz), 8.31 (s, 1H, NH)	65.0 (C-4), 108.1 (C-6), 115.9 (C-9), 119.0 (C-8), 120.8 (C-7), 122.2 (C-4'), 128.3 (C-2' and -6'), 131.0 (C-5a), 131.8 (C-3' and -5'), 139.8 (C-1'), 143.2 (C-9a), 153.3 (C-10a), 155.2 (C-2)

* - Assignments may be reversed.

Table 3

Ethyl 6-Aryl-4-oxo-4,6-dihydro-1(12)(13)*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazole-3-carboxylates

Compound	R	Yield %	Mp (°C)	Molecular Formula	Analysis %, Calcd./Found		
					C	H	N
4a	H	68	319-320	C ₂₁ H ₁₇ N ₅ O ₃	65.11	4.42	18.08
					64.98	4.56	17.95
4b	2-Me	55	319-320	C ₂₂ H ₁₉ N ₅ O ₃	65.83	4.77	17.45
					65.74	4.82	17.32
4c	3-Me	70	300-301	C ₂₂ H ₁₉ N ₅ O ₃	65.83	4.77	17.45
					65.68	4.86	17.31
4d	4-Me	72	322-323	C ₂₂ H ₁₉ N ₅ O ₃	65.83	4.77	17.45
					65.77	4.80	17.34
4e	2-MeO	52	294-295	C ₂₂ H ₁₉ N ₅ O ₄	63.30	4.59	16.78
					63.17	4.64	16.64
4f	3-MeO	60	263-264	C ₂₂ H ₁₉ N ₅ O ₄	63.30	4.59	16.78
					63.15	4.68	16.61
4g	4-MeO	51	305-306	C ₂₂ H ₁₉ N ₅ O ₄	63.30	4.59	16.78
					63.12	4.72	16.56
4h	2-F	68	319-320	C ₂₁ H ₁₆ FN ₅ O ₃	62.22	3.98	17.28
					62.18	4.06	17.22
4i	3-F	58	304-305	C ₂₁ H ₁₆ FN ₅ O ₃	62.22	3.98	17.28
					62.15	4.08	17.21
4j	4-F	65	309-310	C ₂₁ H ₁₆ FN ₅ O ₃	62.22	3.98	17.28
					62.04	4.11	17.07
4k	2-Cl	68	325-326	C ₂₁ H ₁₆ ClN ₅ O ₃	59.79	3.82	16.60
					59.70	4.02	16.43
4l	3-Cl	50	298-299	C ₂₁ H ₁₆ ClN ₅ O ₃	59.79	3.82	16.60
					59.55	4.12	16.38
4m	4-Cl	70	318-319	C ₂₁ H ₁₆ ClN ₅ O ₃	59.79	3.82	16.60
					59.68	3.97	16.55
4n	2-Br	51	326-327	C ₂₁ H ₁₆ BrN ₅ O ₃	54.09	3.46	15.02
					53.96	3.63	14.86
4o	3-Br	66	306-307	C ₂₁ H ₁₆ BrN ₅ O ₃	54.09	3.46	15.02
					53.99	3.58	14.90
4p	4-Br	68	320-321	C ₂₁ H ₁₆ BrN ₅ O ₃	54.09	3.46	15.02
					53.91	3.62	14.87

Table 4

Spectral Data of Ethyl 6-Aryl-4-oxo-4,6-dihydro-1(12)(13)*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazole-3-carboxylates

Compound	IR, potassium bromide, ν (cm ⁻¹)	¹ H nmr (300 MHz), dimethyl sulfoxide-d ₆ /TMS, δ (ppm)	¹³ C nmr (75 MHz), dimethyl sulfoxide-d ₆ /TMS, δ (ppm)
4a	NH 3490, CH 3100-2600, C=O 1706, 1637, 1558, 1507, 1474, 1402, 1322, 1295, 1244, 1124, 796, 749	1.22 (dd, 3H, CH ₂ CH ₃ , <i>J</i> = 7.1, 7.1 Hz), 4.12 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 13.9, 7.1 Hz), 4.16 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 13.9, 7.1 Hz), 7.17 (td, 1H, H-9, <i>J</i> = 7.2, 1.1 Hz), 7.22 (td, 1H, H-10, <i>J</i> = 7.2, 1.1 Hz), 7.32-7.41 (m, 4H, H-11, -3', -4' and -5'), 7.54 (dd, 2H, H-2' and -6', <i>J</i> = 7.9, 1.9 Hz), 7.60 (dd, 1H, H-8, <i>J</i> = 7.2, 1.1 Hz), 8.05 (s, 1H, H-6), 8.47 (s, 1H, H-2), 13.12 (br s, 1H, NH)	14.1 (Me), 59.5 (CH ₂), 65.1 (C-6), 105.4 (C-3), 110.5 (C-8), 112.8 (C-11), 122.8 (C-10), 123.8 (C-9), 126.6 (C-2' and -6'), 128.2 (C-7a), 129.0 (C-3' and -5'), 129.7 (C-4'), 132.3 (C-11a), 137.3 (C-1'), 149.2 (C-13a), 154.9 (C-12a), 156.8 (C-4), 160.3 (C-2), 163.3 (COOEt)
4b	NH 3508, CH 3100-2600, C=O 1706, 1636, 1557, 1504, 1477, 1401, 1321, 1294, 1243, 1127, 799, 745	1.20 (dd, 3H, CH ₂ CH ₃ , <i>J</i> = 7.0, 7.0 Hz), 2.75 (s, 3H, ArMe), 4.10 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 10.6, 7.0 Hz), 4.15 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 10.6, 7.0 Hz), 7.09-7.25 (m, 6H, H-9, -10, -3', -4', -5' and -6'), 7.37 (d, 1H, H-11, <i>J</i> = 7.5 Hz), 7.40 (d, 1H, H-8, <i>J</i> = 7.9 Hz), 7.96 (s, 1H, H-6), 8.44 (s, 1H, H-2), 13.17 (br s, 1H, NH)	14.2 (Me), 18.7 (ArMe), 59.5 (CH ₂), 64.4 (C-6), 105.2 (C-3), 110.2 (C-8), 112.8 (C-11), 122.8 (C-10), 123.7 (C-9), 127.0* (C-5'), 127.1* (C-6'), 128.2 (C-7a), 129.5 (C-4'), 130.9 (C-3'), 132.5 (C-11a), 136.0 (C-2'), 138.3 (C-1'), 148.8 (C-13a), 154.9 (C-12a), 157.1 (C-4), 160.0 (C-2), 163.2 (COOEt)
4c	NH 3455, CH 3100-2600, C=O 1702, 1636, 1556, 1506, 1472, 1401, 1320, 1297, 1248, 1127, 797, 746	1.22 (dd, 3H, CH ₂ CH ₃ , <i>J</i> = 7.2, 7.2 Hz), 2.25 (s, 3H, ArMe), 4.11 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 10.5, 7.2 Hz), 4.16 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 10.5, 7.2 Hz), 7.14 (d, 1H, H-4', <i>J</i> = 7.5 Hz), 7.18 (t, 1H, H-9, <i>J</i> = 7.2 Hz), 7.22 (t, 1H, H-10, <i>J</i> = 7.2 Hz), 7.25 (t, 1H, H-5', <i>J</i> = 7.3 Hz), 7.33 (d, 1H, H-6', <i>J</i> = 7.5 Hz), 7.36 (s, 1H, H-2'), 7.38 (dd, 1H, H-11, <i>J</i> = 7.7, 1.1 Hz), 7.59 (dd, 1H, H-8, <i>J</i> = 7.2, 1.1 Hz), 7.97 (s, 1H, H-6), 8.47 (s, 1H, H-2), 13.11 (br s, 1H, NH)	14.1 (Me), 20.9 (ArMe), 59.5 (CH ₂), 65.1 (C-6), 105.4 (C-3), 110.5 (C-8), 112.7 (C-11), 122.8 (C-10), 123.8 (C-9 and -6'), 127.0 (C-2'), 128.1 (C-7a), 128.8 (C-5'), 130.4 (C-4'), 132.1 (C-11a), 137.3 (C-1'), 138.3 (C-3'), 149.1 (C-13a), 154.8 (C-12a), 156.7 (C-4), 160.2 (C-2), 163.3 (COOEt)

Table 4 (continued)

Compound	IR, potassium bromide, ν (cm ⁻¹)	¹ H nmr (300 MHz), dimethyl sulfoxide-d ₆ /TMS, δ (ppm)	¹³ C nmr (75 MHz), dimethyl sulfoxide-d ₆ /TMS, δ (ppm)
4d	NH 3480, CH 3150-2600, C=O 1706, 1638, 1557, 1507, 1476, 1439, 1403, 1322, 1296, 1245, 1127, 795, 750	1.22 (dd, 3H, CH ₂ CH ₃ , $J = 7.2, 7.2$ Hz), 2.21 (s, 3H, ArMe), 4.12 (dq, 1H, CH ₂ CH ₃ , $J = 10.9, 7.2$ Hz), 4.16 (dq, 1H, CH ₂ CH ₃ , $J = 10.9, 7.2$ Hz), 7.16 (d, 2H, H-3' and -5', $J = 8.1$ Hz), 7.17 (td, 1H, H-9, $J = 7.5, 1.1$ Hz), 7.22 (td, 1H, H-10, $J = 7.5, 1.1$ Hz), 7.37 (d, 1H, H-11, $J = 7.9$ Hz), 7.40 (d, 2H, H-2' and -6', $J = 8.1$ Hz), 7.57 (dd, 1H, H-8, $J = 7.5, 1.1$ Hz), 7.99 (s, 1H, H-6), 8.45 (s, 1H, H-2), 13.07 (br s, 1H, NH)	14.1 (Me), 20.6 (ArMe), 59.5 (CH ₂), 64.9 (C-6), 105.5 (C-3), 110.5 (C-8), 112.7 (C-11), 122.7 (C-10), 123.7 (C-9), 126.5 (C-2' and -6'), 128.2 (C-7a), 129.4 (C-3' and -5'), 132.4 (C-11a), 134.4 (C-1'), 139.4 (C-4'), 149.2 (C-13a), 154.8 (C-12a), 156.7 (C-4), 160.1 (C-2), 163.4 (COOEt)
4e	NH 3450, CH 3090-2580, C=O 1738, C=O 1707, 1637, 1557, 1505, 1475, 1440, 1321, 1299, 1252, 1131, 799, 749	1.20 (dd, 3H, CH ₂ CH ₃ , $J = 7.2, 7.2$ Hz), 3.68 (s, 3H, OMe), 4.10 (dq, 1H, CH ₂ CH ₃ , $J = 10.2, 7.2$ Hz), 4.14 (dq, 1H, CH ₂ CH ₃ , $J = 10.2, 7.2$ Hz), 6.97 (d, 1H, H-3', $J = 7.9$ Hz), 7.00 (t, 1H, H-5', $J = 7.4$ Hz), 7.11 (td, 1H, H-9, $J = 7.5, 1.1$ Hz), 7.17 (td, 1H, H-10, $J = 7.5, 1.1$ Hz), 7.25-7.36 (m, 3H, H-11, -4' and -6'), 7.78 (dd, 1H, H-8, $J = 7.7, 1.3$ Hz), 7.93 (s, 1H, H-6), 8.44 (s, 1H, H-2), 12.98 (br s, 1H, NH)	14.2 (Me), 55.5 (OMe), 59.4 (CH ₂), 64.9 (C-6), 105.2 (C-3), 110.0 (C-8), 112.1 (C-3'), 112.9 (C-11), 120.1 (C-5'), 122.3 (C-10), 123.3 (C-9), 124.2 (C-1'), 128.5 (C-7a), 131.1 (C-4' and -6'), 132.6 (C-11a), 148.7 (C-13a), 154.9 (C-12a), 156.8 (C-4), 157.0 (C-2'), 160.2 (C-2), 163.4 (COOEt)
4f	NH 3380, CH 3090-2600, C=O 1736, C=O 1701, 1636, 1604, 1559, 1495, 1468, 1440, 1320, 1287, 1256, 1128, 800, 745	1.23 (dd, 3H, CH ₂ CH ₃ , $J = 7.5, 7.5$ Hz), 3.71 (s, 3H, OMe), 4.13 (dq, 1H, CH ₂ CH ₃ , $J = 14.5, 7.5$ Hz), 4.17 (dq, 1H, CH ₂ CH ₃ , $J = 14.5, 7.5$ Hz), 6.90 (dd, 1H, H-4', $J = 8.3, 2.6$ Hz), 6.99 (d, 1H, H-2', $J = 7.5$ Hz), 7.11-7.22 (m, 3H, H-9, -10 and -6'), 7.26 (t, 1H, H-5', $J = 7.9$ Hz), 7.40 (d, 1H, H-11, $J = 7.2$ Hz), 7.63 (d, 1H, H-8, $J = 7.2$ Hz), 8.01 (s, 1H, H-6), 8.48 (s, 1H, H-2), 12.90 (br s, 1H, NH)	14.2 (Me), 55.1 (OMe), 59.4 (CH ₂), 64.7 (C-6), 104.7 (C-3), 110.4 (C-8), 113.3 (C-2'), 113.3 (C-11), 114.2 (C-4'), 118.0 (C-6'), 122.4 (C-10), 123.4 (C-9), 128.6 (C-7a), 130.3 (C-5'), 134.1 (C-11a), 138.9 (C-1'), 149.8 (C-13a), 155.0 (C-12a), 156.9 (C-4), 159.2 (C-3'), 160.3 (C-2), 163.5 (COOEt)
4g	NH 3450, CH 3080-2580, C=O 1705, 1636, 1613, 1557, 1508, 1475, 1440, 1404, 1321, 1296, 1244, 1175, 1125, 797, 750	1.23 (dd, 3H, CH ₂ CH ₃ , $J = 7.2, 7.2$ Hz), 3.69 (s, 3H, OMe), 4.13 (dq, 1H, CH ₂ CH ₃ , $J = 10.9, 7.2$ Hz), 4.18 (dq, 1H, CH ₂ CH ₃ , $J = 10.9, 7.2$ Hz), 6.90 (dd, 1H, H-3' and -5', $J = 8.6$ Hz), 7.18 (t, 1H, H-9, $J = 7.5$ Hz), 7.23 (t, 1H, H-10, $J = 7.2$ Hz), 7.39 (d, 1H, H-11, $J = 7.5$ Hz), 7.47 (d, 2H, H-2' and -6', $J = 8.6$ Hz), 7.58 (d, 1H, H-8, $J = 7.5$ Hz), 8.00 (s, 1H, H-6), 8.47 (s, 1H, H-2), 12.84 (br s, 1H, NH)	14.1 (Me), 55.1 (OMe), 59.5 (CH ₂), 64.7 (C-6), 105.4 (C-3), 110.5 (C-8), 112.7 (C-11), 114.2 (C-3' and -5'), 122.7 (C-10), 123.7 (C-9), 128.1 (C-2' and -6'), 128.2 (C-7a), 129.4 (C-1'), 132.3 (C-11a), 149.2 (C-13a), 154.8 (C-12a), 156.7 (C-4), 160.0 (C-4'), 160.2 (C-2), 163.4 (COOEt)
4h	NH 3445, CH 3080-2550, C=O 1705, 1636, 1557, 1508, 1475, 1398, 1366, 1321, 1298, 1248, 1128, 767, 750	1.21 (dd, 3H, CH ₂ CH ₃ , $J = 7.2, 7.2$ Hz), 4.11 (dq, 1H, CH ₂ CH ₃ , $J = 10.9, 7.2$ Hz), 4.14 (dq, 1H, CH ₂ CH ₃ , $J = 10.9, 7.2$ Hz), 7.14-7.46 (m, 3H, H-8, -9, -10, -11, -3', -4' and -6'), 7.85 (td, 1H, H-5', $J = 7.5, 1.5$ Hz), 8.03 (s, 1H, H-6), 8.47 (s, 1H, H-2), 13.14 (br s, 1H, NH)	14.1 (Me), 59.5 (CH ₂), 62.9 (C-6), 105.2 (C-3), 109.6 (C-8), 113.0 (C-11), 116.1 (d, C-3', $J = 20.6$ Hz), 122.7 (C-10), 123.7 (C-9), 123.9 (d, C-1', $J = 12.4$ Hz), 124.8 (d, C-5', $J = 2.9$ Hz), 128.1 (C-7a), 130.6 (d, C-6', $J = 2.9$ Hz), 132.0 (d, C-4', $J = 8.2$ Hz), 132.5 (C-11a), 148.6 (C-13a), 154.5 (C-12a), 156.8 (C-4), 159.7 (d, C-2', $J = 248.1$ Hz), 160.2 (C-2), 163.3 (COOEt)
4i	NH 3440, CH 3080-2600, C=O 1728, C=O 1706, 1638, 1556, 1505, 1475, 1320, 1295, 1244, 1133, 803, 750	1.23 (dd, 3H, CH ₂ CH ₃ , $J = 7.2, 7.2$ Hz), 4.12 (dq, 1H, CH ₂ CH ₃ , $J = 10.5, 7.2$ Hz), 4.17 (dq, 1H, CH ₂ CH ₃ , $J = 10.5, 7.2$ Hz), 7.15-7.27 (m, 3H, H-8, -9, -10 and -4'), 7.30 (d, 1H, H-2', $J = 7.5$ Hz), 7.36-7.47 (m, 2H, H-11 and -5'), 7.51 (ddd, 1H, H-6', $J = 9.4, 1.9, 1.9$ Hz), 7.65 (dd, 1H, H-8, $J = 7.3, 1.3$ Hz), 8.05 (s, 1H, H-6), 8.47 (s, 1H, H-2), 13.20 (br s, 1H, NH)	14.1 (Me), 59.5 (CH ₂), 64.5 (C-6), 105.4 (C-3), 110.5 (C-8), 112.9 (C-11), 114.3 (d, C-2', $J = 22.9$ Hz), 116.7 (d, C-4', $J = 20.6$ Hz), 122.3 (d, C-6', $J = 2.9$ Hz), 122.8 (C-10), 123.8 (C-9), 128.1 (C-7a), 131.4 (d, C-5', $J = 8.2$ Hz), 132.3 (C-11a), 139.7 (d, C-1', $J = 6.5$ Hz), 149.1 (C-13a), 154.6 (C-12a), 156.8 (C-4), 160.1 (C-2), 161.8 (d, C-3', $J = 245.8$ Hz), 163.3 (COOEt)
4j	NH 3510, CH 3070-2550, C=O 1702, 1635, 1556, 1509, 1475, 1440, 1402, 1321, 1296, 1245, 1125, 797, 749	1.22 (dd, 3H, CH ₂ CH ₃ , $J = 7.2, 7.2$ Hz), 4.13 (dq, 1H, CH ₂ CH ₃ , $J = 10.9, 7.2$ Hz), 4.16 (dq, 1H, CH ₂ CH ₃ , $J = 10.9, 7.2$ Hz), 7.15-7.26 (m, 4H, H-9, -10, -3' and -5'), 7.39 (d, 1H, H-11, $J = 7.2$ Hz), 7.56-7.65 (m, 3H, H-8, -2' and -6'), 8.06 (s, 1H, H-6), 8.47 (s, 1H, H-2), 12.56 (br s, 1H, NH)	14.1 (Me), 59.5 (CH ₂), 64.4 (C-6), 105.4 (C-3), 110.4 (C-8), 112.8 (C-11), 115.9 (d, C-3' and -5', $J = 22.3$ Hz), 122.8 (C-10), 123.8 (C-9), 128.1 (C-7a), 129.1 (d, C-2' and -6', $J = 8.8$ Hz), 132.4 (C-11a), 133.7 (d, C-1', $J = 2.9$ Hz), 149.2 (C-13a), 154.7 (C-12a), 156.8 (C-4), 160.2 (C-2), 162.4 (d, C-4', $J = 247.0$ Hz), 163.3 (COOEt)
4k	NH 3480, CH 3100-2600, C=O 1703, 1638, 1556, 1507, 1476, 1402, 1321, 1297, 1249, 1131, 1111, 795, 745	1.20 (dd, 3H, CH ₂ CH ₃ , $J = 7.2, 7.2$ Hz), 4.10 (dq, 1H, CH ₂ CH ₃ , $J = 10.5, 7.2$ Hz), 4.15 (dq, 1H, CH ₂ CH ₃ , $J = 10.5, 7.2$ Hz), 7.15 (t, 1H, H-9, $J = 7.3$ Hz), 7.16-7.28 (m, 2H, H-10 and -5'), 7.34-7.50 (m, 4H, H-8, -11, -4' and -6'), 7.81 (dd, 1H, H-3', $J = 7.0, 2.4$ Hz), 8.00 (s, 1H, H-6), 8.45 (s, 1H, H-2), 13.16 (br s, 1H, NH)	14.2 (Me), 59.5 (CH ₂), 65.9 (C-6), 105.1 (C-3), 109.7 (C-8), 113.0 (C-11), 122.7 (C-10), 123.7 (C-9), 127.9 (C-5'), 128.3 (C-7a), 130.2 (C-6'), 131.2* (C-3'), 131.4* (C-4'), 131.6 (C-2'), 132.5 (C-11a), 134.3 (C-1'), 148.6 (C-13a), 154.5 (C-12a), 156.9 (C-4), 159.9 (C-2), 163.2 (COOEt)

Table 4 (continued)

Compound	IR, potassium bromide, ν (cm^{-1})	^1H nmr (300 MHz), dimethyl sulfoxide- d_6 /TMS, δ (ppm)	^{13}C nmr (75 MHz), dimethyl sulfoxide- d_6 /TMS, δ (ppm)
4l	NH 3465, CH 3070-2570, C=O 1704, 1635, 1557, 1501, 1475, 1440, 1401, 1320, 1295, 1244, 1127, 796, 754	1.22 (dd, 3H, CH_2CH_3 , $J = 7.2, 7.2$ Hz), 4.13 (dq, 1H, CH_2CH_3 , $J = 10.7, 7.2$ Hz), 4.16 (dq, 1H, CH_2CH_3 , $J = 10.7, 7.2$ Hz), 7.19 (t, 1H, H-9, $J = 7.5$ Hz), 7.24 (t, 1H, H-10, $J = 7.2$ Hz), 7.35-7.46 (m, 4H, H-11, -4', -5' and -6'), 7.64 (d, 1H, H-8, $J = 7.2$ Hz), 7.74 (s, 1H, H-2'), 8.04 (s, 1H, H-6), 8.47 (s, 1H, H-2), 13.19 (br s, 1H, NH)	14.1 (Me), 59.5 (CH_2), 64.5 (C-6), 105.4 (C-3), 110.5 (C-8), 112.9 (C-11), 122.9 (C-10), 123.9 (C-9), 125.0 (C-6'), 127.1 (C-2'), 128.1 (C-7a), 129.8* (C-5'), 131.2* (C-4'), 132.3 (C-11a), 133.3 (C-3'), 139.4 (C-1'), 149.1 (C-13a), 154.6 (C-12a), 156.8 (C-4), 160.1 (C-2), 163.2 (COOEt)
4m	NH 3505, CH 3080-2600, C=O 1704, 1638, 1558, 1507, 1476, 1417, 1321, 1297, 1245, 1125, 1111, 795, 749	1.23 (dd, 3H, CH_2CH_3 , $J = 7.0, 7.0$ Hz), 4.13 (dq, 1H, CH_2CH_3 , $J = 14.2, 7.0$ Hz), 4.17 (dq, 1H, CH_2CH_3 , $J = 14.2, 7.0$ Hz), 7.19 (td, 1H, H-9, $J = 7.5, 1.1$ Hz), 7.24 (td, 1H, H-10, $J = 7.5, 1.1$ Hz), 7.40 (dd, 1H, H-11, $J = 7.2, 1.1$ Hz), 7.45 (d, 2H, H-3' and -5', $J = 8.3$ Hz), 7.60 (d, 2H, H-2' and -6', $J = 8.7$ Hz), 7.60 (d, 1H, H-8, $J = 7.2$ Hz), 8.07 (s, 1H, H-6), 8.49 (s, 1H, H-2), 13.22 (br s, 1H, NH)	14.2 (Me), 59.5 (CH_2), 64.6 (C-6), 105.5 (C-3), 110.5 (C-8), 112.9 (C-11), 122.8 (C-10), 123.9 (C-9), 128.1 (C-7a), 128.7 (C-2' and -6'), 129.0 (C-3' and -5'), 132.4 (C-11a), 134.4 (C-1'), 136.2 (C-4'), 149.1 (C-13a), 154.6 (C-12a), 156.8 (C-4), 160.2 (C-2), 163.3 (COOEt)
4n	NH 3460, CH 3070-2550, C=O 1702, 1638, 1556, 1505, 1476, 1441, 1403, 1320, 1296, 1250, 1132, 1111, 795, 745	1.21 (dd, 3H, CH_2CH_3 , $J = 7.0, 7.0$ Hz), 4.11 (dq, 1H, CH_2CH_3 , $J = 10.9, 7.0$ Hz), 4.14 (dq, 1H, CH_2CH_3 , $J = 10.9, 7.0$ Hz), 7.16 (t, 1H, H-9, $J = 7.7$ Hz), 7.22 (t, 1H, H-10, $J = 7.2$ Hz), 7.27-7.34 (m, 2H, H-5' and -6'), 7.38 (d, 1H, H-11, $J = 7.6$ Hz), 7.43 (t, 1H, H-4', $J = 7.9$ Hz), 7.65 (d, 1H, H-8, $J = 7.2$ Hz), 7.73 (d, 1H, H-3', $J = 7.5$ Hz), 7.94 (s, 1H, H-6), 8.45 (s, 1H, H-2), 13.19 (br s, 1H, NH)	14.2 (Me), 59.5 (CH_2), 67.8 (C-6), 105.1 (C-3), 110.0 (C-8), 113.0 (C-11), 121.5 (C-2'), 122.7 (C-10), 123.8 (C-9), 128.3 (C-7a), 128.6 (C-5'), 130.9 (C-6'), 131.5 (C-3'), 132.6 (C-11a), 133.4 (C-4'), 136.1 (C-1'), 148.6 (C-13a), 154.5 (C-12a), 157.0 (C-4), 159.7 (C-2), 163.2 (COOEt)
4o	NH 3465, CH 3080-2600, C=O 1734, 1668, 1627, 1561, 1496, 1466, 1440, 1389, 1272, 1254, 1228, 1122, 800, 753	1.23 (dd, 3H, CH_2CH_3 , $J = 7.2, 7.2$ Hz), 4.13 (dq, 1H, CH_2CH_3 , $J = 10.7, 7.2$ Hz), 4.16 (dq, 1H, CH_2CH_3 , $J = 10.7, 7.2$ Hz), 7.20 (t, 1H, H-9, $J = 7.2$ Hz), 7.24 (t, 1H, H-10, $J = 7.2$ Hz), 7.32 (t, 1H, H-5', $J = 8.0$ Hz), 7.40 (d, 1H, H-11, $J = 7.2$ Hz), 7.48 (d, 1H, H-4', $J = 7.9$ Hz), 7.55 (d, 1H, H-6', $J = 7.9$ Hz), 7.65 (d, 1H, H-8, $J = 7.9$ Hz), 7.88 (s, 1H, H-2'), 8.03 (s, 1H, H-6), 8.48 (s, 1H, H-2), 13.15 (br s, 1H, NH)	14.1 (Me), 59.6 (CH_2), 64.5 (C-6), 105.4 (C-3), 110.5 (C-8), 112.9 (C-11), 121.8 (C-3'), 122.9 (C-10), 123.9 (C-9), 125.3 (C-6'), 128.1 (C-7a), 129.9 (C-2), 131.4 (C-5'), 132.5 (C-11a), 132.7 (C-4'), 139.6 (C-1'), 149.1 (C-13a), 154.6 (C-12a), 156.8 (C-4), 160.1 (C-2), 163.2 (COOEt)
4p	NH 3455, CH 3070-2560, C=O 1704, 1634, 1559, 1508, 1476, 1413, 1321, 1296, 1245, 1126, 795, 750	1.23 (dd, 3H, CH_2CH_3 , $J = 7.2, 7.2$ Hz), 4.13 (dq, 1H, CH_2CH_3 , $J = 14.5, 7.2$ Hz), 4.17 (dq, 1H, CH_2CH_3 , $J = 14.5, 7.2$ Hz), 7.18 (td, 1H, H-9, $J = 7.5, 1.1$ Hz), 7.24 (td, 1H, H-10, $J = 7.5, 1.1$ Hz), 7.40 (d, 1H, H-11, $J = 7.2$ Hz), 7.52 (d, 2H, H-3' and -5', $J = 8.7$ Hz), 7.59 (d, 2H, H-2' and -6', $J = 8.7$ Hz), 7.60 (d, 1H, H-8, $J = 7.2$ Hz), 8.05 (s, 1H, H-6), 8.48 (s, 1H, H-2), 13.21 (br s, 1H, NH)	14.2 (Me), 59.5 (CH_2), 64.7 (C-6), 105.4 (C-3), 110.5 (C-8), 112.9 (C-11), 122.8 (C-10), 123.1 (C-4'), 123.9 (C-9), 128.1 (C-7a), 128.9 (C-2' and -6'), 132.0 (C-3' and -5'), 132.4 (C-11a), 136.6 (C-1'), 149.1 (C-13a), 154.6 (C-12a), 156.8 (C-4), 160.2 (C-2), 163.3 (COOEt)

* - Assignments may be reversed .

Table 5

Ethyl 6-Aryl-13-methyl-4-oxo-6,13-dihydro-4*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazole-3-carboxylates

Compound*	R	Yield %	Mp ($^{\circ}\text{C}$)	Molecular Formula	Analysis %, Calcd./Found		
					C	H	N
9a	H	52	247-248	$\text{C}_{22}\text{H}_{19}\text{N}_5\text{O}_3$	65.83	4.77	17.45
					65.60	4.85	17.32
9b	2-Me	62	260-261	$\text{C}_{23}\text{H}_{21}\text{N}_5\text{O}_3$	66.49	5.09	16.86
					66.22	5.35	16.68
9c	3-Me	58	205-206	$\text{C}_{23}\text{H}_{21}\text{N}_5\text{O}_3$	66.49	5.09	16.86
					66.24	5.32	16.55
9d	4-Me	70	257-259	$\text{C}_{23}\text{H}_{21}\text{N}_5\text{O}_3$	66.49	5.09	16.86
					66.25	5.28	16.63

Table 6

Spectral Data of Ethyl 6-Aryl-13-methyl-4-oxo-6,13-dihydro-4*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazole-3-carboxylates

Compound	IR, potassium bromide, ν (cm ⁻¹)	¹ H nmr (300 MHz), dimethyl sulfoxide- <i>d</i> ₆ /TMS, δ (ppm)	¹³ C nmr (75 MHz), dimethyl sulfoxide- <i>d</i> ₆ /TMS, δ (ppm)
9a	CH 2790-3090, C=O 1740, 1671, 1560, 1520, 1497, 1455, 1286, 1253, 1127, 1111, 766, 744, 699	1.24 (dd, 3H, CH ₂ CH ₃ , <i>J</i> = 7.2, 7.2 Hz), 3.79 (s, 3H, NMe), 4.16 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 11.3, 7.0 Hz), 4.21 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 11.3, 7.0 Hz), 7.13 (td, 1H, H-9, <i>J</i> = 7.3, 1.2 Hz), 7.18 (td, 1H, H-10, <i>J</i> = 7.3, 1.5 Hz), 7.31-7.39 (m, 3H, H-3', -4' and -5'), 7.48-7.57 (m, 3H, H-11, -2' and -6'), 7.67 (dd, 1H, H-8, <i>J</i> = 7.2, 1.5 Hz), 8.07 (s, 1H, H-6), 8.58 (s, 1H, H-2)	14.0 (CH ₂ Me), 31.6 (NMe), 60.1 (CH ₂), 64.8 (C-6), 108.4 (C-3), 110.3 (C-8), 117.9 (C-11), 122.0 (C-10), 122.8 (C-9), 126.6 (C-2' and -6'), 129.0 (C-3' and -5'), 129.7 (C-4'), 131.3 (C-7a), 136.4 (C-1'), 141.6 (C-11a), 144.4 (C-13a), 149.9 (C-12a), 155.6 (C-4), 159.3 (C-2), 162.9 (COOEt)
9b	CH 2790-3100, C=O 1710, 1684, 1560, 1523, 1496, 1456, 1301, 1294, 1261, 1135, 795, 739	1.22 (dd, 3H, CH ₂ CH ₃ , <i>J</i> = 7.2, 7.2 Hz), 2.80 (s, 3H, ArMe), 3.83 (s, 3H, NMe), 4.15 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 10.9, 7.2 Hz), 4.20 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 10.9, 7.2 Hz), 7.08-7.25 (m, 6H, H-9, -10, -3', -4', -5' and -6'), 7.35 (d, 1H, H-11, <i>J</i> = 7.9 Hz), 7.54 (dd, 1H, H-8, <i>J</i> = 7.9, 1.1 Hz), 7.94 (s, 1H, H-6), 8.57 (s, 1H, H-2)	14.1 (CH ₂ Me), 18.8 (ArMe), 31.6 (NMe), 60.1 (CH ₂), 64.1 (C-6), 108.1 (C-3), 109.5 (C-8), 117.9 (C-11), 122.1 (C-10), 122.8 (C-9), 126.7 (C-5)*, 127.2 (C-6)*, 129.5 (C-4'), 130.9 (C-3'), 131.3 (C-7a), 135.2 (C-1'), 136.3 (C-2'), 141.5 (C-11a), 143.7 (C-13a), 149.7 (C-12a), 155.9 (C-4), 159.2 (C-2), 162.8 (COOEt)
9c	CH 2790-3120, C=O 1742, 1712, 1683, 1519, 1496, 1456, 1400, 1286, 1259, 1134, 1113, 745, 711	1.24 (dd, 3H, CH ₂ CH ₃ , <i>J</i> = 7.2, 7.2 Hz), 2.24 (s, 3H, ArMe), 3.79 (s, 3H, NMe), 4.16 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 11.1, 7.0 Hz), 4.20 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 11.1, 7.0 Hz), 7.08-7.19 (m, 3H, H-9, -10 and -4'), 7.22 (t, 1H, H-5', <i>J</i> = 7.5 Hz), 7.29 (d, 1H, H-6', <i>J</i> = 7.5 Hz), 7.36 (s, 1H, H-2'), 7.54 (dd, 1H, H-11, <i>J</i> = 6.8, 1.5 Hz), 7.64 (dd, 1H, H-8, <i>J</i> = 6.8, 1.5 Hz), 7.99 (s, 1H, H-6), 8.57 (s, 1H, H-2)	14.0 (CH ₂ Me), 20.8 (ArMe), 31.6 (NMe), 60.1 (CH ₂), 64.9 (C-6), 108.4 (C-3), 110.3 (C-8), 117.8 (C-11), 122.0 (C-10), 122.7 (C-9), 123.7 (C-6), 127.1 (C-2'), 128.9 (C-5'), 130.5 (C-4'), 131.2 (C-7a), 136.4 (C-1'), 138.4 (C-3'), 141.6 (C-11a), 144.3 (C-13a), 149.9 (C-12a), 155.5 (C-4), 159.3 (C-2), 162.9 (COOEt)
9d	CH 2750-3095, C=O 1720, 1694, 1558, 1517, 1498, 1456, 1291, 1267, 1254, 1133, 796, 736	1.24 (dd, 3H, CH ₂ CH ₃ , <i>J</i> = 7.0, 7.0 Hz), 2.20 (s, 3H, ArMe), 3.78 (s, 3H, NMe), 4.16 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 11.3, 7.0 Hz), 4.21 (dq, 1H, CH ₂ CH ₃ , <i>J</i> = 11.3, 7.0 Hz), 7.12 (td, 1H, H-9, <i>J</i> = 7.3, 1.2 Hz), 7.13 (d, 2H, H-3' and -5', <i>J</i> = 8.0 Hz), 7.18 (td, 1H, H-10, <i>J</i> = 7.6, 1.5 Hz), 7.39 (d, 2H, H-2' and -6', <i>J</i> = 8.0 Hz), 7.54 (dd, 1H, H-11, <i>J</i> = 7.2, 1.5 Hz), 7.63 (dd, 1H, H-8, <i>J</i> = 7.2, 1.5 Hz), 8.02 (s, 1H, H-6), 8.57 (s, 1H, H-2)	14.0 (CH ₂ Me), 20.6 (ArMe), 31.6 (NMe), 60.1 (CH ₂), 64.7 (C-6), 108.4 (C-3), 110.3 (C-8), 117.8 (C-11), 122.0 (C-10), 122.7 (C-9), 126.5 (C-2' and -6'), 129.4 (C-3' and -5'), 131.2 (C-7a), 133.5 (C-1'), 139.4 (C-4'), 141.6 (C-11a), 144.4 (C-13a), 149.9 (C-12a), 155.5 (C-4), 159.3 (C-2), 162.9 (COOEt)

* - Assignments may be reversed .

EXPERIMENTAL

Melting points (uncorrected) were determined on a Gallenkamp melting point apparatus. The infrared spectra were performed on a Jasco FT-IR-430 spectrophotometer in potassium bromide pellets. ¹H and ¹³C nmr spectra were recorded on a Bruker DPX-300 spectrometer in dimethyl sulfoxide-*d*₆ solution using TMS as an internal reference.

2-Guanidinobenzimidazole (**1**) was prepared from *o*-phenylenediamine according to the reported method [24]. Synthesis and properties of 4-aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines (**2a**, **2h-j**) were described in our previous reports [2,3].

General Procedure for Preparation of 4-Aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines (**2b-g**, **k-p**).

A solution of 2-guanidinobenzimidazole **1** (1.75 g, 10.0 mmol), appropriate benzaldehyde (10.0 mmol) and 0.5 mL piperidine in ethanol (30-50 mL) was heated under reflux for 1-4 h. After cooling, the product was filtered, washed with ethanol, dried and recrystallized from DMF/ethanol.

General Procedure for Preparation of Ethyl 6-Aryl-4-oxo-4,6-dihydro-1(12)(13)*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazole-3-carboxylates (**4a-p**).

A solution of appropriate 4-aryl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazole-2-amines **2a-p** (2.5 mmol) and diethyl ethoxymethylenemalonate (0.5 mL, 2.5 mmol) in DMF (15 mL) was heated under reflux for 3-18 h. After cooling, the product was filtered, washed with ethanol, dried and recrystallized from DMF.

General Procedure for Preparation of Ethyl 6-Aryl-13-methyl-4-oxo-6,13-dihydro-4*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazole-3-carboxylates (**9a-d**).

A mixture of the appropriate ethyl 6-aryl-4-oxo-4,6-dihydro-1(12)(13)*H*-pyrimido[2',1':4,5][1,3,5]triazino[1,2-*a*]benzimidazole-3-carboxylate **4a-d** (1.0 mmol) and anhydrous potassium carbonate (0.27 g, 1.5 mmol) in 7 mL DMF was stirred at room temperature while iodomethane (0.71 g, 5.0 mmol) was added dropwise over a period of 10 min. The mixture was stirred for 24 h at room temperature. At the end of this time, the reaction mixture was poured into 25 mL of ice cold water and allowed to stand at 4° for 5-10 h. The

precipitate was collected by filtration and recrystallized from ethanol to give pure products **9a-d**.

Acknowledgement.

This work is supported by the Academic Research Fund from the National University of Singapore.

REFERENCES

- [1] Part 4 in the series "Fused heterocyclic systems with *s*-triazine ring", for part 3 see A. V. Dolzhenko, W. K. Chui, and A. V. Dolzhenko, *Synthesis*, 597 (2006).
- [2] A. V. Dolzhenko and W. K. Chui, *J. Heterocyclic Chem.*, **43**, 95 (2006).
- [3] A. V. Dolzhenko, W. K. Chui, and A. V. Dolzhenko, *J. Fluorine Chem.*, **126**, 759 (2005).
- [4] G. Gulyas, T. Emri, A. Simon, and Z. Gyorgydeak, *Folia Microbiol.*, **47**, 29 (2002).
- [5] T. Toyoda, R. K. B. Brobey, G. Sano, T. Horii, N. Tomioka, and A. Itai, *Biochem. Biophys. Res. Comm.*, **235**, 515 (1997).
- [6] A. Itai and T. Toyota, Japanese Patent, 10,310,526 (1998); *Chem. Abstr.*, **130**, 62956 (1999).
- [7] Z. Brzozowski, *Acta Polon. Pharm.*, **55**, 49 (1998).
- [8] C. E. Ward, R. V. Berthold, J. F. Koerwer, J. B. Tomlin, and D. T. Manning, *J. Agric. Food Chem.*, **34**, 1005 (1986).
- [9] E. Schiewald, H. W. Graubaum, H. D. Martin, W. Steinke, W. Kramer, N. Lange, W. Mory, and G. Wolter, East German Patent, 227,035 (1985); *Chem. Abstr.*, **104**, 143975 (1986).
- [10] E. Schiewald, H. W. Graubaum, H. D. Martin, N. Lange, G. Wolter, W. Kochmann, W. Kramer, and W. Steinke, East German Patent, 214,054 (1984); *Chem. Abstr.*, **102**, 127347 (1985).
- [11] C. Bennion and D. Robinson, European Patent, 93,515 (1983); *Chem. Abstr.*, **100**, 85727 (1984).
- [12] J. F. Koerwer, Canadian Patent, 1,146,376 (1983); *Chem. Abstr.*, **99**, 175809 (1983).
- [13] C. E. Ward and R. V. Berthold, Canadian Patent, 1,159,065 (1983); *Chem. Abstr.*, **100**, 209880 (1984).
- [14] F. Saczewski, T. Debowski, and J. Szmigiel, *Heterocycles*, **48**, 1879 (1998).
- [15] J. Svetlik, *Heterocycles*, **20**, 1495 (1983).
- [16] K. Senga, R. K. Robins, and D. E. O'Brien, *J. Heterocyclic Chem.*, **12**, 899 (1975).
- [17] R. Bossio, S. Marcaccini, V. Parrini, and R. Pepino, *J. Heterocyclic Chem.*, **23**, 889 (1986).
- [18] R. Bossio, S. Marcaccini, V. Parrini, and R. Pepino, *J. Heterocyclic Chem.*, **22**, 1147 (1985).
- [19] R. Bossio, S. Marcaccini, V. Parrini, and R. Pepino, *Heterocycles*, **23**, 391 (1985).
- [20] C. E. Hoesl, A. Nefzi, and R. A. Houghten, *J. Comb. Chem.*, **6**, 220 (2004).
- [21] M. S. R. Murty, T. Ramalingam, and P. B. Sattur, *J. Heterocyclic Chem.*, **27**, 949 (1990).
- [22] G. Primofiore, F. Da Settimo, G. Pardi, F. Simorini, C. La Motta, S. Salerno, S. Taliani, and A. M. Marini, *J. Heterocyclic Chem.*, **42**, 1417 (2005).
- [23] K. Nagarajan, V. R. Rao, and A. Venkateswarlu, *Indian J. Chem.*, **8**, 126 (1970).
- [24] F. E. King, R. M. Acheson, and P.C. Spensley, *J. Chem. Soc.*, 1366 (1948).