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Unique substituted 3-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]benzimidazole-1-carboxamides generated by Ugi 3CC using bifunctional starting material

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ABSTRACT

2-(2-Formyl-1*H*-benzimidazol-1-yl)acetic acid, as a bifunctional formyl-acid was prepared in four steps. This compound underwent one-pot reaction with primary amines, and alkyl isocyanides under Ugi conditions. A series of novel 3-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]benzimidazole-1-carboxamides were obtained in moderate to excellent yields.

1. Introduction

Multicomponent reactions (MCRs)[1] in general and isocyanide-based multicomponent reactions (IMCRs)[2] in particular have attracted the chemist attentions during the past years. These reactions are well defined and suited for combinational library synthesis due to the fact that products are formed in one-pot reactions.[3] The most popular IMCR is probably the Ugi reaction in which a carboxylic acid, a primary amine, an aldehyde, and an isocyanide react in a one-pot manner to afford *N*-substituted acyl aminoamide containing four independently varying groups in one reaction.[4]

Piperazines, and their keto analogs are among the most important backbones in today's drug discovery.[5] Piperazines are the unique class of compounds with the privileged structures in molecules involved in the regulation of a wide variety of biological processes.[6] A privileged structure is a molecular scaffold that is able to provide potent and selective ligands for a range of different biological targets through modification of functional groups, and usually exhibits good drug-like properties that lead to more drug-like compound libraries and leads.[7] Heteroaryl-fused pyrazin-3-one fragments are present in a number of natural and synthetic physiologically active agents.[8] Among them are antineoplastic and antibacterial alkaloids longamide, longamide **B** (structures **Ia**,**b**), and phakellstatins (**IIa**,**b**) isolated from marine organisms *Agelas* genus, *Homaxinella* sp., and *Phakellia mauritiana*,[9] antitromboticagent **III**[10] and potential antiprotozoal drug **IV**[11] (Fig. 1). Given the success of privileged structures in medicinal chemistry, and benzimidazoles with the known extensive biochemical and pharmacological properties,[12] we envisioned that fusion of these moieties could rapidly identify new novel compounds. We have carried out the synthesis of 2-(2-formyl-1*H*-benzoimidazol-1-yl)acetic acid **4** in four steps (Scheme 1) in order to use it as a formyl-acid bifunctional starting material with isocyanides and primary amines in Ugi three-component reaction. We expected to obtain the novel pyrazino[1,2-*a*]benzimidazole-3-one (structure **A**) heterocycles (Fig. 1).

2. Results and discussion

2.1. Preparation of 2-(2-formyl-1*H*-benzoimidazol-1-yl)acetic acid (4)

The 2-(2-formyl-1*H*-benzoimidazol-1-yl)acetic acid **4** chosen for this study was synthesized according to the procedure presented in Scheme 1. 2-(Diethoxymethyl)-1*H*-benzimidazole **1** was prepared on the basis of the previously reported method. The spectral data of **1** were similar to that of the authentic sample.[13] Subsequent treatment of **1** with methyl chloroacetate in the presence of K_2CO_3 in refluxing CH_3CN for 6 h afforded the methyl 2-(2-(diethoxymethyl)-1*H*-benzoimidazol-1-yl)acetate **2** in 91%. Transformation of **2** to 2-(2-(diethoxymethyl)-1*H*-benzoimidazol-1-yl)acetic acid **3** was then to carried out in a mixture of methanolic NaOH at rt for 4 h in 95%. Reaction of **3** with HCl in THF/H_2O under reflux for 24 h finally afforded the desired bifunctional compound **4** in 92%. The structure of compounds **2** and **3** was confirmed by their analytical and spectral data.

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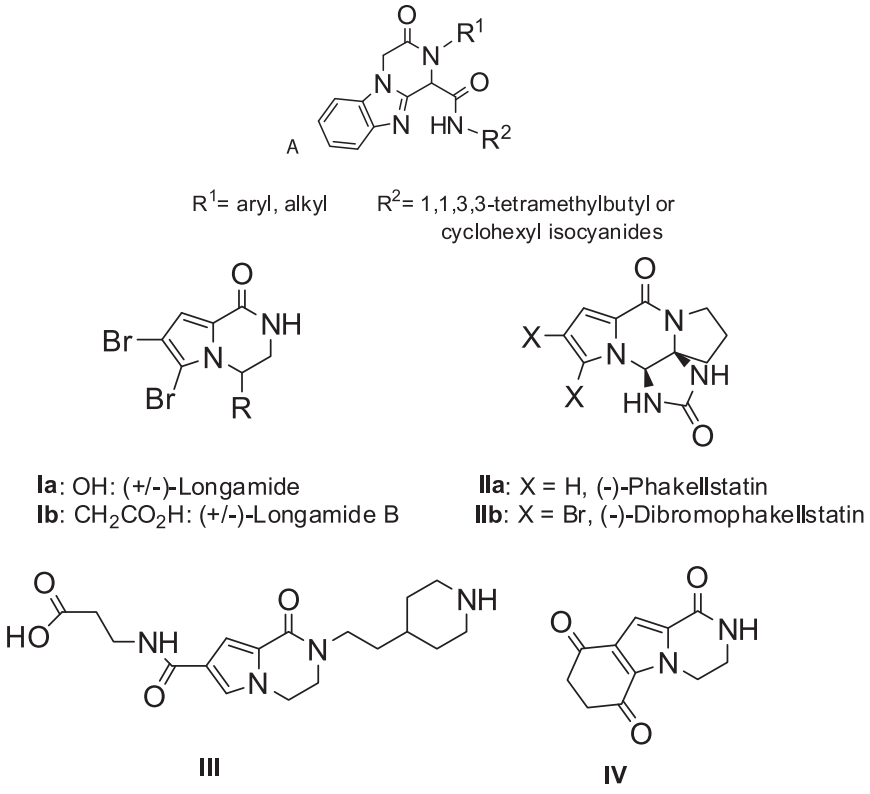
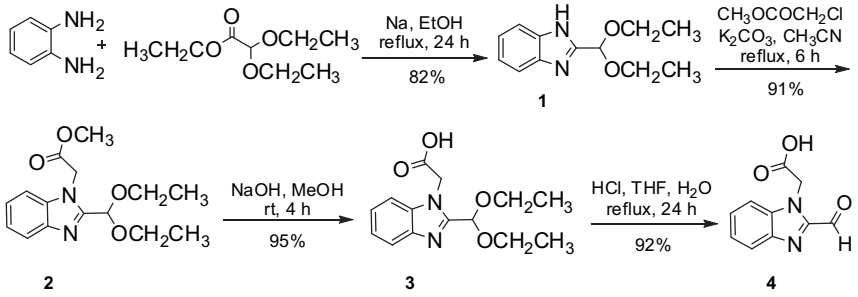
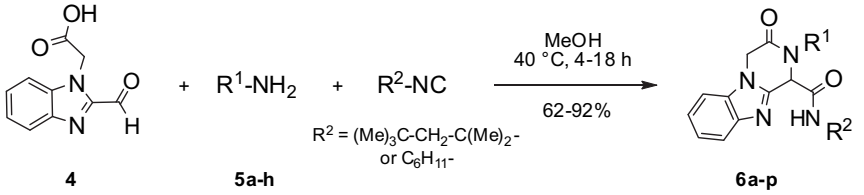


Figure 1. Some natural and synthetic physiologically active heteroaryl-fused pyrazin-3-ones.



Scheme 1. Synthesis of formyl acid **4**.



Scheme 2. Synthesis of benzimidazoketopiprazines **6a**–**p**.

2.2. Preparation of substituted 3-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]benzimidazole-1-carboxamide (6a–p)

Formyl-acid acid **4** reacted with commercially available primary amines **5a**–**h** and isocyanides to give the 3-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]benzimidazole-1-carboxamides **6a**–**p** (Scheme 2). Various amines and the commercial 1,1,3,3- tetramethylbutyl or cyclohexyl isocyanides were incorporated into this structure in moderate to high yields (Table 1). For example, 2-formyl-acid reacted with 3,4-dimethylaniline and 1,1,3,3-tetramethylbutyl isocyanide at 40 °C in 4 h to afford **6d** in 90% yield (entry 4, Table 1). These reactions demonstrated that ketopiperazine annulated benzimidazoles can be prepared through 3CC Ugi reactions.

The structure of compounds **6a**–**p** was confirmed by their analytical and spectral data. The mass spectra of **6a** displayed the molecular ion peak at 419 for M^++1 consistent with the molecular structure. The IR spectrum of **6a** displayed characteristic absorption bands at 3399 and 1672 cm^{-1} due to N–H and C=O stretching vibrations, respectively. The ^1H NMR spectrum of **6a** consisted characteristic singlets at δ 0.73 (9H, 3Me), 1.16 (3H, Me) and 1.27 (3H, Me), two doublets at 1.45 (1H, *J* 14.8 Hz, CCHC), 1.76 (1H, *J*

Table 1
Structure and yields of compounds **6a**–**p** obtained from **4**, amines **5a**–**h**, and 1,1,3,3-tetramethylbutyl or cyclohexyl isocyanides

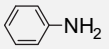
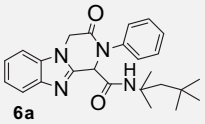
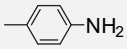
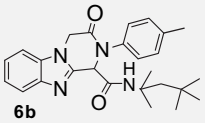
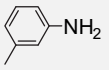
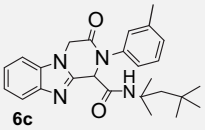
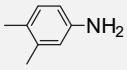
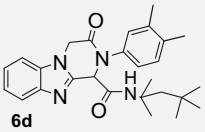
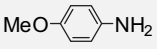
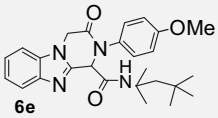
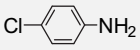
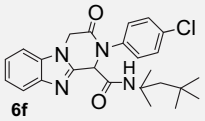
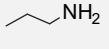
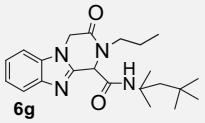
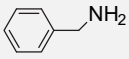
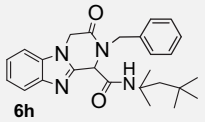
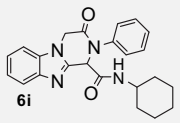
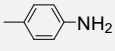
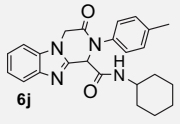
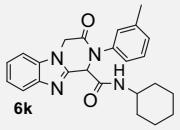
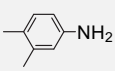
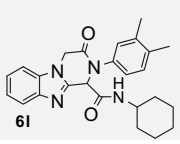
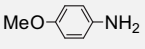
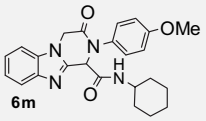
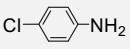
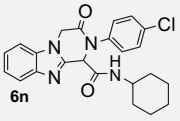
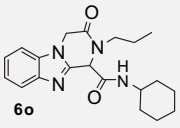
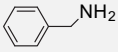
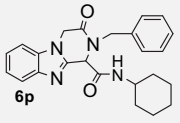
Entry	R^1	Product	Time (h)	Yield[a] (%)
1		 **6a**	6	76
2		 **6b**	4	92
3		 **6c**	5	72
4		 **6d**	4	90
5		 **6e**	6	67
6		 **6f**	5	82
7		 **6g**	15	68
8		 **6h**	8	88
9		 **6i**	6	80
10		 **6j**	4	90
11		 **6k**	6	77
12		 **6l**	4	91

Table 1 (*continued*)

Entry	R^1	Product	Time (h)	Yield[a] (%)
13		 **6m**	7	76
14		 **6n**	5	85
15		 **6o**	18	62
16		 **6p**	8	82

[a] Based on isolated products.

14.8 Hz, CCHC) together with two doublets and a singlet at 5.05 (1H, *J* 16.6 Hz, NCHCO), 5.22 (1H, *J* 16.6 Hz, NCHCO), 6.07 (1H, NCOCHN) and a broad singlet at 7.12 (1H, NH). The presence of two C═O groups was further confirmed by the appearance of two signals at δ 165.1 and 165.3 in the ^{13}C NMR spectrum of **6a**. The ^{1}H NMR and ^{13}C NMR spectra of **6b**–**p** were similar to that of **6a**.

As has been rationalized in Scheme 3, it is conceivable that the initial event is the formation of iminium ion **I** from the amine, and aldehyde **4** followed by activation of the imine by carboxylic acid. Subsequent addition of the nucleophilic isocyanide to the activated iminium followed by trapping of the nitrilium intermediate by carboxylate affords the iminolactone **II**. The irreversible acyl transfer step (Mumm rearrangement)[5] associated with Ugi reaction finally gives the desired 3-oxo-1,2,3,4- tetrahydropyrazino[1,2-*a*] benzimidazole-1-carboxamides **6a**–**p**.

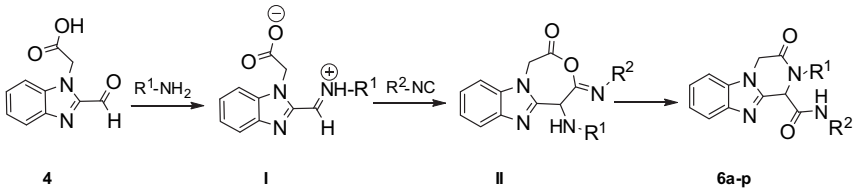
3. Conclusions

In conclusion, by using a bifunctional starting material containing an aldehyde and carboxylic acid functional group in a 3CC reaction, novel heteroaryl-fused pyrazinones **6a**–**p** were prepared. The method offers several advantages including moderate to high yields of products and an easy experimental work-up procedure. These new structures broaden the scaffolds that are accessible through Ugi reactions, and many of them may represent interesting pharmacophores.

4. Experimental section

4.1. General information

All commercially available chemicals and reagents were used without further purification. Melting points were determined with an Electrothermal model 9100 apparatus and are uncorrected. IR spectra were recorded on a Shimadzu 4300 spectrophotometer, in cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500-AVANCE spectrometer at 500 (^{1}H) and 125 MHz (^{13}C) using $CDCl_3$ as solvent and with the residual solvent signal as internal reference ($CDCl_3$, 7.24 and 77.0 ppm). Mass spectra of the products were obtained with a HP (Agilent technologies) 5937 Mass Selective



Scheme 3. Mechanism evoked for the formation of **6a**–**p**.

Detector. Elemental analyses were carried out by a CHN-Rapid Heraeus elemental analyzer (Wellesley, MA).

4.2. Preparation of 2-(diethoxymethyl)-1*H*-benzoimidazole

To a solution of sodium ethoxide (1.20 g, 52.2 mmol Na in 30 mL dry ethanol) were added *o*-phenylenediamine (2.73 g, 25.3 mmol) and ethyl diethoxyacetate (5.35 g, 30.3 mmol), and the mixture was heated to reflux for 24 h. After evaporation of solvent under reduced pressure, the residue was dissolved in water and neutralized with acetic acid. Filteration of the solid followed by recrystallization from ethyl acetate/hexane (1:1) afforded compound **1**.

*4.2.1. 2-(Diethoxymethyl)-1H-benzoimidazole (**1**).* White solid (4.55 g, 82%), mp 174–176 °C. Found: C, 65.40; H, 7.33; N, 12.72. $C_{12}H_{16}N_2O_2$ requires C, 65.43; H, 7.32; N, 12.72%. ν_{max} (KBr) 3327, 1070 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.20 (6H, t, *J* 7.2 Hz, $2OCH_2CH_3$), 3.62–3.75 (4H, m, $2OCH_2CH_3$), 5.71 (1H, s, $CH(OC_2H_5)_2$), 7.25–7.78 (4H, m, Ar), 9.89 (1H, s, N*H*); δ_c (125 MHz, $CDCl_3$) 15.3 ($2OCH_2CH_3$), 62.5 ($2OCH_2CH_3$), 99.6 ($CH(OC_2H_5)_2$), 111.3, 120.4, 122.5, 123.6, 133.0, 143.3, 151.4 (C–Ar); *m*/*z* (EI, 70 eV) 221 (100, M^++1), 176 (65), 117 (20), 77 (6%).

4.3. Preparation of methyl 2-(2-(diethoxymethyl)-1*H*-benzoimidazol-1-yl)acetate 2

To a solution of **1** (4.40 g, 20 mmol) in CH_3CN (40 mL) were added methyl chloroacetate (2.19 g, 20.2 mmol) and K_2CO_3 (2.76 g, 20 mmol) and the mixture was heated to reflux for 6 h. The solid was filtered, and the filtrate was concentrated under reduced pressure to afford compound **2** as a brown oil.

*4.3.1. Methyl 2-(2-(diethoxymethyl)-1H-benzoimidazol-1-yl)acetate (**2**).* Brown oil (5.32 g, 91%). Found: C, 61.23; H, 6.59; N, 9.63. $C_{15}H_{20}N_2O_4$ requires C, 61.63; H, 6.90; N, 9.58%. ν_{max} (KBr) 1752 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.18 (6H, t, *J* 7.0 Hz, $2OCH_2CH_3$), 3.50–3.56 (2H, m, OCH_2CH_3), 3.69 (3H, s, OCH_3), 3.72–3.78 (2H, m, OCH_2CH_3), 5.14 (2H, s, NCH_2CO_2), 5.63 (1H, s, $CH(OC_2H_5)_2$), 7.23–7.28 (3H, m, Ar), 7.75 (1H, d, *J* 7.6 Hz, Ar); δ_c (125 MHz, $CDCl_3$) 15.3 ($2OCH_2CH_3$), 45.6 (NCH_2CO_2), 52.7 (OCH_3), 64.1 ($2OCH_2CH_3$), 99.8 ($CH(OC_2H_5)_2$), 109.6, 120.7, 122.8, 124.1, 136.4, 142.1, 150.7 (C–Ar), 168.7 (C=O); *m*/*z* (EI, 70 eV) 293 (100, M^++1), 248 (68), 219 (80), 191 (9), 131 (16), 77 (6), 47 (8%).

4.4. Preparation of 2-(2-(diethoxymethyl)-1*H*-benzoimidazol-1-yl)acetic acid 3

To a stirred solution of methyl 2-(2-(diethoxymethyl)-1*H*-benzoimidazol-1-yl)acetate **2** (5.85 g, 20 mmol) in methanol (20 mL), a solution of NaOH (0.96 g, 24 mmol) in water (10 mL) was added dropwise. The reaction mixture was stirred for 4 h at rt (TLC monitoring). After evaporation of the volatiles, the mixture was diluted with water (5 mL), and the pH of the reaction mixture was then adjusted to about pH 3–4 with HCl solution. Filteration of the mixture and recrystallization of the solid from ethanol afforded compound **3**.

*4.4.1. 2-(2-(Diethoxymethyl)-1H-benzoimidazol-1-yl)acetic acid (**3**).* White solid (5.30 g, 95%), mp 173–175 °C. Found: C, 60.06; H, 6.28; N, 10.12. $C_{14}H_{18}N_2O_4$ requires C, 60.42; H, 6.52; N, 10.07%. ν_{max} (KBr) 2800–3300, 1707 cm^{-1}; δ_H (500 MHz, DMSO-d_6) 1.14 (6H, t, *J* 7.0 Hz, $2OCH_2CH_3$), 3.48–3.54 (2H, m, OCH_2CH_3), 3.68–3.75 (2H, m, OCH_2CH_3), 5.16 (2H, s, NCH_2CO_2H), 5.66 (1H, s, $CH(OC_2H_5)_2$), 7.22 (1H, t, *J* 7.2 Hz, Ar), 7.27 (1H, t, *J* 7.2 Hz, Ar), 7.55 (1H, d, *J* 7.9 Hz, Ar), 7.64 (1H, d, *J* 7.9 Hz, Ar), 13.03 (1H, br s, O*H*); δ_c (125 MHz, DMSO-d_6) 15.7 ($2OCH_2CH_3$), 45.9 (NCH_2CO_2H), 63.7 ($2OCH_2CH_3$), 99.2 ($CH(OC_2H_5)_2$), 111.5, 120.2, 122.7, 123.8, 137.0, 142.1, 151.1 (C–Ar), 170.2 (C=O); *m*/*z* (EI, 70 eV) 278 (4, M^+), 234 (68), 205 (100), 177 (27), 159 (24), 131 (59), 104 (16), 77 (31), 47 (19%).

4.5. Preparation of 2-(2-formyl-1*H*-benzoimidazol-1-yl)acetic acid 4

Water (15 mL) and 37% hydrochloride acid (13 mL) were added to a THF (60 mL) solution of the crude 2-(2-(diethoxymethyl)-1*H*-benzoimidazol-1-yl)acetic acid **3** (5.57 g, 20 mmol), and the mixture was heated to reflux for 24 h. After evaporation of the volatiles, the mixture was diluted with water (10 mL) and the pH of the reaction mixture was then adjusted to about 3–4 with saturated potassium carbonate solution. Filteration of the mixture and recrystallization of the solid from ethanol afforded compound **4**.

*4.5.1. 2-(2-Formyl-1H-benzoimidazol-1-yl)acetic acid (**4**).* White solid (3.76 g, 92%), mp 230–232 °C. Found: C, 58.80; H, 3.90; N, 13.57. $C_{10}H_8N_2O_3$ requires C, 58.82; H, 3.95; N, 13.72%. ν_{max} (KBr) 2900–3381, 1699 cm^{-1}; δ_H (500 MHz, DMSO-d_6) 5.38 (2H, s, NCH_2CO_2H), 7.40 (1H, t, *J* 7.6 Hz, Ar), 7.50 (1H, t, *J* 7.6 Hz, Ar), 7.83 (1H, d, *J* 8.2 Hz, Ar), 7.90 (1H, d, *J* 8.2 Hz, Ar), 10.01 (1H, s, CO*H*); δ_c (125 MHz, DMSO-d_6) 46.7 (NCH_2CO_2H), 112.6, 122.5, 124.8, 127.5, 137.2, 142.7, 147.0 (C–Ar), 170.1 (C=O), 186.3 (C=O); *m*/*z* (EI, 70 eV) 204 (M^+, 83), 159 (33), 131 (100), 104 (33), 77 (51), 69 (20), 51 (20), 43 (15%).

4.6. Representative procedure for the synthesis of 3-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]benzimidazole-1-carboxamides 6a–p

A solution of 2-(2-formyl-1*H*-benzoimidazol-1-yl)acetic acid **4** (0.20 g, 1.0 mmol), amine (1.0 mmol), and isocyanide (1.0 mmol) in methanol (3 mL) was stirred at 40 °C for the appropriate time (see Table 1). The progress of the reaction was monitored by TLC. On completion, the reaction mixture was cooled to rt, the crude solid was filtered and recrystallized from ethanol to afford compounds **6a**–**p**.

*4.6.1. 3-Oxo-2-phenyl-N-(1,1,3,3-tetramethylbutyl)-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6a**).* White solid (0.32 g, 76%), mp 225–227 °C. Found: C, 71.38; H, 7.62; N, 13.25. $C_{25}H_{30}N_4O_2$ requires C, 71.74; H, 7.22; N, 13.39%. ν_{max} (KBr) 3399, 1672 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.73 (9H, s, CMe_3), 1.16 (3H, s,

C*Me*$_2$), 1.27 (3H, s, C*Me*$_2$), 1.45 (1H, d, *J* 14.8 Hz, CC*H*C), 1.76 (1H, d, *J* 14.8 Hz, CC*H*C), 5.05 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.22 (1H, d, *J* 16.6 Hz, NC*H*CO), 6.07 (1H, s, NCOC*H*N), 7.29–7.50 (9H, m, Ar), 7.12 (1H, br s, N*H*); δ_c (125 MHz, $CDCl_3$) 28.9 (C*Me*$_2$), 29.4 (C*Me*$_2$), 31.5 (C*Me*$_3$), 31.7 (*C*Me$_3$), 47.4 (NCH_2CO), 51.6 (CCH_2C), 56.8 (*C*Me$_2$), 64.2 (NCO*C*HN), 110.0, 119.9, 123.8, 124.1, 127.7, 128.8, 130.1, 134.0, 140.8, 142.9, 145.5 (C–Ar), 165.1 (C=O), 165.3 (C=O); *m*/*z* (EI, 70 eV) 419 (9, M^++1), 297 (43), 263 (100), 234 (83), 219 (9), 158 (16), 131 (51), 104 (23), 77 (29), 57 (64), 41 (24%).

*4.6.2. 3-Oxo-2-p-tolyl-N-(1,1,3,3-tetramethylbutyl)-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6b**).* White solid (0.40 g, 92%), mp 256–258 °C. Found: C, 72.50; H, 7.75; N, 12.73. $C_{26}H_{32}N_4O_2$ requires C, 72.19; H, 7.46; N, 12.95%. ν_{max} (KBr) 3397, 1656 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.73 (9H, s, C*Me*$_3$), 1.12 (3H, s, C*Me*$_2$), 1.25 (3H, s, C*Me*$_2$), 1.43 (1H, d, *J* 14.7 Hz, CC*H*C), 1.78 (1H, d, *J* 14.7 Hz, CC*H*C), 2.44 (3H, s, *Me*), 5.05 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.24 (1H, d, *J* 16.6 Hz, NC*H*CO), 6.18 (1H, s, NCOC*H*N), 7.24–7.32 (6H, m, Ar), 7.36 (1H, br s, N*H*), 7.40 (1H, t, *J* 7.7 Hz, Ar), 7.44 (1H, d, *J* 8.0 Hz, Ar); δ_c (125 MHz, $CDCl_3$) 21.6 (*Me*), 28.8 (C*Me*$_2$), 29.3 (C*Me*$_2$), 31.5 (C*Me*$_3$), 31.7 (*C*Me$_3$), 47.4 (NCH_2CO), 51.6 (CCH_2C), 56.8 (*C*Me$_2$), 64.2 (NCO*C*HN), 110.0, 119.9, 123.6, 124.0, 127.4, 130.7, 134.1, 138.2, 138.8, 143.0, 145.7 (C–Ar), 165.2 (C=O), 165.6 (C=O); *m*/*z* (EI, 70 eV) 433 (7, M^++1), 277 (100), 248 (62), 131 (35), 91 (16), 77 (5), 57 (41), 41 (15%).

*4.6.3. 3-Oxo-2-m-tolyl-N-(1,1,3,3-tetramethylbutyl)-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6c**).* White solid (0.31 g, 72%), mp 231–233 °C. Found: C, 72.05; H, 7.49; N, 12.92. $C_{26}H_{32}N_4O_2$ requires C, 72.19; H, 7.46; N, 12.95%. ν_{max} (KBr) 3335, 1686 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.73 (9H, s, C*Me*$_3$), 1.11 (3H, s, C*Me*$_2$), 1.25 (3H, s, C*Me*$_2$), 1.45 (1H, d, *J* 14.8 Hz, CC*H*C), 1.79 (1H, d, *J* 14.8 Hz, CC*H*C), 2.36 (3H, s, *Me*), 5.05 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.24 (1H, d, *J* 16.6 Hz, NC*H*CO), 6.17 (1H, s, NCOC*H*N), 7.21–7.40 (8H, m, N*H*, Ar), 7.44 (1H, d, *J* 8.0 Hz, Ar); δ_c (125 MHz, $CDCl_3$) 21.7 (*Me*), 28.8 (C*Me*$_2$), 29.4 (C*Me*$_2$), 31.5 (C*Me*$_3$), 31.7 (*C*Me$_3$), 47.4 (NCH_2CO), 51.5 (CCH_2C), 56.8 (*C*Me$_2$), 64.2 (NCO*C*HN), 110.0, 119.8, 123.7, 124.0, 124.6, 128.2, 129.6, 130.0, 134.1, 140.2, 140.7, 143.1, 145.7 (C–Ar), 165.2 (C=O), 165.6 (C=O); *m*/*z* (EI, 70 eV) 430 (2, M^+–2), 277 (100), 248 (45), 219 (79), 178 (38), 131 (39), 97 (29), 81 (38), 69 (75), 57 (71), 43 (65%).

*4.6.4. 2-(3,4-Dimethylphenyl)-3-oxo-N-(1,1,3,3-tetramethylbutyl)-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6d**).* White solid (0.40 g, 90%), mp 238–241 °C. Found: C, 72.51; H, 7.86; N, 12.51. $C_{27}H_{34}N_4O_2$ requires C, 72.62; H, 7.67; N, 12.55%. ν_{max} (KBr) 3410, 1663 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.75 (9H, s, C*Me*$_3$), 1.17 (3H, s, C*Me*$_2$), 1.28 (3H, s, C*Me*$_2$), 1.48 (1H, d, *J* 14.8 Hz, CC*H*C), 1.79 (1H, d, *J* 14.8 Hz, CC*H*C), 2.25 (3H, s, *Me*), 2.33 (3H, s, *Me*), 5.03 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.21 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.98 (1H, s, NCOC*H*N), 7.13 (1H, d, *J* 7.9 Hz, Ar), 7.17 (1H, s, Ar), 7.23 (1H, d, *J* 8.0 Hz, Ar), 7.32 (1H, d, *J* 6.9 Hz, Ar), 7.35 (1H, t, *J* 7.1 Hz, Ar), 7.39 (1H, t, *J* 7.4 Hz, Ar), 7.44 (1H, d, *J* 8.0 Hz, Ar), 7.04 (1H, br s, N*H*); δ_c (125 MHz, $CDCl_3$) 19.9 (*Me*), 20.2 (*Me*), 28.8 (C*Me*$_2$), 29.4 (C*Me*$_2$), 31.5 (C*Me*$_3$), 31.7 (*C*Me$_3$), 47.4 (NCH_2CO), 51.6 (CCH_2C), 56.8 (*C*Me$_2$), 64.4 (NCO*C*HN), 109.9, 119.9, 123.6, 124.0, 124.9, 128.6, 131.2, 134.1, 137.6, 138.4, 138.6, 143.1, 145.6 (C–Ar), 165.2 (C=O), 165.6 (C=O); *m*/*z* (EI, 70 eV) 447 (8, M^++1), 446 (M^+, 2), 291 (100), 262 (30), 247 (7), 235 (4), 158 (4), 131 (16), 105 (8), 77 (5), 57 (20), 41 (6%).

*4.6.5. 2-(4-Methoxyphenyl)-3-oxo-N-(1,1,3,3-tetramethylbutyl)-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6e**).* White solid (0.30 g, 67%), mp 230–233 °C Found: C, 69.74; H, 7.49; N, 12.49. $C_{26}H_{32}N_4O_3$ requires C, 69.62; H, 7.19; N, 12.49%. ν_{max} (KBr) 3272, 1679 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.75 (9H, s, C*Me*$_3$), 1.14 (3H, s, C*Me*$_2$), 1.26 (3H, s, C*Me*$_2$), 1.45 (1H, d, *J* 14.7 Hz, CC*H*C), 1.77 (1H, d, *J* 14.7 Hz, CC*H*C), 3.86 (3H, s, O*Me*), 5.04 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.22 (1H, d, *J* 16.6 Hz, NC*H*CO), 6.13 (1H, s, NCOC*H*N), 6.97 (2H, d, *J* 8.8 Hz, Ar), 7.30–7.34 (5H, m, N*H*, Ar), 7.38 (1H, t, *J* 6.9 Hz, Ar), 7.44 (1H, d, *J* 7.9 Hz, Ar); δ_c (125 MHz, $CDCl_3$) 28.8 (C*Me*$_2$), 29.3 (C*Me*$_2$), 31.5 (C*Me*$_3$), 31.7 (*C*Me$_3$), 47.3 (NCH_2CO), 51.6 (CCH_2C), 56.0 (O*Me*), 56.8 (*C*Me$_2$), 64.4 (NCO*C*HN), 110.0, 115.3, 119.9, 123.7, 124.0, 129.0, 133.5, 134.1, 143.1, 145.7, 159.8 (C–Ar), 165.4 (C=O), 165.6 (C=O); *m*/*z* (EI, 70 eV) 448 (5, M^+), 293 (100), 264 (23), 219 (24), 205 (13), 131 (19), 77 (7), 57 (12%).

*4.6.6. 2-(4-Chlorophenyl)-3-oxo-N-(1,1,3,3-tetramethylbutyl)-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6f**).* White solid (0.37 g, 82%), mp 256–257 °C. Found: C, 66.45; H, 6.39; N, 12.30. $C_{25}H_{29}ClN_4O_2$ requires C, 66.29; H, 6.45; N, 12.37%. ν_{max} (KBr) 3415, 1669 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.76 (9H, s, C*Me*$_3$), 1.23 (3H, s, C*Me*$_2$), 1.31 (3H, s, C*Me*$_2$), 1.51 (1H, d, *J* 14.8 Hz, CC*H*C), 1.77 (1H, d, *J* 14.8 Hz, CC*H*C), 5.04 (1H, d, *J* 16.7 Hz, NC*H*CO), 5.16 (1H, d, *J* 16.7 Hz, NC*H*CO), 5.86 (1H, s, NCOC*H*N), 6.86 (1H, br s, N*H*), 7.28–7.48 (8H, m, Ar); δ_c (125 MHz, $CDCl_3$) 29.0 (C*Me*$_2$), 29.4 (C*Me*$_2$), 31.5 (C*Me*$_3$), 31.7 (*C*Me$_3$), 47.3 (NCH_2CO), 51.6 (CCH_2C), 57.0 (*C*Me$_2$), 64.2 (NCO*C*HN), 109.9, 120.0, 123.9, 124.2, 129.2, 130.2, 134.0, 134.7, 139.2, 143.1, 145.0 (C–Ar), 164.9 (C=O), 165.2 (C=O); *m*/*z* (EI, 70 eV) 453 (2, M^++1), 297 (100), 269 (53), 53 (12), 158 (14), 131 (48), 111 (12), 77 (11), 57 (59), 41 (22%).

*4.6.7. 3-Oxo-2-propyl-N-(1,1,3,3-tetramethylbutyl)-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6g**).* White solid (0.26 g, 68%), mp 185–188 °C. Found: C, 67.73; H, 8.80; N, 14.57. $C_{22}H_{32}N_4O_2$ requires C, 68.72; H, 8.39; N, 14.57%. ν_{max} (KBr) 3292, 1688 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.80 (9H, s, C*Me*$_3$), 0.95 (3H, t, *J* 7.3 Hz, $CH_2CH_2CH_3$), 1.22 (3H, s, C*Me*$_2$), 1.29 (3H, s, C*Me*$_2$), 1.56 (1H, d, *J* 14.8 Hz, CC*H*C), 1.63–1.76 (2H, m, $CH_2CH_2CH_3$), 1.77 (1H, d, *J* 14.8 Hz, CC*H*C), 3.11–3.17 (1H, m, $CH_2CH_2CH_3$), 4.04–4.10 (1H, m, $CH_2CH_2CH_3$), 4.93 (1H, d, *J* 16.5 Hz, NC*H*CO), 5.00 (1H, d, *J* 16.5 Hz, NC*H*CO), 5.81 (1H, s, NCOC*H*N), 7.38–7.41 (3H, m, N*H*, Ar), 7.43 (1H, d, *J* 6.5 Hz, Ar), 7.73 (1H, d, *J* 6.1 Hz, Ar); δ_c (125 MHz, $CDCl_3$) 11.7 ($CH_2CH_2CH_3$), 21.0 ($CH_2CH_2CH_3$), 29.1 (C*Me*$_2$), 29.4 (C*Me*$_2$), 31.5 (C*Me*$_3$), 31.8 (*C*Me$_3$), 46.9 (NCH_2CO), 49.0 ($CH_2CH_2CH_3$), 50.6 (CCH_2C), 56.8 (*C*Me$_2$), 60.4 (NCO*C*HN), 110.1, 119.6, 123.9, 124.0, 134.1, 143.1, 145.8 (C–Ar), 164.9 (C=O), 165.3 (C=O); *m*/*z* (EI, 70 eV) 385 (9, M^++1), 384 (M^+, 2), 229 (100), 200 (64), 186 (6), 158 (14), 131 (15), 57 (14), 41 (7%).

*4.6.8. 2-Benzyl-3-oxo-N-(1,1,3,3-tetramethylbutyl)-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6h**).* White solid (0.38 g, 88%), mp 210–212 °C. Found: C, 72.03; H, 7.60; N, 12.41. $C_{26}H_{32}N_4O_2$ requires C, 72.19; H, 7.46; N, 12.95%. ν_{max} (KBr) 3287, 1684 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.86 (9H, s, C*Me*$_3$), 1.33 (3H, s, C*Me*$_2$), 1.35 (3H, s, C*Me*$_2$), 1.63 (1H, d, *J* 14.9 Hz, CC*H*C), 1.79 (1H, d, *J* 14.9 Hz, CC*H*C), 4.09 (1H, d, *J* 15.0 Hz, NC*H*CO), 4.97 (2H, s, CH_2Ph), 5.28 (1H, s, NCOC*H*N), 5.53 (1H, d, *J* 15.0 Hz, NC*H*CO), 6.78 (1H, br s, N*H*), 7.18–7.26 (5H, m, Ar), 7.36–7.37 (2H, m, Ar), 7.40 (1H, d, *J* 7.6 Hz, Ar), 7.71 (1H, d, *J* 7.1 Hz, Ar); δ_c (125 MHz, $CDCl_3$) 29.2 (C*Me*$_2$), 29.5 (C*Me*$_2$), 31.6 (C*Me*$_3$), 31.9 (*C*Me$_3$), 46.6 (NCH_2CO), 49.8 (CH_2Ph), 51.8 (CCH_2C), 56.8 (*C*Me$_2$), 59.2 (NCO*C*HN), 109.9, 120.0, 123.8, 123.9, 128.5, 129.0, 129.2, 134.0, 135.4, 143.2, 145.0 (C–Ar), 164.5 (C=O), 165.0 (C=O); *m*/*z* (EI, 70 eV) 433 (5, M^++1), 277 (100), 186 (61), 158 (5), 131 (10), 91 (30), 57 (15), 41 (6%).

*4.6.9. N-Cyclohexyl-3-oxo-2-phenyl-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6i**).* White solid (0.31 g, 80%), mp 280–281 °C. Found: C, 71.39; H, 6.52; N, 14.43. $C_{23}H_{24}N_4O_2$ requires C, 71.11; H, 6.23; N, 14.42%. ν_{max} (KBr) 3217, 1672 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.86–1.88 (m, 10H, 5CH_2 of cyclohexyl), 3.50–3.55 (1H, m, C*H*NH of cyclohexyl), 5.00 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.17 (1H, d, *J* 16.6 Hz, NC*H*CO), 6.03 (1H, s, NCOC*H*N),

7.26–7.41 (9H, m, Ar), 8.14 (1H, d, *J* 6.2 Hz, N*H*); δ_c (125 MHz, $CDCl_3$) 25.0 ($2CH_2$), 25.6 (CH_2), 32.3 (CH_2), 33.1 (CH_2), 47.2 (NCH_2CO), 50.1 (*C*HNH of cyclohexyl), 63.3 (NCO*C*HN), 100.4, 110.0, 119.6, 123.8, 124.1, 127.6, 128.8, 130.1, 133.9, 140.6, 145.4 (C–Ar), 165.0 (C=O), 166.2 (C=O); *m*/*z* (EI, 70 eV) 388 (2, M^+), 263 (100), 234 (98), 219 (16), 158 (17), 131 (64), 104 (35), 77 (51), 55 (22), 41 (16%).

*4.6.10. N-Cyclohexyl-3-oxo-2-p-tolyl-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6j**).* White solid (0.37 g, 90%), mp 252–254 °C. Found: C, 71.49; H, 6.20; N, 13.73. $C_{24}H_{26}N_4O_2$ requires C, 71.62; H, 6.51; N, 13.92%. ν_{max} (KBr) 3208, 1672 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.84–2.00 (10H, m, 5C*H*$_2$ of cyclohexyl), 2.44 (3H, s, *Me*), 3.56–3.62 (1H, m, C*H*NH of cyclohexyl), 5.05 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.23 (1H, d, *J* 16.6 Hz, NC*H*CO), 6.09 (1H, s, NCOC*H*N), 7.20 (1H, d, *J* 8.0 Hz, Ar), 7.25 (4H, br s, Ar), 7.30 (1H, t, *J* 7.6 Hz, Ar), 7.39 (1H, t, *J* 7.6 Hz, Ar), 7.44 (1H, d, *J* 8.0 Hz, Ar), 8.03 (1H, d, *J* 6.4 Hz, N*H*); δ_c (125 MHz, $CDCl_3$) 21.6 (*Me*), 25.1 ($2CH_2$), 25.6 (CH_2), 32.4 (CH_2), 33.3 (CH_2), 47.2 (NCH_2CO), 50.2 (*C*HNH of cyclohexyl), 63.7 (NCO*C*HN), 110.0, 119.7, 123.6, 124.0, 127.5, 130.8, 134.0, 138.0, 138.9, 142.9, 145.6 (C–Ar), 165.0 (C=O), 166.3 (C=O); *m*/*z* (EI, 70 eV) 401 (5, M^+-1), 355 (46), 236 (20), 268 (23), 149 (19), 236 (100), 91 (85), 77 (9), 59 (16%).

*4.6.11. N-Cyclohexyl-3-oxo-2-m-tolyl-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6k**).* White solid (0.31 g, 77%), mp 250–252 °C. Found: C, 71.50; H, 6.59; N, 14.02. $C_{24}H_{26}N_4O_2$ requires C, 71.62; H, 6.51; N, 13.92%. ν_{max} (KBr) 1678, 3210 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.83–2.01 (10H, m, 5C*H*$_2$ of cyclohexyl), 2.32 (3H, s, *Me*), 3.56–3.62 (1H, m, C*H*NH of cyclohexyl), 5.06 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.25 (1H, d, *J* 16.6 Hz, NC*H*CO), 6.20 (1H, s, NCOC*H*N), 7.16–7.19 (3H, m, Ar), 7.26 (1H, d, *J* 7.6 Hz, Ar), 7.32 (1H, d, *J* 7.8 Hz, Ar), 7.36 (1H, t, *J* 8.1 Hz, Ar), 7.40 (1H, t, *J* 7.6 Hz, Ar), 7.46 (1H, d, *J* 8.0 Hz, Ar). 8.22 (1H, br s, N*H*); δ_c (125 MHz, $CDCl_3$) 21.7 (*Me*), 25.0 ($2CH_2$), 25.6 (CH_2), 32.3 (CH_2), 33.3 (CH_2), 47.2 (NCH_2CO), 50.2 (*C*HNH of cyclohexyl), 63.5 (NCO*C*HN), 110.0, 119.5, 123.9, 124.2, 124.7, 128.3, 129.8, 130.0, 133.9, 140.3, 140.4, 142.6, 145.6 (C–Ar); 164.8 (C=O), 166.3 (C=O); *m*/*z* (EI, 70 eV) 416 (4, M^+), 293 (23), 277 (100), 248 (56), 219 (27), 177 (4), 131 (42), 97 (26), 81 (42), 69 (83), 57 (63), 43 (50%).

*4.6.12. N-Cyclohexyl-2-(3,4-dimethylphenyl)-3-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6l**).* White solid (0.38 g, 91%), mp 262–265 °C. Found: C, 72.00; H, 6.82; N, 13.15. $C_{25}H_{28}N_4O_2$ requires C, 72.09; H, 6.78; N, 13.45%. ν_{max} (KBr) 3381, 1654 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.78–1.93 (10H, m, 5C*H*$_2$ of cyclohexyl), 2.11 (3H, s, *Me*), 2.25 (3H, s, *Me*), 3.46–3.53 (1H, m, C*H*NH of cyclohexyl), 4.97 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.16 (1H, d, *J* 16.6 Hz, NC*H*CO), 6.11 (1H, s, NCOC*H*N), 6.99 (1H, d, *J* 7.9 Hz, Ar), 7.02 (1H, s, Ar), 7.04 (1H, d, *J* 8.1 Hz, Ar), 7.12 (1H, d, *J* 7.8 Hz, Ar), 7.21 (1H, t, *J* 7.3 Hz, Ar), 7.30 (1H, t, *J* 7.8 Hz, Ar), 7.37 (1H, d, *J* 8.0 Hz, Ar), 8.46 (1H, d, *J* 6.3 Hz, N*H*); δ_c (125 MHz, $CDCl_3$) 19.8 (*Me*), 20.1 (*Me*), 25.0 ($2CH_2$), 25.6 (CH_2), 32.2 (CH_2), 33.2 (CH_2), 47.1 (NCH_2CO), 50.0 (*C*HNH of cyclohexyl), 63.4 (NCO*C*HN), 110.0, 119.4, 123.4, 123.8, 124.9, 128.5, 131.1, 133.9, 137.4, 138.1, 138.5, 142.8, 145.7 (C–Ar), 164.9 (C=O), 166.6 (C=O); *m*/*z* (EI, 70 eV) 416 (2, M^+), 291 (100), 262 (30), 247 (6), 235 (4), 158 (4), 131 (19), 105 (10), 77 (8), 55 (12), 41 (7%).

*4.6.13. N-Cyclohexyl-2-(4-methoxyphenyl)-3-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6m**).* White solid (0.32 g, 76%), mp 257–260 °C. Found: C, 68.96; H, 6.40; N, 13.58. $C_{24}H_{26}N_4O_3$ requires C, 68.88; H, 6.26; N, 13.39%. ν_{max} (KBr) 3365, 1658 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.77–1.86 (10H, m, 5C*H*$_2$ of cyclohexyl), 3.42–3.49 (1H, m, C*H*NH of cyclohexyl), 2.74 (3H, s, O*Me*), 4.93 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.11 (1H, d, *J* 16.6 Hz, NC*H*CO), 6.02 (1H, s, NCOC*H*N), 6.82 (2H, d, *J* 8.9 Hz, Ar), 7.12–7.16 (3H, m, Ar), 7.18 (1H, t, *J* 7.6 Hz, Ar), 7.26 (1H, t, *J* 10.6 Hz, Ar), 7.34 (1H, d, *J* 8.0 Hz, Ar), 8.44 (1H, d, *J* 6.5 Hz, N*H*); δ_c (125 MHz, $CDCl_3$) 25.0 ($2CH_2$), 25.6 (CH_2), 32.3 (CH_2), 33.1 (CH_2), 47.1 (NCH_2CO), 50.0 (*C*HNH of cyclohexyl), 55.9 (O*Me*), 63.6 (NCO*C*HN), 110.0, 115.2, 119.6, 123.4, 123.8, 128.8, 133.2, 133.9, 143.0, 145.6, 159.6 (C–Ar), 165.1 (C=O), 166.5 (C=O); *m*/*z* (EI, 70 eV) 418 (9, M^+), 293 (96), 264 (32), 248 (23), 219 (100), 205 (26), 131 (44), 69 (30), 57 (44), 43 (40%).

*4.6.14. 2-(4-Chlorophenyl)-N-cyclohexyl-3-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6n**).* White solid (0.36 g, 85%), mp 270–271 °C. Found: C, 65.10; H, 6.08; N, 12.85. $C_{23}H_{23}ClN_4O_2$ requires C, 65.32; H, 5.48; N, 13.25%. ν_{max} (KBr) 3212, 1675 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.91–1.98 (10H, m, 5C*H*$_2$ of cyclohexyl), 3.59–3.62 (1H, m, C*H*NH of cyclohexyl), 5.06 (1H, d, *J* 16.7 Hz, NC*H*CO), 5.21 (1H, d, *J* 16.7 Hz, NC*H*CO), 6.04 (1H, s, NCOC*H*N), 7.28–7.48 (8H, m, Ar), 7.83 (1H, br s, N*H*); δ_c (125 MHz, $CDCl_3$) 25.0 (CH_2), 25.6 (CH_2), 31.3 (CH_2), 32.4 (CH_2), 33.2 (CH_2), 47.1 (NCH_2CO), 50.4 (*C*HNH of cyclohexyl), 63.3 (NCO*C*HN), 110.2, 119.4, 124.4, 124.6, 129.2, 130.4, 133.7, 134.3, 138.9, 142.6, 145.6 (C–Ar), 164.8 (C=O), 165.3 (C=O); *m*/*z* (EI, 70 eV) 423 (2, M^++1), 297 (100), 268 (57), 186 (31), 158 (17), 131 (66), 111 (18), 91 (21), 77 (16), 55 (33), 41 (25%).

*4.6.15. N-Cyclohexyl-3-oxo-2-propyl-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6o**).* White solid (0.22 g, 62%), mp 207–208 °C. Found: C, 67.34; H, 7.84; N, 14.71. $C_{20}H_{26}N_4O_2$ requires C, 67.77; H, 7.39; N, 15.81%. ν_{max} (KBr) 1685, 3218 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.3 Hz, $CH_2CH_2CH_3$), 0.96–2.11 (12H, m, 5C*H*$_2$ of cyclohexyl, $CH_2CH_2CH_3$), 3.20–3.26 (1H, m, $CH_2CH_2CH_3$), 3.62–3.67 (1H, m, C*H*NH of cyclohexyl), 3.90–3.96 (1H, m, $CH_2CH_2CH_3$), 4.94 (1H, d, *J* 16.5 Hz, NC*H*CO), 5.07 (1H, d, *J* 16.5 Hz, NC*H*CO), 5.88 (1H, s, NCOC*H*N), 7.40–7.43 (2H, m, Ar), 7.46 (1H, d, *J* 7.5 Hz, Ar), 7.73 (1H, d, *J* 7.2 Hz, Ar), 8.36 (1H, d, *J* 6.1 Hz, N*H*); δ_c (125 MHz, $CDCl_3$) 11.6 ($CH_2CH_2CH_3$), 21.0 ($CH_2CH_2CH_3$), 25.1 (CH_2), 25.2 (CH_2), 25.7 (CH_2), 32.7 (CH_2), 33.4 (CH_2), 46.8 (NCH_2CO), 48.9 ($CH_2CH_2CH_3$), 50.3 (*C*HNH of cyclohexyl), 60.0 (NCO*C*HN), 110.2, 119.3, 124.0, 124.1, 134.1, 142.9, 145.8 (C–Ar), 164.7 (C=O), 166.3 (C=O); *m*/*z* (EI, 70 eV) 353 (2, M^+-1), 229 (100), 200 (10), 186 (9), 158 (14), 131 (14), 55 (10), 43 (10%).

*4.6.16. 2-Benzyl-N-cyclohexyl-3-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazole-1-carboxamide (**6p**).* White solid (0.33 g, 82%), mp 284–286 °C. Found: C, 71.75; H, 6.84; N, 13.60. $C_{24}H_{26}N_4O_2$ requires C, 71.62; H, 6.51; N, 13.92%. ν_{max} (KBr) 3217, 1676 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.00–1.81 (10H, m, 5C*H*$_2$ of cyclohexyl), 3.45–3.52 (1H, m, C*H*NH of cyclohexyl), 4.00 (1H, d, *J* 14.9 Hz, C*H*$_2$Ph), 4.86 (1H, d, *J* 16.6 Hz, NC*H*CO), 4.96 (1H, d, *J* 16.6 Hz, NC*H*CO), 5.30 (1H, d, *J* 14.9 Hz, C*H*$_2$Ph), 5.31 (1H, s, NCOC*H*N), 7.15 (5H, br s, Ar), 7.23–7.28 (2H, m, Ar), 7.32 (1H, d, *J* 7.9 Hz, Ar), 7.60 (1H, d, *J* 7.6 Hz, Ar), 7.64 (1H, d, *J* 6.9 Hz, N*H*); δ_c (125 MHz, $CDCl_3$) 25.0 (CH_2), 25.1 (CH_2), 25.7 (CH_2), 32.6 (CH_2), 33.2 (CH_2), 46.7 (NCH_2CO), 49.6 (*C*H$_2$Ph), 50.0 (*C*HNH of cyclohexyl), 58.8 (NCO*C*HN), 110.0, 119.7, 123.8, 124.0, 128.3, 128.9, 129.1, 133.8, 135.5, 143.2, 145.1 (C–Ar), 165.0 (C=O), 135.4 (C=O); *m*/*z* (EI, 70 eV) 402 (2, M^+), 277 (100), 186 (85), 158 (7), 131 (15), 91 (52), 55 (10), 41 (9%).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.08.057.

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