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SYNTHESIS OF 2-ALKYL AND 2-ARYL PYRIMIDINES FROM β-CHLOROVINYL KETONES OF CYCLOPENTANONE TYPE

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ABSTRACT

Amidines react in the presence of $NaHCO_3$ with β-chlorovinyl ketones, prepared regioselectively by the reaction of 2-acetylcyclopentanone-type diketones with PPh_3-CCl_4 in 73–78% yield, to afford 2-alkyl (aryl)-pyrimidines annelated with cyclopentane derivatives in 79–87% yields.

β-Chlorovinyl carbonyl compounds are versatile reagents known to be used for preparation of aza-heterocycles (1,2), organometallic derivatives (3), cyclopentadienyl complexes (4). Here we report the regioselective synthesis of β-chlorovinyl ketones from readily accessible chiral β-difunctional derivatives of monoterpenes limonene and (+)-3-carene (5,6), as well as the simplest analogue (2-acetylcyclopentanone) and their use for the synthesis of annelated pyrimidines whose preparation from β-diketones directly by traditional methods results in poor yields of the desired pyrimidins.

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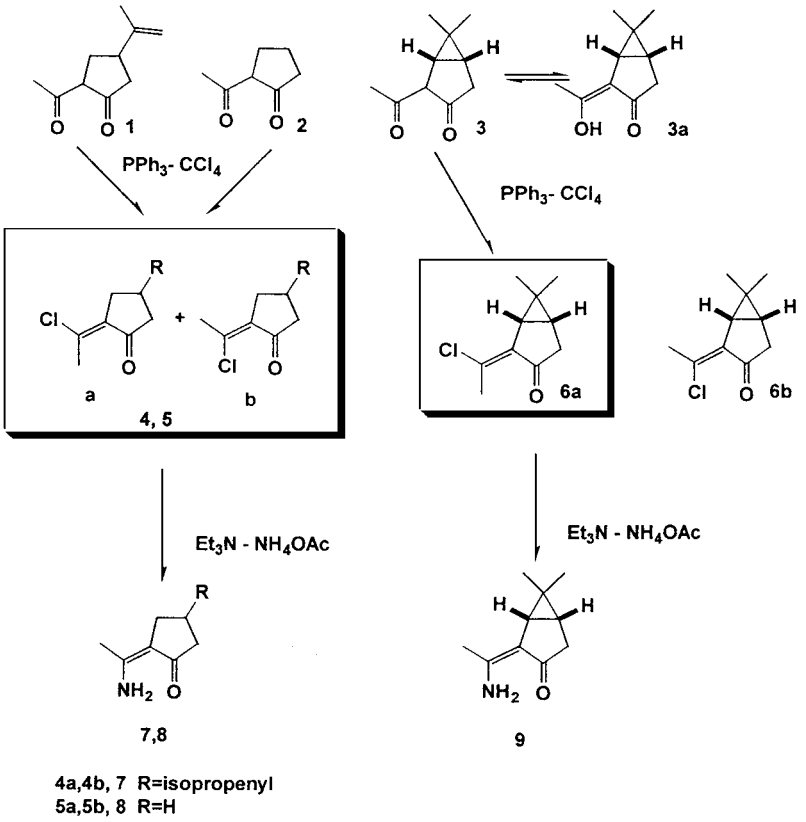
We studied the reaction of 2-acetylcyclopentanone-type diketones **1**–**3** with PPh_3-CCl_4 [with $CHCl_3$ as co-solvent (7)] and found that formation of β-chlorovinyl ketones proceeds regioselectively to provide good yields of β-chlorovinyl ketones **4**, **5** and **6**.



Formation of 2 pairs of isomers is possible in the reaction of 2-acetyl cyclopentanone-type diketones with CCl_4-PPh_3. According to NMR data, the reaction of diketones **1** or **2** provided a mixture of only 2 isomers **4** or **5** (with carbonyl in the cyclopentene moiety). Treatment of the mixtures **4a** + **4b** or **5a** + **5b** with ammonium acetate-Et_3N gave enaminone **7** [identical to that obtained earlier from diketone **1** (8)] or enaminone **8** (9) as the only isomers (yields 85% and 83%, correspondingly). So the positional isomers with acetyl group and chlorocyclopentene moiety are not formed in this reaction in a significant yield (Table 1).

The value of the NMR-^{1}H shifts of the *E*-methyl group for certain cyclic isopopylidene-2-enones are 0.19–0.08 ppm less than the corresponding values for

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Table 1.

Entry	Product	Reaction Conditions	Yield, %	The Ratio of the Isomers **a**:**b**
1	**4a**,**b**	reflux, 5 h	72	1.0:0.26
2	**5a**,**b**	12 h at 20°C→ reflux, 15 min	78	1.0:0.69
3	**6a**	reflux, 5 h	78	100:0

Z-methyl (10). In the minor isomers **4b** and **5b**, NMR-^{1}H shifts of the methyl 3H-1 are 2.36 and 2.41 ppm, whereas the corresponding values for major isomers **4a** and **5a** are 2.46 and 2.53 ppm. Additionally, according to the molecular mechanics (MM2) and semi-empirical quantum chemical calculations (AM1, PM3), *E*-isomers **4a**, **5a** are more stable than *Z*-isomers **4b**, **5b** [$\Delta H^\circ_{f\,\mathbf{4a}} - \Delta H^\circ_{f\,\mathbf{4b}} = -1.64$ (MM2), -2.32 (AM1), -0.47 (PM3) kcal/mol; ($\Delta H^\circ_{f\,\mathbf{5a}} - \Delta H^\circ_{f\,\mathbf{5b}} = -1.54$ (MM2), -2.35 (AM1), -0.46 (PM3) kcal/mol], and that might be the reason for predominant formation of the isomers **4a** and **5a**.

Surprisingly, the single isomer of chlorovinyl ketone **6** was isolated in the reaction of diketone **3** with PPh_3-CCl_4, which was proved by NMR (both ^{1}H and ^{13}C shifts of the methyl are quite similar to the corresponding values for compounds **4a**, **5a)** and preparation of the enaminone **9**[3] (82%) as the single product by the reaction of **6** with NH_4OAc-Et_3N. Formation of 1-(2-chloro-cyclopent-1-enyl)-ethanone type isomers is hardly possible due to steric reasons; moreover, according to NMR data, diketone **3** exists predominantly as isomer **3a**. Taking into account the NMR data and greater stability of the *E*-isomer **6a** by 1.82 (MM2), 2.28 (AM1), and 0.59 (PM3) kcal/mol, the most probable structure of the product should be drawn as **6a**.

Cyclopentanoids annelated with the nitrogen containing aromatic systems (mostly pyridines) are known to be presented in alkaloid series (11). On the other hand, pyrimidine derivatives fused with alicyclic fragments are the less known class of compounds (12). The combination of pharmacophoric pyrimidine nuclei and cyclopentane moiety especially those, which comprise chiral fragments in the molecule, is of interest from the viewpoint of bioactivity, so we attempted the work designed at preparation of fused pyrimidines.

Reaction of β-diketones with amidines is one of the most common routes to pyrimidines. We tried to prepare 2-alkyl- or 2-aryl pyrimidines by the reaction of β-diketones **1** and **3** and 2-acetylcyclopentanone with amidines, but our attempts were unsuccessful due to the retrocondensation reactions of the named β-diketones resulted in the ring cleavage. For example, unlike the reaction of 2-formylcyclopentanone with amidines (2), ω-keto esters were the main products when solutions of diketones **1**–**3** in *n*-BuOH or MeOH were treated with amidines or with carbonates or bicarbonates of amidines (only traces of pyrimidine-type compounds were detected).

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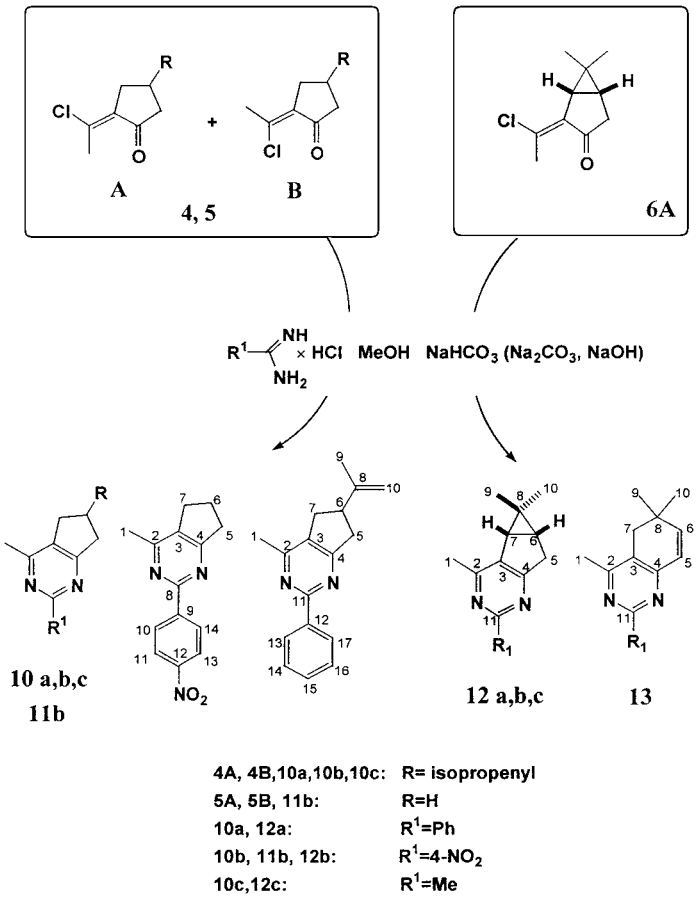

The numbering scheme of the carbons does not coincide with the numbering of the system according to IUPAC and is given for NMR interpretation only.

β-Chlorovinyl carbonyl compounds are known to react readily with amidines in the presence of NaOH to give 2-substituted pyrimidines in quite good yield (13). We found that the reaction of chlorovinylketone **6a** with amidine hydrochlorides in the presence of a strong base (like NaOH) was always accompanied with destruction of cyclopropane ring. Formation of 4,6,6-trimethyl-5,6-dihydro-quinazoline-type by-products **13** was observed.

The relative amount of the by-product **13** is strongly dependent on the type of base. Thus, in the reaction of **6a** with benzamidine hydrochloride, the ratio **12a**:**13a** was 1:1, 5:1, 50:1 when NaOH, Na_2CO_3, and $NaHCO_3$, correspondingly,

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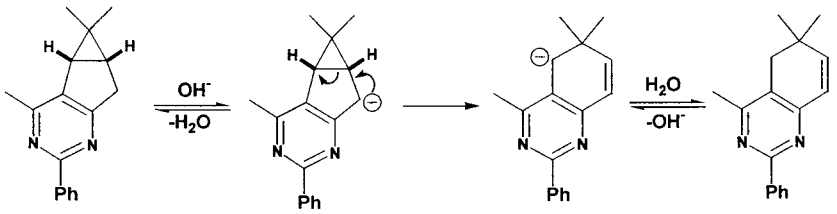
were used as the base. Generally, when $NaHCO_3$ was used in the reaction of **6a** with amidines, the relative amount of **13** in the mixture of isomers did not exceed 3% and compound **12** was purified readily *via* crystallization (compound **12c** was purified as adduct with picric acid). Mixtures of the isomers **4** and **5** are less strained as compared to **6a**, so their reactions with amidines are less sensitive to the type of the base. At the same time, the best yields of annelated pyrimidines in the reactions of amidines with **4**, **5** were obtained in the presence of $NaHCO_3$. Compounds **12** can be easily transformed to **13** by treatment with alkali. Thus, reaction of **12a** with KOH in methanol under reflux for 20 h results in compound **13a** (yield 58%). The transformation **12** → **13** can be explained in terms of nucleophylic rearrangement of α-cyclopropyl anion:



12a **13a**

Thus, in the case of certain terpenoid-based molecules, application of β-chlorovinyl ketones for the syntheses of fused pyrimidines is advantageous over the parent diketones (14).

EXPERIMENTAL

General Experimental Procedures

Analytical TLC plates were Silufol® (Silpearl on aluminum foil, Czech Republic). Preparative column chromatography was performed on SiO_2 ("KSK," Russia, 100–200 mesh, air dried, and activated at 140°C for 5 h) or Al_2O_3. IR spectra were recorded on a Specord M-80 spectrometer. UV spectra were obtained for 1% solutions in EtOH using a *Specord UV VIS* spectrometer. A Polamat A polarimeter was used to measure optical rotation at 578 nm. Melting points were measured using a Kofler melting point apparatus. Mass spectra were obtained on a Finnigan MAT 8200 instrument using the Electron Impact Ionization technique (50°–150°C, 70 eV). ^1H and ^{13}C NMR spectra were recorded at room temperature for 5–10% solutions in $CDCl_3$-CCl_4 (2:3 v/v) using standard Bruker NMR Software System on a Bruker AC 200 instrument (^1H 200.13 MHz, ^{13}C 50.32 MHz) locked to the deuterium resonance of the solvent. Chemical shifts were calculated

relative to the solvent signal ($CDCl_3$) used as the internal standard: δ_H 7.24 ppm and δ_C 76.90 ppm.

Diketones **1** and **3** were prepared by known methods (6,8) from (±)-3-(1-methyl-ethenyl)-6-oxoheptanenitrile and (1R,3S)-2,2-dimethyl-3-(2-oxo-propyl)-cyclopropyl]-acetonitrile (purchased from *Acros*), correspondingly.

Synthesis of β-Chlorovinyl Ketones from Diketones **1**, **2**, **3**

(1R,5R)-2-(1-Chloroethylidene)-6, 6-dimethyl-bicyclo[3.1.0]hexan-3-one **6**

A mixture of diketone **3** (20.0 g, 120 mmol) and triphenylphosphane (53.6 g, 204 mmol) in a mixture of CCl_4 (80 mL) and $CHCl_3$ (200 mL) was refluxed for 4 h. The mixture was worked according to the procedure described in ref. (7) and the crude product was distilled in vacuum to afford compound **6** (17.3 g, 78%) as a pale yellow oil, which was solidified in a refrigerator to give yellow crystals with m.p. 27°–28°C (pentane) and b.p. 85°–87°C/6 mm Hg; $[\alpha]^{19}$ −331 (c 3.5, $CHCl_3$). IR ($CHCl_3$) ν_{max} = 1715, 1612, 1267, 1235, 1212, 1130, 1102, 1071, 1042, 1012, 927, 873 cm^{-1}. UV (EtOH) λ_{max} = 277 nm (ε 8030). MS (m/z, %): 184.0651 (M^+, 100%, $C_{10}H_{13}OCl$, requires 184.0655), 169 (74), 149 (37), 133 (65), 121 (21), 105 (36), 91 (19), 79 (22), 67 (16), 51 (12). NMR ^1H: δ = 0.82 s (3H-10), 1.11 s (3H-9), 1.34 ddd (J = 7.3, 6.5 and 1.0, 1H-6), 2.08 d (J = 7.3, 1H-7), 2.27 dd (J = 19.5 and 1.0, 1H-5a), 2.49 s (3H-1), 2.56 dd (J = 19.5 and 6.5, 1H-5b). NMR ^{13}C: δ = 15.05 (C-10), 22.49 (C-1), 22.67 (C-6), 24.00 (C-8), 26.71 (C-9), 33.86 (C-7), 39.68 (C-5), 133.67 (C-3 or C-2), 144.20 (C-2 or C-3), 203.06 (C-4).

A mixture of *(E)-(±)-2-(1-Chloro-ethylidene)-4-isopropenyl-cyclopentanone* **4a** and *(Z)-(±)-2-(1-Chloro-ethylidene)-4-isopropenyl-cyclopentanone* **4b** (1:0.26 according to NMR) was prepared from diketone **2** by the above method in 72% yield as yellow oil with b.p. 86°–90°C/6mm Hg. IR ($CHCl_3$) ν_{max} = 1714, 1627, 1438, 1404, 1208, 1066, 1004, 971, 897, 785 cm^{-1}. UV (EtOH) λ_{max} = 253 nm (ε 12280). MS (m/z, %): 184.0653 (M^+, 4%, $C_{10}H_{13}OCl$, requires 184.0655) 169 (7), 149 (8), 144 (20), 142 (62), 121 (7), 118 (10), 116(32), 107 (100), 95 (2), 91 (21), 88 (57), 81 (4), 77 (18), 67 (15), 55(3), 53 (27), 43 (38). Major isomer **4a**, NMR ^1H: δ = 1.67 s (3H-9), 2.46 s (3H-1), 4.64 m (1H-10a), 4.68 m (1H-10b); NMR ^{13}C: δ = 20.48 (C-9), 22.74 (C-1), 36.24 (C-7), 38.82 (C-6), 45.61 (C-5), 110.00 (C-10), 132 87 (C-2), 144.55 (C-3), 145.54 (C-8), 201.82 (C-4). Minor isomer **4b**, NMR ^1H: 1.63 s (3H-9), 2.36 s (3H-1); NMR ^{13}C: δ = 20.15 (C-9), 30.00 (C-1), 36.98 (C-7), 41.20 (C-6), 45.44 (C-5), 110.00 (C-10), 136.70 (C-2), 144.55 (C-3), 145.54 (C-8), 194.80 (C-4).

A mixture of *(E)-2-(1-Chloro-ethylidene)-cyclopentanone* **5a** and *(Z)-2-(1-Chloro-ethylidene)-cyclopentanone* **5b** (1.0:0.69 according to NMR) was prepared from diketone **2** by the above method in 78% yield as yellow oil with

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b.p. 58°–61°C/5 mm Hg. IR ($CHCl_3$) ν_{max} = 1712 1659, 1625, 1459, 1410, 1211, 1132 cm^{-1}. UV (EtOH) λ_{max} = 251 nm (ε 10200). MS (m/z, %): 144.0337 (M^+, 100%, C_7H_9OCl, requires 144.0342), 129 (81), 116 (12), 102 (17), 88 (27), 81 (30), 65 (44), 53 (32), 43 (59). Major isomer **5a**, NMR ^1H: δ = 2.53 t (J = 2.3, 3H) NMR ^{13}C: δ = 19.53 (C-7), 23.59 (C-1), 32.14 (C-6), 41.61 (C-5), 133.85 (C-2), 145.13 (C-3), 203.63 (C-4). Minor isomer **5b**, NMR ^1H: δ = 2.41 s (3H). NMR ^{13}C: δ = 20.82 (C-7), 31.05 (C-1), 33.27 (C-6), 42.20 (C-5), 138.16 (C-2), 141.24 (C-3), 194.80 (C-4).

Synthesis of Pyrimidines from Chlorovinyl Ketones **4**, **5** and **6**

A solution of a chlorovinyl ketone **4**, **5** or **6** (10 mmol) in MeOH (10 mL) was added to a stirred mixture of an amidine hydrochloride (15 mmol) and $NaHCO_3$ (50 mmol) in MeOH (75 mL). The reaction mixture was stirred at ambient temperature for 5 h and then refluxed for 2 h. The solvent was distilled off and the residue was treated with water (150 mL) and extracted with $CHCl_3$ (2 × 20 mL). Then the combined organic extracts were treated according to the following procedures.

*2-Methyl pyrimidines **10c** and **12c***

The combined extracts were washed with 1M H_2SO_4 (3 × 20 mL). The combined aqueous extracts were neutralized with aq. NH_4OH (50 mL) and extracted with $CHCl_3$ (3 × 30 mL). The combined chloroform extracts were concentrated at reduced pressure followed by chromatography on a short alumina column (EtOAc) to afford pure compounds. An analytical sample of compound **12c** was obtained by additional purification via adduct with picric acid.

*2-Aryl pyrimidines **10a**, **10b**, **11a**, **12a** and **12b***

The combined extracts were washed with 1M H_2SO_4 (2 × 20 mL), dried over Na_2SO_4, and concentrated at reduced pressure to afford the crude pyrimidines, which were then purified by chromatography on a short alumina column (EtOAc) and crystallized from MeCN to give pure pyrimidines **10a**, **10b**, **11a**, **12a** or **12b**.

The reaction in the presence of NaOH or Na_2CO_3 was carried out by adding a stirring solution of a chlorovinyl ketone **3** or **4** (10 mmol) in MeOH (10 mL) to a stirred mixture of an amidine hydrochloride (15 mmol) and NaOH (15 mmol) or Na_2CO_3 (50 mmol) in MeOH (75 mL), followed by isolation (described above) and analysis of the reaction mixture by NMR.

(±)-6-Isopropenyl-4-methyl-2-phenyl-6,7-dihydro-5-H-cyclopentapyrimidine **10a**, **y**ield 83%, pale yellow needles with m.p. 78°–79°C (pentane). IR

($CHCl_3$) $\nu_{max} = 1647, 1566, 1439, 1392, 1224, 1206, 1179, 1070, 1027, 897\,cm^{-1}$. UV (EtOH) $\lambda_{max} = 260$ nm (ε 17180). MS (m/z, %): 250.1473 (M^+, 96%, $C_{17}H_{18}N_2$, requires 250.1470), 235 (22), 221 (4), 209 (12), 194 (9), 180 (2), 167 (5), 146 (5), 131 (5), 118 (1), 104 (15), 91 (16), 77 (14), 65 (8), 53 (7), 43 (1). NMR ^{1}H: $\delta = 1.73$ s (3H-9), 2.35 s (3H-1), 2.5–3.2 m (5H, H-5,6,7), 4.73 dm (J = 0.9, H-10a), 4.76 m (H-10b), 7.25–7.45 m (3H, Ar-H), 8.25–8.45 m (2H, Ar-H). NMR ^{13}C: $\delta = 19.81$ (C-9), 20.75 (C-1), 32.34 (C-7), 37.92 (C-5), 42.68 (C-6), 109.32 (C-10), 127.10 (4C, aromatic carbons), 128.68 (C-15), 128.82 (C-3), 137.32 (C-12), 145.38 (C-8), 159.98 (C-11 or C-2), 161.78 (C-2 or C-11), 171.57 (C-4).

(±)-6-Isopropenyl-4-methyl-2-(4-nitro-phenyl)-6,7-dihydro-5H-cyclopentapyrimidine **10b**, yield 81%, pale yellow needles, dec. at ≈110°C. IR ($CHCl_3$) $\nu_{max} = 1648, 1578, 1521, 1421, 1393, 1347, 1214, 1106, 1014, 697, 870, 853\,cm^{-1}$. UV (EtOH) $\lambda_{max} = 299$ nm (ε 18860). MS (m/z, %): 295.1317 (M^+, 96%, $C_{17}H_{18}N_3O_2$, requires 295.1321) 280 (27), 266 (4), 248 (15), 239 (12), 207 (5), 219 (3), 193 (3), 167 (2), 149 (2), 146 (3), 131 (4), 118 (1), 104 (4), 91 (15), 79 (5), 77 (7), 65 (6), 53 (6). NMR ^{1}H: $\delta = 1.79$ s (3H-9), 2,46 s (3H-1), 2.71–2.33 m (5H-5,6,7), 4.82 m (H-10a), 4.79 m (H-10b), 8.16 m (2H, Ar-H), 8.52 m (2H, Ar-H). NMR ^{13}C: $\delta = 20.65$ (C-9), 21.62 (C-1), 33.41 (C-7), 38.86 (C-5), 43.67 (C-6), 110.47 (C-10), 123.18(2C, C-14, 16), 128.69 (2C, C-13, 17), 131.19 (C-3), 146.01 (C-8), 148.77 (C-15), 160.78 (C-11 or C-2), 161.55 (C-2 or C-11), 173.13 (C-4).

(±)-6-Isopropenyl-2,4-dimethyl-6,7-dihydro-5-H-cyclopentapyrimidine **10c**, yield 84%, pale yellow oil. IR ($CHCl_3$) $\nu_{max} = 1647, 1585, 1566, 1434, 1409, 1227, 1207, 1161, 1088, 1024, 932, 896\,cm^{-1}$. UV (EtOH) $\lambda_{max} = 213$ nm (ε 5560), 260 nm (ε 4582). MS (m/z, %): 188.1296 (M^+, 77%, $C_{12}H_{16}N_2$, requires 188.1314), 187 (100), 173 (49), 146 (25), 132 (32), 118 (5), 105 (19), 91 (16), 79 (11), 65 (9), 53 (9). NMR ^{1}H: $\delta = 1.54$ s (3H-9), 2.12 s (3H-1), 2.44 s (3H-12), 2.45–2.9 m (5H-5,6,7) 4.53 m (1-10a), 4.56 m (H-10b). NMR ^{13}C: $\delta = 20.34$ (C-1), 21.06 (C-9), 25.17 (C-12), 33.12 (C-7), 38.66 (C-5), 43.49 (C-6), 110.02 (C-10), 128.09 (C-3), 146.12 (C-8), 160.54 (C-11 or C-2), 165.94 (C-2 or C-11), 172.14 (C-4).

4-Methyl-2-(4-nitro-phenyl)-6,7-dihydro-5H-cyclopentapyrimidine **11b**, yield 79%, pale yellow crystals with m.p. 172°–174°C (CH_3CN). IR ($CHCl_3$) $\nu_{max} = 1714, 1627, 1439, 1404, 1373, 1214, 1208, 1146, 1066, 1004\,cm^{-1}$. UV (EtOH) λ_{max}=299 nm (ε 17910). MS (m/z, %): 255.0968 (M^+, 100%, $C_{14}H_{13}N_3O_2$, requires 255.1008), 225 (11), 214 (18), 209 (43), 179 (8), 166 (10), 150 (14), 125 (4), 103 (10), 91 (3), 76 (8), 65 (13), 53 (5). NMR ^{1}H: $\delta = 2.19$ tt (J = 8.0 and 7.6, 2H-6), 2.48 s (3H-1), 2.92 t (J = 7.6, 2H-5 or 2H-7), 3.03 t (J = 8.0, 2H-7 or 2H-5), 8.23 m (2H, Ar-H), 8.56 m (2H, Ar-H). NMR ^{13}C: $\delta = 21.72$ (C-1), 21.78 (C-6), 28.22 (C-7), 34.00 (C-5), 123.37 (2C, aromatic carbons), 128.72 (2C, aromatic carbons), 132.05 (C-3), 144.18 (C-9), 160.81 (C-8), 161.99 (C-2), 174.42 (C-4).

(1aR,6aR)-1,1,2-Trimethyl-4-phenyl-1,1a,6,6a-tetrahydro-3,5-diaza-cyclopropa[a]indene **12a**, yield 86%, white crystals with m.p. 74°–75°C (pentane-toluene) and $[\alpha]^{21}$ +160 (c 1.3, $CHCl_3$). IR ($CHCl_3$) ν_{max} = 1560, 1448, 1421, 1398, 1300, 1214, 119, 1075, 1042, 1020, 927, 864 cm^{-1}. UV (EtOH) λ_{max} = 274 nm (ε 57780). MS (m/z, %): 250.1468 (M^+, 96%, $C_{17}H_{18}N_2$, requires 250.1470), 235 (100), 208 (18), 194 (52), 167 (3), 132 (3), 117 (5), 104 (9), 91 (21), 77 (12), 65 (6), 51 (4). NMR ^{1}H: δ = 0.64 s (3H-10), 1.17 s (3H-9), 1.54 ddd (J = 6.7, 6.7 and 1.0, 1H-6), 2.08 dd (J = 6.7 and 1.4, 1H-7), 2.48 s (3H-10), 2.82 ddd (19.0, 1.4 and 1.4, 1H-5a), 3.15 dd (J = 19.0 and 7.3, 1H-5b), 7.36 m (3H, Ar-H), 8.36 m (2H, Ar-H). NMR ^{13}C: δ = 14.00 (C-10), 21.68 (C-1), 22.22 (C-8), 26.50 (C-6), 26.71 (C-9), 32.01 (C-7), 33.90 (C-5), 127.94 (C-15), 128.00 (2C, aromatic carbons), 129.57 (2C, aromatic carbons), 131.02 (C-3), 138.06 (C-12), 160.97 (C-11), 161.94 (C-2), 174.77 (C-4).

(1aR,6aR)-1,1,2-Trimethyl-4-(4-nitro-phenyl)-1,1a,6,6a-tetrahydro-3,5-diazacyclopropa[a]indene **12b**, yield 87%, pale yellow crystals with m.p. 149°–151°C (dec., MeCN) and $[\alpha]^{21}$ +145 (c 0.4, $CHCl_3$). IR ($CHCl_3$) ν_{max} = 1600, 1574, 1556, 1521, 1420, 1397, 1212, 1102, 1044, 1010 cm^{-1}. UV (EtOH) λ_{max} = 313 nm (19390). MS (m/z, %): 295.1329 (M^+, 99.6%, $C_{17}H_{18}N_3O_2$, requires 295.1321), 280 (100), 253 (18), 239 (74), 234 (15), 219 (6), 207 (8), 193 (16), 166 (2), 150 (1), 132 (2), 116 (7), 105 (5), 91 (22), 77 (10), 65 (8), 51 (4). NMR ^{1}H: δ = 0.65 s (3H-10), 1.21 s (3H-9), 1.64 dm (J = 6.6, 1H-6), 2.14 d (J = 7.0, 1H-7), 2.51 s (3H-1), 2.85 d (J = 19.0, 1H-5a), 3.16 dd (J = 19.0 and 7.0, 1H-5b). NMR ^{13}C: δ = 14.05 (C-10), 21.65 (C-1), 22.66 (C-8), 26.73 (C-9), 26.90 (C-6), 32.13 (C-7), 33.91 (C-5), 123.23 (2C, aromatic carbons), 128.61 (2C, aromatic carbons), 132.72 (C-3), 143.79 (C-12), 148.71 (C-15), 159.61 (C-11), 161.49 (C-2), 175.22 (C-4).

(1aR,6aR)-1,1,2,4-Tetramethyl-1,1a,6,6a-tetrahydro-3,5-diaza-cyclopropa-[a]indene **12c**. Yield 82% as pale yellow oil. $[\alpha]^{24}$ +99 (c 2.7, $CHCl_3$). IR ($CHCl_3$) ν_{max} = 1722, 1585, 1566, 1411, 1298, 1225, 1122, 1046, 966, 927, 874, 828 cm^{-1}. UV (EtOH) λ_{max} = 230 nm (ε 7084), 273 nm (ε4106). MS (m/z, %): 188.1305 (M^+, 77%, $C_{12}H_{16}N_2$, requires 188.1314), 173 (100), 159 (3), 146 (25), 132 (97), 117 (7), 105 (15), 91 (26), 77 (12), 65 (10), 61 (76). NMR ^{1}H: δ = 0.62 s (3H-10), 1.18 s (3H-9), 1.54 ddd (J = 6.8, 6.8 and 1.4, 1H-6), 2.08 dd (J = 6.8 and 1.4, 1H-7), 2.40 s (3H-1), 2.56 s (3H-12), 2.74 ddd (J = 19.0, 1.4 and 1.4, 1H-5α), 3.08 dd (J = 19.0 and 6.8, 1H-5β). NMR ^{13}C: δ = 13.73 (C-10), 20.61 (C-1), 21.15 (C-8), 25.20 (C-12), 26.11 (C-6), 26.59 (C-9), 32.50 (C-7), 33.65 (C-5), 129.56 (C-3), 160.64 (C-11 or C-2), 164.81 (C-2 or C-11), 174.41 (C-4).

4,6,6-Trimethyl-2-phenyl-5,6-dihydro-quinazoline **13a**. Potassium hydroxide (1.0 g, 18 mmol) was added to a solution of phenyl pyrimidine **12a** (0.060 g, 0.24 mmol) in MeOH (15 mL) and the mixture was stirred under reflux for 20 h. The solvent was distilled off and the residue was diluted with water and taken up in CH_2Cl_2 (3 × 10 mL). The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was crystallized to afford 35 mg

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(58 %) of the title compound as white crystals with m.p. 67°–69°C (hexane-*t*-Bu-O-Me). IR ($CHCl_3$) ν/cm^{-1} 1629, 1556, 1468, 1397, 1361. UV (EtOH) λ_{max}/nm 252 (ε 42200). MS (m/z, %): 250.1453 (M^+, 70%, $C_{17}H_{18}N_2$, requires 250.1470), 235 (27), 221 (3), 209 (10), 194 (100), 132 (3), 104 (7), 91 (21), 77 (11), 65 (9). NMR ^1H: 1.11 s (6H-9,10), 2.50 s (3 H-1), 2.69 s (2H-7), 6.50 d (J = 9.8, 1H-5), 6.24 d (J = 9.8, 1H-6). NMR ^{13}C: 21.17 (C-1), 26.64 (C-9,10), 29.56 (C-8), 37.14 (C-7), 126.27 (C-5), 128.18 (C-13, 15, 17), 129.63 (C-14, 16), 131.37 (C-3), 138.39 (C-12), 148.36 (C-6), 161.36 (C-11), 162.25 (C-2), 175.09 (C-4).

Synthesis of Enaminones **7**, **8**, and **9**

Ammonium acetate (1.0 g, 13 mmol) and Et_3N (2.0 g, 20 mmol) were added to a stirred solution of a chlorovinylketone **4** or **5** or **6** (1.6 mmol) in MeOH (10 mL) and the reaction mixture was stirred at ambient temperature for 12 h. The solvent was distilled off under reduced pressure and the residue was treated with water (60 ml) and extracted with CH_2Cl_2 (2 × 30 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuum followed by chromatography on a short alumina column (EtOAc) to afford enaminones **7**, **8**, **9** as pale yellow crystals identical to those described previously (8).

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