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Synthesis of the novel pyrimido[1,6-*a*]pyrimidine and imidazo[1,2-*c*]pyrimidine derivatives based on heterocyclic ketene aminals

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ABSTRACT

A concise and efficient route for the synthesis of pyrimido[1,6-*a*]pyrimidines and imidazo[1,2-*c*]pyrimidines by simply refluxing a reaction mixture of different heterocyclic ketene aminals and *N*,*N*′-bis(arylmethylidene)arylmethane was developed. This protocol provides an alternative method for application in combinatorial and parallel synthesis in drug discovery.

1. Introduction

In last few years, combinatorial methods using multicomponent reactions have been closely examined as a fast and convenient solution for the synthesis of diverse classes of compounds.[1,2] Multicomponent reactions (MCRs), defined as one-pot reactions in which at least three functional groups join through covalent bonds, have been steadily gaining importance in synthetic organic chemistry.[1–4]

Heterocyclic ketene aminals (HKAs), because of their distinctive electronic features, have been significantly used as flexible synthons for the construction of a variety of fused-ring polycyclic heterocycles and therefore are highly noteworthy in contemporary organic synthesis.[5] These fused heterocyclic structures are frequently found in pharmacophores and play important roles in drug discovery and are also used as herbicides, pesticides,[6] antianxiety agents,[7] antileishmanial agents,[8] and antibacterial drugs.[9] For example, imidazoindoles are present as the key structural motif in the core structures of novel marine natural products and biologically active molecules, including the potent cholecystokinin antagonist asperlicin (**7**)[10] and the antifungal and moderately cytotoxic fumiquinazolines A (**8**) and B (**9**)[11,12] (Fig. 1).

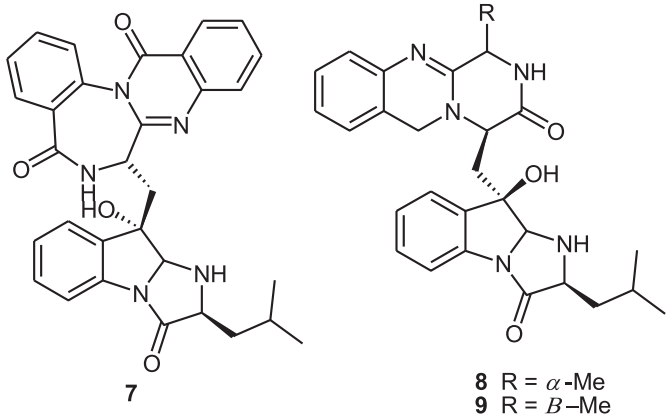

Fig. 1. Structures of novel marine natural products and biologically active compounds.

N,*N*′-Bis(arylmethylidene)arylmethanes serve as good precursors for the synthesis of numerous organic compounds, especially aza-cyclic compounds.[13–17] This easily accessible precursor can be produced by the reaction of aromatic aldehydes and ammonia solution.

As part of our continuing effort into the design of new routes for the preparation of biologically active compounds,[18–21] herein, we describe a simple, one-pot, three-component synthesis of pyrimido

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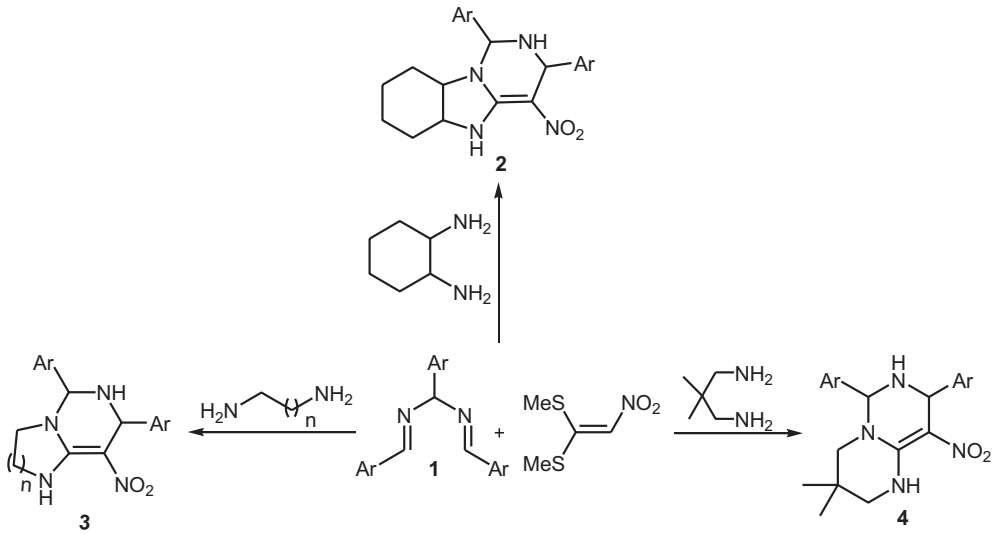
[1,6-*a*]pyrimidines and imidazo[1,2-*c*]pyrimidines from heterocyclic ketene aminals. The reaction of *N*,*N*′-bis(arylmethylidene)arylmethanediamine **1** and different diamines in the presence of 1,1-bis(methylthio)-2-nitroethylene in anhydrous ethanol under reflux produces compounds **2**–**4** in 72–88% yields (Table 2).

2. Results and discussion

The choice of an appropriate reaction medium is of crucial importance for successful synthesis. Initially, the three-component reaction of *N*,*N*′-bis(arylmethylidene)arylmethanediamine **1** and different diamines in the presence of 1,1-bis(methylthio)-2-nitroethylene as a simple model substrate was investigated to establish the feasibility of the strategy and to optimize the reaction conditions (Scheme 1).

Encouraged by this success, we extended this reaction of *N*,*N*′-bis(arylmethylidene)arylmethanediamine **1** and different diamines in the presence of 1,1-bis(methylthio)-2-nitroethylene. The corresponding products **2**–**4** were synthesized in high yield (74–85%) and the results are summarized in Table 2.

The structures of compounds **2**–**4** were deduced from their elemental analysis, IR and high-field ^{1}H and ^{13}C NMR spectra. The mass spectrum of **2** displayed the molecular ion peak at *m*/*z* 376, which is in agreement with the proposed structure. The IR spectrum of this compound showed absorption bands due to the NH, CH, and NO_2 groups at 3372, 3251, and 2924 and 1379 cm^{-1}, respectively. The ^{1}H NMR spectrum of **2** showed two multiplets for the CH_2 groups (δ=0.91–1.23 and 1.51–1.68 ppm), two singlets for the CH (δ=4.77 and 5.46), two multiplets for the CH (δ=3.30–3.34 and 4.05–4.07), two singlets for the NH groups (δ=2.58 and 8.61),



Scheme 1. Reaction of heterocyclic ketene aminals with *N*,*N*′-bis(arylmethylidene)arylmethane.

Different solvents, such as methanol, ethanol, acetonitrile, tetrahydrofuran (THF), and dichloromethane were explored. The results are summarized in Table 1.

Table 1
Synthetic results of **2** under different reactions conditions

Entry	Solvent	Temp	Time/h	Yield[a] (%)
1	MeOH	Reflux	12	54
2	EtOH	Reflux	8	74
3	H_3CCN	Reflux	8	57
4	THF	Reflux	10	69
5	CH_2Cl_2	Reflux	10	21

[a] Isolated yield.

Table 2
Synthesis of pyrimido[1,6-*a*]pyrimidine and imidazo[1,2-*c*]pyrimidine

Product	Ar	*n*	Time	Yield (%)
2	Ph	—	8	74
3a	Ph	1	8	80
3b	*p*-$MeOC_6H_4$	1	8	81
3c	Ph	2	8	83
3d	*p*-$MeOC_6H_4$	2	10	75
3e	Ph	3	10	80
3f	*p*-$MeOC_6H_4$	3	10	85
4a	Ph	—	10	79
4b	*p*-$MeOC_6H_4$	—	10	78

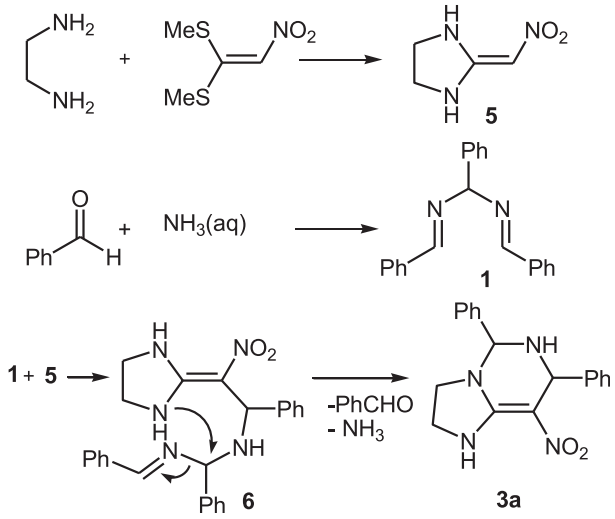
As can be seen from Table 1, the best results were obtained by refluxing the reaction mixture in EtOH to yield product **2** in good yield (Table 1, entry 2).

and the aromatic moieties gave rise to multiplets in the aromatic region of the spectrum (δ=7.26–7.40 ppm). The ^{1}H-decoupled ^{13}C NMR spectrum of **2** showed 18 distinct resonances in agreement with the suggested structure. This process was successfully applied to other aldehydes as summarized in Table 2 and Scheme 1. As shown in Scheme 1 and Table 2, the reaction of various aldehydes with ammonia followed by reaction with different diamines and 1,1-bis(methylthio)-2-nitroethylene, afforded pyrimido[1,6-*a*]pyrimidine and imidazo[1,2-*c*]pyrimidine **2**–**4** in good yields.

Although we have not established the mechanism of reaction experimentally, a possible explanation is proposed in Scheme 2. Compound **3a** could result from the initial addition of the ethylenediamine to 1-bis(methylthio)-2-nitroethylene and subsequent attack of the resulting reactive compound **5** on the compound **1a** to yield intermediate **6**. Cyclization of **6** and subsequent loss of aldehyde lead to compound **3a** (Scheme 2).

3. Conclusion

In summary, a simple and easy method has been developed for the quick construction of novel pyrimido[1,6-*a*]pyrimidines and imidazo[1,2-*c*]pyrimidines by the reaction of HKAs with *N*,*N*′-bis(arylmethylidene)arylmethanediamine. These types of heterocycles contain a number of functional groups and are therefore valuable precursors for the diversity orientated synthesis of pyrimido[1,6-*a*]pyrimidine and imidazo[1,2-*c*]pyrimidine libraries, which are of potential use in the facile preparation of biologically active molecules. Further work on the reactions of compound **1** is under way.



Scheme 2. Proposed mechanism.

4. Experimental

4.1. General

All reactions were carried out in oven-dried glassware. Progress of reactions was monitored by thin layer chromatography while purification was effected by column chromatography, using silica gel (Merck 230–240 mesh). Diamines, aldehydes, and ammonia were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H, and N were performed using a Heraeus CHN–O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 70 eV. ^{1}H and ^{13}C NMR spectra were measured (DMSO-d_6) with a Bruker DRX-500 AVANCE spectrometer at 500.13 and 125.8 MHz, respectively. IR spectra were recorded on a Shimadzu IR-460 spectrometer, absorbances are reported in cm^{-1}.

4.2. General procedure for the preparation of compounds 1

The benzaldehyde (for **1a**) or 4-methoxybenzaldehyde (for **1b**) (3 mmol) was added to NH_4OH (30%, 10 mL) and the solution was stirred for 5 h at reflux. During this time, a white precipitate formed. The precipitate was removed by filtration and dried.

4.3. General procedure for the preparation of compounds 2–4, exemplified on 2

A mixture of cyclohexane-1,2-diamine (0.11 g, mmol), 1,1-bis(methylthio)-2-nitroethylene (0.16 g, 1 mmol) in a 50 mL flask was stirred at reflux for 12 h, then *N*,*N*′-bis(phenylmethylidene) phenylmethanediamine **1a** (0.3 g, 1 mmol) was added and the reaction mixture heated at reflux for the time period as indicated in Table 1. When the reaction mixture was cooled to room temperature, a white solid precipitated. The precipitates were filtered and washed with diethyl ether to give product **2** in 74% yields. All products gave satisfactory spectral data in accordance with the assigned structures.

*4.3.1. 4-Nitro-1,3-diphenyl-1,2,3,5,5a,6,7,8,9,9a-decahydropyrimido [1,6-a][1,3]benzimidazole (**2**).* White powder, mp=245 °C (dec), 0.28 g, yield 74%. IR (KBr): 3372 (NH), 3251 (NH), 2924 (CH), 1587 and 1494 (Ar), 1379 (NO_2). Anal. Calcd for $C_{22}H_{24}N_4O_2$ (376.45): C, 70.19; H, 6.43; N, 14.88%. Found: C, 70.12; H, 6.36; N, 14.81%. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ=0.91–1.23 (2H, m, CH_2), 1.51–1.68 (6H, m, $3CH_2$), 2.58 (1H, s, NH), 3.30–3.34 (1H, m, CH–NH), 4.05–4.07 (1H, m, CH–N), 4.77 (1H, s, CH), 5.46 (1H, s, CH), 7.26–7.40 (10H, m, Ar), 8.61 (1H, s, NH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ=19.71 (CH_2), 20.80 (CH_2), 25.60 (CH_2), 25.79 (CH_2), 53.88 (CH), 54.26 (CH), 58.03 (CH), 66.39 (CH), 106.31 (C–NO_2), 126.95 (2CH of Ar), 127.49 (CH of Ar), 127.74 (2CH of Ar), 128.52 (2CH of Ar), 129.26 (2CH of Ar), 129.56 (CH of Ar), 136.82 (C_{ipso}), 140.62 (C_{ipso}), 157.57 (*C*=CNO_2). MS (EI, 70 eV): *m*/*z* (%)=376 (1) [M^+], 330 (8), 272 (100), 225 (32), 194 (8), 169 (12), 128 (13), 104 (25), 91 (1), 77 (16).

*4.3.2. 8-Nitro-5,7-diphenyl-1,2,3,5,6,7-hexahydroimidazo[1,2-c]pyrimidine (**3a**).* White powder, mp=240 °C (dec), 0.26 g, yield 80%. IR (KBr): 3281 (NH), 3044 (NH), 2924 (CH), 1592 and 1528 (Ar), 1405 (NO_2). Anal. Calcd for $C_{18}H_{18}N_4O_2$ (322.36): C, 67.07; H, 5.63; N, 17.38%. Found: C, 67.02; H, 5.57; N, 17.31%. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ=2.72 (1H, br, NH), 3.21–3.32 (2H, m, CH_2–NH), 3.69–3.80 (2H, m, CH_2–N), 4.74 (1H, s, CH), 5.50 (1H, s, CH), 7.24–7.42 (10H, m, Ar), 8.74 (1H, s, NH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ=42.34 (CH_2), 47.13 (CH_2), 54.18 (CH), 68.90 (CH), 106.18 (C–NO_2), 126.97 (2CH of Ar), 127.53 (CH of Ar), 127.71 (2CH of Ar), 128.52 (2CH of Ar), 129.31 (2CH of Ar), 129.65 (CH of Ar), 136.68 (C_{ipso}), 140.39 (C_{ipso}), 157.86 (*C*=CNO_2). MS (EI, 70 eV): *m*/*z* (%)=322 (2) [M^+], 276 (13), 218 (100), 194 (6), 171 (32), 143 (4), 115 (13), 104 (25), 89 (8), 77 (16).

*4.3.3. 4-[5-(4-Methoxyphenyl)-8-nitro-1,2,3,5,6,7-hexahydroimidazo [1,2-c]pyrimidine-7-yl]phenyl methyl ether (**3b**).* White powder, mp=204 °C (dec), 0.31 g, yield 81%. IR (KBr) (ν_{max}, cm^{-1}): 3364 (NH), 3267 (NH), 2861 (CH), 1594 and 1514 (Ar), 1379 (NO_2). Anal. Calcd for $C_{20}H_{22}N_4O_4$ (382.41): C, 62.82; H, 5.80; N, 14.65%. Found: C, 62.79; H, 5.76; N, 14.60%. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ_H=2.83 (1H, s, NH), 3.19–3.25 (2H, m, CH_2–NH), 3.67–3.72 (2H, m, CH_2N), 3.78 (6H, s, OCH_3), 4.70 (1H, s, CH), 5.40 (1H, s, CH), 6.85–6.90 (4H, m, 4CH of Ar), 7.26–7.29 (4H, m, 4CH of Ar), 8.71 (1H, s, NH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ_C=42.38 (CH_2), 47.11 (CH_2), 53.71 (CH), 55.30 (OCH_3), 55.36 (OCH_3), 68.34 (CH), 106.49 (C–NO_2), 113.90 (2CH of Ar), 114.56 (2CH of Ar), 128.36 (2CH of Ar), 128.84 (2CH of Ar), 132.55 ($2C_{ipso}$), 157.73 (*C*=CNO_2), 158.99 (C_{ipso}–OMe), 160.41 (C_{ipso}–OMe) ppm. MS (EI, 70 eV): *m*/*z* (%)=383 (1) [M^++1], 246 (50), 200 (16), 134 (100), 119 (25), 108 (13), 91 (25), 77 (30), 65 (32).

*4.3.4. 9-Nitro-6,8-diphenyl-1,3,4,6,7,8-hexahydro-2H-pyrimido[1,6-a]pyrimidine (**3c**).* White powder, mp=220 °C (dec), 0.28 g, yield 83%. IR (KBr): 3253 (NH), 3037 (NH), 2899 (CH), 1568 (Ar), 1378 (NO_2). Anal. Calcd for $C_{19}H_{20}N_4O_2$ (336.39): C, 67.84; H, 5.99; N, 16.66%. Found: C, 67.79; H, 5.92; N, 16.61%. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ=1.79–1.95 (2H, m, CH_2), 2.80–2.88 (2H, m, CH_2), 2.99 (1H, dd, $^3J_{HH}$=11.8 Hz, $^3J_{HH}$=3.5 Hz, NH), 3.38 (1H, t, $^3J_{HH}$=9.0 Hz, CH_2), 3.52 (1H, dd, $^2J_{HH}$=13.0 Hz, $^3J_{HH}$=4.6 Hz, CH_2), 4.79 (1H, d, $^3J_{HH}$=11.8 Hz, CH), 5.61 (1H, d, $^3J_{HH}$=3.5 Hz, CH), 7.27–7.38 (10H, m, Ar), 11.74 (1H, s, NH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ=20.26 (CH_2), 38.20 (CH_2), 43.67 (CH_2), 53.86 (CH), 73.01 (CH), 107.79 (C–NO_2), 127.09 (2CH of Ar), 127.37 (CH of Ar), 127.53 (2CH of Ar), 128.52 (2CH of Ar), 129.27 (2CH of Ar), 129.34 (CH of Ar), 137.29 (C_{ipso}), 139.26 (C_{ipso}), 153.47 (*C*=CNO_2). MS (EI, 70 eV): *m*/*z* (%)=336 (1) [M^+], 313 (2), 236 (20), 149 (15), 137 (25), 111 (27), 97 (58), 81 (100), 69 (90), 57 (76).

*4.3.5. 4-[6-(4-Methoxyphenyl)-9-nitro-1,3,4,6,7,8-hexahydro-2H-pyrimido[1,6-a]pyrimidine-8-yl]phenyl methyl ether (**3d**).* White powder, mp=165 °C (dec), 0.3 g, yield 75%. IR (KBr): 3244 (NH), 2935 (CH), 1580 (Ar), 1380 (NO_2). Anal. Calcd for $C_{21}H_{24}N_4O_4$ (396.44): C, 63.62; H, 6.10; N, 14.13%. Found: C, 63.57; H, 6.07; N, 14.08%. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ=1.90–1.96 (2H, m, CH_2), 2.84–2.87 (2H, m, CH_2), 3.04 (1H, br, NH), 3.37–3.56 (2H, m, CH_2), 3.81 (s, $2OCH_3$), 4.77 (1H, s, CH), 5.56 (1H, s, CH), 6.90–7.27 (8H, m,

Ar), 11.71 (1H, s, NH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ=20.40 (CH_2), 38.32 (CH_2), 43.65 (CH_2), 53.31 (CH), 55.30 (OCH_3), 55.40 (OCH_3), 72.47 (CH), 107.98 (C–NO_2), 114.04 (2CH of Ar), 114.73 (2CH of Ar), 128.22 (2CH of Ar), 128.65 (2CH of Ar), 129.31 (C_{ipso}), 131.18 (C_{ipso}), 153.50 (*C*=CNO_2), 159.06 (C_{ipso}–OCH_3), 160.41 (C_{ipso}–OCH_3),. MS (EI, 70 eV): *m*/*z* (%)=396 (1) [M^+], 272 (1), 260 (1), 167 (8), 149 (25), 135 (100), 107 (16), 84 (58), 71 (32), 57 (51).

*4.3.6. 10-Nitro-7,9-diphenyl-1,2,3,4,5,7,8,9-octahydropyrimido[1,6-a][1,3]diazepine (**3e**).* White powder, mp=212 °C (dec), 0.28 g, yield 80%. White powder. IR (KBr): 3240 (NH), 2926 (CH), 1576 (Ar), 1379 (NO_2). Anal. Calcd for $C_{20}H_{22}N_4O_2$ (350.42): C, 68.55; H, 6.33; N, 15.99%. Found: C, 68.51; H, 6.27; N, 15.93%. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ=1.18–1.19 (1H, m, CH_2), 1.56–1.57 (2H, m, CH_2), 1.84–1.86 (1H, m, CH_2), 2.95–3.01 (2H, m, CH_2), 3.06 (1H, br, NH), 3.39–3.44 (1H, m, CH_2), 3.66–3.68 (1H, m, CH_2), 4.67 (1H, d, $^3J_{HH}$=12.2 Hz, CH), 5.67 (1H, s, CH), 7.26–7.45 (10H, m, Ar), 11.58 (1H, s, NH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ=25.77 (CH_2), 26.19 (CH_2), 45.75 (CH_2), 51.65 (CH_2), 54.03 (CH), 75.62 (CH), 112.26 (C–NO_2), 127.23 (2CH of Ar), 127.51 (CH of Ar), 127.73 (2CH of Ar), 128.65 (2CH of Ar), 129.06 (2CH of Ar), 129.25 (CH of Ar), 138.41 (C_{ipso}), 138.89 (C_{ipso}), 162.16 (*C*=CNO_2). MS (EI, 70 eV): *m*/*z* (%)=350 (1) [M^+], 304 (16), 246 (100), 199 (54), 160 (8), 140 (10), 104 (50), 91 (13), 77 (32).

*4.3.7. 4-[7-(4-Methoxyphenyl)-10-nitro-1,2,3,4,5,7,8,9-octahydropyrimido[1,6-a][1,3]diazepin-9-yl]phenyl methyl ether (**3f**).* White powder, mp=208 °C (dec), 0.35 g, yield 85%. Anal. Calcd for $C_{22}H_{26}N_4O_4$ (410.47): C, 64.38; H, 6.38; N, 13.65%. Found: C, 64.30; H, 6.31; N, 13.62%. IR (KBr) (ν_{max}, cm^{-1}): 3254 (NH), 2934 (CH), 1576 (Ar), 1390 (NO_2). ^{1}H NMR (500.13 MHz, $CDCl_3$): δ_H=1.17–1.85 (4H, m, CH_2), 2.94–3.01 (2H, m, CH_2), 3.05(1H, br, NH), 3.36–3.41(1H, m, CH_2), 3.65 (1H, m, CH), 3.80 (6H, s, OCH_3), 4.62 (1H, s, CH), 5.58 (1H, s, CH), 6.87–6.90 (4H, m, 4CH of Ar), 7.26–7.37 (4H, m, 4CH of Ar), 11.55 (1H, s, NH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ_C=25.81 (CH_2), 26.19 (CH_2), 45.74 (CH_2), 51.53 (CH_2), 53.46 (CH), 55.29 (OCH_3), 55.33 (OCH_3), 75.08 (CH), 112.44 (C–NO_2), 114.05 (2CH of Ar), 114.37 (2CH of Ar), 128.51 (2CH of Ar), 128.81 (2CH of Ar), 130.49 (C_{ipso}), 130.87 (C_{ipso}), 159.05 (*C*=CNO_2), 160.19 (C_{ipso}–OMe), 162.08 (C_{ipso}–OMe) ppm. MS (EI, 70 eV): *m*/*z* (%)=411 [M^++1], 274 (80), 229 (58), 189 (35), 157 (65), 135 (100), 119 (69), 97 (41), 84 (25), 55 (51).

*4.3.8. 3,3-Dimethyl-9-nitro-6,8-diphenyl-1,3,4,6,7,8-hexahydro-2H-pyrimido[1,6-a]pyrimidine (**4a**).* White powder, mp=205 °C (dec), 0.29 g, yield 79%. IR (KBr): 3257 (NH), 3038 (NH), 2955 (CH), 1586 and 1557 (Ar), 1387 (NO_2). Anal. Calcd for $C_{21}H_{24}N_4O_2$ (364.44): C, 69.21; H, 6.64; N, 15.37%. Found: C, 69.16; H, 6.57; N, 15.32%. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ=0.91 (3H, s, CH_3), 0.92 (3H, s, CH_3), 2.33 (1H, d, $^3J_{HH}$=12.9 Hz, CH_2), 2.57 (1H, d, $^3J_{HH}$=13.0 Hz, CH_2), 3.06–3.10 (2H, m, CH_2), 3.15 (1H, br, NH), 4.73 (1H, s, CH), 5.6 (1H, s, CH), 7.26–7.3 (10H, m, Ar), 11.78 (1H, s, NH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ=23.57 (CH_3), 24.83 (CH_3), 27.39 (*C*(CH_3)$_2$), 49.66 (CH_2), 53.95 (CH_2), 55.66 (CH), 73.41 (CH), 107.63 (C–NO_2), 127.41 (2CH of Ar), 127.43 (CH of Ar), 127.57 (2CH of Ar), 128.44 (2CH of Ar), 128.57 (2CH of Ar), 129.27 (CH of Ar), 137.22 (C_{ipso}), 139.37 (C_{ipso}), 152.68 (*C*=CNO_2). MS (EI, 70 eV): *m*/*z* (%)=364 (1) [M^+], 318 (58), 260 (100), 213 (49), 194 (24), 138 (31), 104 (58), 91 (25), 77 (51).

*4.3.9. 4-[6-(4-Methoxyphenyl)-3,3-dimethyl-9-nitro-1,3,4,6,7,8-hexahydro-2H-pyrimido[1,6-a]pyrimidine-8-yl]phenyl methyl ether (**4b**).* White powder, mp=210 °C (dec), 0.33 g, yield 78%. IR (KBr) (ν_{max}, cm^{-1}): 3285 (NH), 2942 (CH), 1582 (Ar), 1389 (NO_2). Anal. Calcd for $C_{23}H_{28}N_4O_4$ (424.49): C, 65.08; H, 6.65; N, 13.2%. Found: C, 65.01; H, 6.59; N, 13.1%. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ_H=0.91 (6H, s, CH_3), 2.33 (1H, d, $^3J_{HH}$=12.2 Hz, CH_2), 2.56 (1H, d, $^3J_{HH}$=12.6 Hz, CH_2), 2.96 (1H, s, NH), 3.09 (2H, m, CH_2), 3.78 (6H, s, CH_3), 4.70 (1H, s, CH), 5.55 (1H, s, CH), 6.87–6.90 (4H, m, 4CH of Ar), 7.27 (4H, m, 4CH of Ar), 11.75 (1H, s, NH). ^{13}C NMR (125.75 MHz, $CDCl_3$): δ_C=23.60 (CH_3), 24.85 (CH_3), 27.36 (*C*(CH_3)$_2$), 49.66 (CH_2), 53.38 (CH_2), 55.28 (OCH_3), 55.35 (OCH_3), 55.56 (CH), 72.82 (CH), 107.86 (C–NO_2), 113.82 (2CH of Ar), 114.60 (2CH of Ar), 128.64 (4CH of Ar), 129.23 (C_{ipso}), 131.29 (C_{ipso}), 152.58 (*C*=CNO_2), 159.00 (C_{ipso}–OMe), 160.31 (C_{ipso}–OMe) ppm. MS (EI, 70 eV): *m*/*z* (%)=424 (1) [M^+], 288 (1), 217 (30), 203 (8), 150 (60), 134 (100), 112 (20), 91 (16), 77 (14), 57 (25).

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.10.035.

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