Synthesis of Bioactive Heterocycles: Sigmatropic Rearrangements of 1,3-Dimethyl-6-[methyl(4-aryloxybut-2-ynyl)amino]pyrimidine-2,4(1*H*,3*H*)-diones

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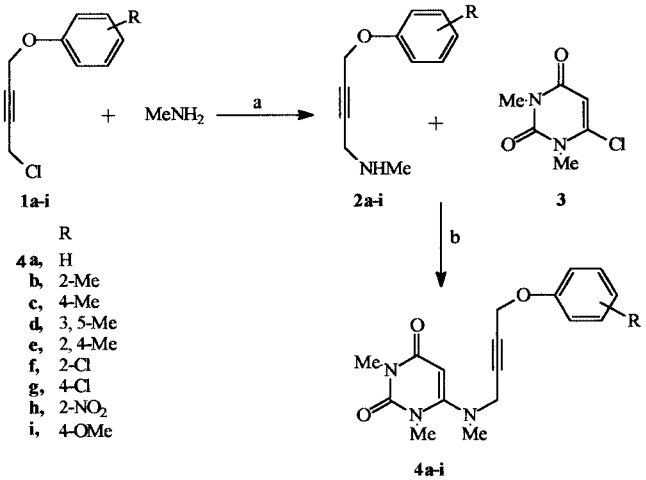
Abstract: A number of 1,3-dimethyl-6-[methyl(4-aryloxybut-2-ynyl)amino]pyrimidine-2,4(1*H*,3*H*)-diones **4a**–**i** were synthesised in 69 to 80% yields by the reaction of 6-chloro-1,3-dimethyluracil (6-chloro-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-diones) and 1-aryloxy-4-*N*-methylaminobut-2-yne in refluxing ethanol for 12 hours. The tertiary amines **4a**–**i** were then heated in refluxing 1,2-dichlorobenzene for 17 hours to give 5-[(*E*)-aryloxymethylidene]-1,3,8-trimethyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **5a**–**i** in 55 to 75% yields.

Key words: aza-Claisen rearrangement, cyclizations, heterocycles, pyrido[2,3-*d*]pyrimidine-2,4-diones, sigmatropic rearrangement

The biological importance of pyrimidine and its derivatives is well known.[1,2] Numerous pyrimidine and uracil (pyrimidine-2,4(1*H*,3*H*)-dione) based molecules have found wide application in medicine and therapeutics. Thus FU (5-fluorouracil) and FUDR (5-fluoro-2'-deoxyuridine) are used in chemotherapy for the treatment of cancer.[3] F_3TDR (trifluorothymidine), BVDU [(*E*)-5-(2-bromovinyl-2'-deoxyuridine)], AZT (3'-azido-3'-deoxythymidine)[4–7] and 5-(2-chloroethyl-2'-deoxyuridine (CEDU)[8] are used against viral diseases. Both BVDU and CEDU compounds effectively inhibit herpes simples type 1 virus (HSV-1) and Varicella zoster virus (VZV) replication in vitro[4,8–11] and AZT[12] is an anti AIDS drug. Functionalisation of uracils at 5- and 6-positions lead to biologically interesting molecules.[13–15] Recently a 6-substituted uracil derivative, 1-[(2-hydroxyethoxy)methyl]-6-phenylthiothymine (HEPT)[16–18] has attained considerable significance as a specific HIV-1 inhibitor, a causative against AIDS.[19]

Claisen rearrangement has been used for the synthesis of a number of furo[3,2-*d*]pyrimidines, pyrano[3,2-*d*]pyrimidines and dihydrofuro[2,3-*d*]pyrimidine derivatives.[20,21] Recently amine oxide rearrangement[22] has been employed for the synthesis of pyrrolo[3,2-*d*]pyrimidine derivatives starting from 1,3-dimethyl-5-[ethyl(4-aryloxybut-2-ynyl)amino]pyrimidine-2,4(1*H*,3*H*)-diones. Amino-Claisen rearrangement of 5- and 6-substituted allyl and propargyl amines of uracils was studied by Itoh and coworkers.[20,23] This prompted us to undertake a study of the amino-Claisen rearrangement of 1,3-dimethyl-6-[methyl(4-aryloxybut-2-ynyl)amino]pyrimidine-2,4(1*H*,3*H*)-diones **4a–i**.

The starting materials **4a**–**i** were prepared in 69–80% yield by refluxing 6-chloro-1,3-dimethyluracil (**3**) with the corresponding 4-aryloxy-1-*N*-methylaminobut-2-ynes **2a**–**i** in ethanol for 9 to 12 hours (Scheme 1). The amines **2a**–**i** in turn were prepared by dropwise addition of an alcoholic solution of 1-aryloxy-4-chlorobut-2-ynes **1a**–**i** to excess aqueous methylamine (40%) and stirring the reaction mixture at room temperature for 2 h. Excess methylamine and alcohol were distilled off under reduced pressure and the compounds **2a**–**i**, isolated after usual workup, were used without further purification in the next step. Compounds **4a**–**i** were characterised from their elemental analyses and spectral data.



Reagents: a, EtOH, r.t, 2h; b, EtOH, reflux

Scheme 1

The substrates **4a**–**i** possess two potential sites for Claisen rearrangement. The aryloxy propargyl ether part may undergo oxygen-Claisen rearrangement while the vinyl propargyl amine part may undergo amino-Claisen rearrangement. Hence the substrate provides an excellent scope for competitive study of oxygen-Claisen rarrangement versus amino-Claisen rearrangement in the same molecule. It is well known that amino-Claisen rearrangement requires higher activation energy[24] than the oxygen-

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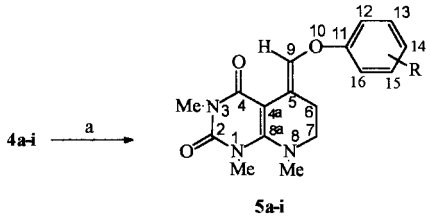
Claisen rearrangement. But the activation energy required for the propargyl vinyl ether[25] rearrangement is much less than that of aryl propargyl ether rearrangement.[26]

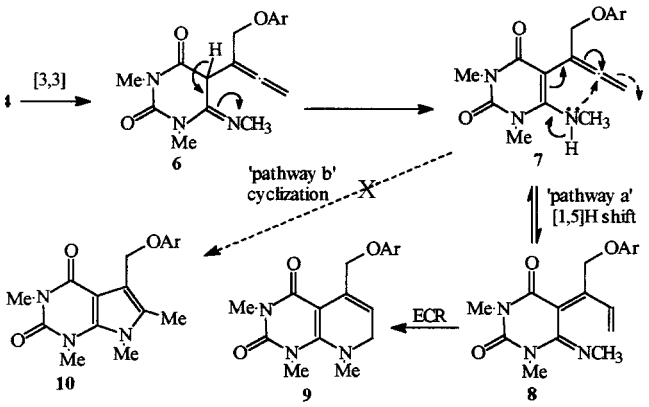
The substrates **4a–i** were refluxed in 1,2-dichlorobenzene at 180 °C for 17 hours to give **5a–i** in 55–75% yield (Scheme 2). The compounds **5a–i** were characterised on the basis of their elemental analyses and spectral data.[27]



Reagents: a, *o*-dichlorobenzene, reflux, 17h

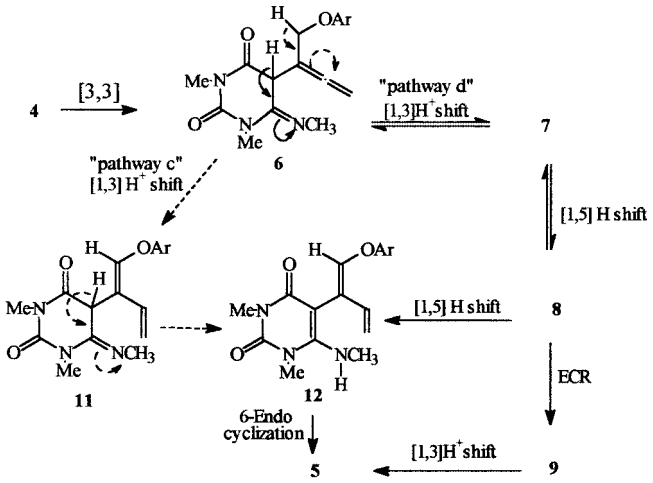
Scheme 2

As in the case of amino-Claisen rearrangement of 1,3-dimethyl-6-(*N*-methyl-*N*-propargyl)aminouracil,[20] we expected dihydropyrido[2,3-*d*]pyrimidine derivative **9** via "pathway a" or pyrrolo[2,3-*d*]pyrimidine derivative **10** via "pathway b" for this type of usual Claisen rearrangement. Initially **4** may undergo a [3,3] sigmatropic rearrangement to the allene **6**, followed by enamine **7** formation, which may then proceed via "pathway a", *viz.* [1,5] hydrogen shift, followed by electrocyclic ring closure to **9**, or via "pathway b", *viz.* cyclisation of the enamine **7** to **10** (Scheme 3).



Scheme 3

The formation of product **5** from **4** may be explained by an initial [3,3] sigmatropic shift to give the intermediate allene **6**, which can then proceed via "pathway c" *viz.* 1,3-H^+ shift to give butadienyl intermediate **11**, enamine formation and 6-*endo* cyclisation to give the product **5**. Another "pathway d" has been considered as an alternative to 1,3-H^+ shift. This may involve [1,5] H shift of enamine H to the central allene carbon in **13**, followed by another [1,5] H shift (or tautomerism) to give **12** which then undergoes 6-*endo* cyclisation (Scheme 4). There is a literature report[28] for the 1,3-H^+ shift in an allene to give



Scheme 4

butadienyl derivative. An additional 1,3-prototropic shift in **9** may also lead to product **5**.

There are some reports on the formation of products similar to **5** with exocyclic double bond from the Claisen rearrangement. Thus only in one case (4-cresoxyether), the rearrangement of aryloxybutynyl ethers of 4-hydroxycoumarin yielded *exo*-methylene pyranocoumarins along with the normal Claisen rearrangement products.[29] In the case of 2-cresoxy ether also, a furocoumarin with an exocyclic double bond was formed along with the normal Claisen rearrangement product.[29] In another instance, in the case of alkylation[30] of 4-hydroxy-1-methylquinolone with 1-(2-chloroaryloxy)-4-chlorobut-2-ynes, a similar kind of product was obtained. 4-(4-Aryloxybut-2-ynyloxy)[1]benzopyran-2-thiones also gave *exo*-methylene products along with normal endocyclic products.[31]

It is interesting to note that all the substrates studied so far underwent [3,3] sigmatropic rearrangement at the propargyl vinyl amine moiety in preference to the aryl propargyl ether part of the substrates. However, it has been recently reported[32] that the thermal rearrangement of 1,3-dimethyl-5-[methyl(4-aryloxybut-2-ynyl)amino]pyrimidine-2,4(1*H*,3*H*)-diones furnished exclusively the corresponding 5-[(2*H*-chromen-4-yl)(methyl)amino]-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-diones by the [3,3] sigmatropic rearrangement at the aryloxypropynyl moiety. In the case of uracil, the amino-Claisen rearrangement at the 6-position is preferred over oxygen-Claisen rearrangement perhaps due to the high reactivity of the 5-position of uracil. In the case of 5-substituted uracil the low reactivity of the 6-position pushes the reaction towards the more favourable oxygen-Claisen rearrangement pathway. This work derives additional interest from the fact that pyrido[2,3-*d*]pyrimidines are shown to be biologically highly active compounds possessing antitumour, antibacterial and anticonvulsive activities.[33]

Melting points are uncorrected. UV absorption spectra were recorded in absolute EtOH on a Hitachi 200-20 Spectrophotometer. IR spectra were run on KBr discs on a Perkin-Elmer 1330 apparatus.

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^{1}H NMR spectra were recorded for solutions in $CDCl_3$ with $SiMe_4$ as an internal standard on Jeol Fx-100 at IICB, Calcutta, Bruker (300 MHz) spectrometer at IICB, Calcutta and Bruker (500 MHz) spectrometer at Bose Institute, Calcutta. Elemental analyses and recording of mass spectra (EI) were carried out by RSIC (CDRI), Lucknow. Silica gel (60–120 mesh) was used for chromatograpic separation.

4-Aryloxy-1-N-methylaminobut-2-ynes 2a–i; General Procedure

To an aqueous methylamine solution (40%, 10 mL, excess) was added dropwise a solution of **1a–i** (6 mmol) in EtOH (20 mL) and stirred at r.t. for 2 h. The excess methylamine and EtOH were distilled off under reduced pressure. The residue was then extracted with $CHCl_3$ (3 × 20 mL). The $CHCl_3$ extract was washed with water (3 × 20 mL) and dried (Na_2SO_4). The solvent was evaporated and the residual liquid obtained was used in the next step without further purification.

1,3-Dimethyl-6-[methyl(4-aryloxybut-2-ynyl)amino]pyrimidine-2,4(1H,3H)-diones 4a–i; General Procedure

A mixture of an ethanolic solution (100 mL) of **3** (0.872 g, 5 mmol) and **2a–i** (12 mmol) was refluxed for 9 to12 h on a water bath. The alcohol was then removed under reduced pressure and the residue was extracted with $CHCl_3$ (3 × 20 mL). The extract was washed with water (2 × 20 mL) and dried (Na_2SO_4). After removal of $CHCl_3$, the crude mass was chromatographed over silica gel and elution of the column with EtOAc–benzene (1:3) gave products **4a–i**.

4a

Yield: 72%; viscous liquid.

UV (EtOH): λ_{max} (log ε) = 216 (2.95), 276 nm (2.89).

IR (KBr): ν = 2980, 2860, 1710, 1640, 1250 cm^{-1}.

^{1} H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.71 (s, 3 H), 3.32 (s, 3 H), 3.35 (s, 3 H), 3.76 (s, 2 H), 4.72 (s, 2 H), 5.34 (s, 1 H), 6.93–7.02 (m, 3 H), 7.28–7.33 (m, 2 H).

MS: *m*/*z* = 313 (M^+).

Anal. Calcd for $C_{17}H_{19}N_3O_3$: C, 65.17; H, 6.07; N, 13.41. Found: C, 65.25; H, 5.98; N, 13.35.

4b

Yield: 75%; mp 64 °C.

UV (EtOH): λ_{max} (log ε) = 215 (2.48), 276 nm (2.49).

IR (KBr): ν = 2960, 1700, 1640, 1230 cm^{-1}.

^{1} H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.23 (s, 3 H), 2.71 (s, 3 H), 3.32 (s, 3 H), 3.36 (s, 3 H), 3.76 (s, 2 H), 4.74 (s, 2 H), 5.34 (s, 1 H), 6.88–6.92 (m, 2 H), 7.13–7.16 (m, 2 H).

MS: *m*/*z* = 327 (M^+).

Anal. Calcd for $C_{18}H_{21}N_3O_3$: C, 66.05; H, 6.42; N, 12.84. Found: C, 66.14; H, 6.51; N, 12.81.

4c

Yield 73%; viscous liquid.

UV (EtOH): λ_{max} (log ε) = 219 (2.62), 276 nm (2.56).

IR (KBr): ν = 2960, 1690, 1640, 1220 cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.29 (s, 3 H), 2.72 (s, 3 H), 3.32 (s, 3 H), 3.36 (s, 3 H), 3.79 (s, 2 H), 4.69 (s, 2 H), 5.35 (s, 1 H) 6.84 (d, *J* = 9 Hz, 2 H), 7.10 (d, *J* = 9 Hz, 2 H).

MS: *m*/*z* = 327 (M^+).

Anal. Calcd for $C_{18}H_{21}N_3O_3$: C, 66.05; H, 6.42; N, 12.84. Found: C, 66.13; H, 6.44; N, 12.92.

4d

Yield 80%; mp 84 °C.

UV (EtOH): λ_{max} (log ε) = 210 (2.83), 276 nm (2.67).

IR (KBr): ν = 2920, 1680, 1630, 1290 cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.28 (s, 6 H), 2.73 (s, 3 H), 3.31 (s, 3 H), 3.36 (s, 3 H), 3.76 (s, 2 H), 4.68 (s, 2 H), 5.34 (s, 1 H), 6.57 (s, 2 H), 6.64 (s, 1 H).

MS: *m*/*z* = 341 (M^+).

Anal.Calcd for $C_{19}H_{23}N_3O_3$: C, 66.86; H, 6.74; N, 12.31. Found: C, 67.92; H, 6.62; N, 12.30.

4e

Yield 76%; viscous liquid.

UV (EtOH): λ_{max} (log ε) = 214 (3.39), 276 nm (3.30).

IR (KBr): ν = 2935, 1690, 1640, 1220 cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.19 (s, 3 H), 2.26 (s, 3 H), 2.71 (s, 3 H), 3.32 (s, 3 H), 3.36 (s, 3 H), 3.75 (s, 2 H), 4.70 (s, 2 H), 5.34 (s, 1 H), 6.77–6.79 (m, 1 H), 6.93–6.96 (m, 2 H).

MS: *m*/*z* = 341 (M^+).

Anal. Calcd for $C_{19}H_{23}N_3O_3$: C, 66.86; H, 6.74; N, 12.31. Found: C, 66.98; H, 6.64; N, 12.28.

4f

Yield: 70%; viscous liquid.

UV (EtOH): λ_{max} (log ε) = 218 (2.54), 275 nm (2.47).

IR (KBr): ν = 2900, 1680, 1635, 1260 cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS, 100 MHz): δ = 2.68 (s, 3 H), 3.30 (s, 3 H), 3.33 (s, 3 H), 3.77 (s, 2 H), 4.83 (s, 2 H), 5.35 (s, 1 H), 6.88–7.48 (m, 4 H).

MS: *m*/*z* = 349 and 347 (M^+).

Anal. Calcd for $C_{17}H_{18}ClN_3O_3$: C, 58.78; H, 5.18; N, 12.10. Found: C, 58.90; H, 5.08; N, 12.18.

4g

Yield: 72%; viscous liquid.

UV (EtOH): λ_{max} (log ε) = 218 (2.76), 276 nm (2.39).

IR (KBr): ν = 2940, 1690, 1630, 1215 cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS, 500 MHz): δ = 2.64 (s, 3 H), 3.24 (s, 3 H), 3.28 (s, 3 H), 3.69 (s, 2 H), 4.62 (s, 2 H), 5.27 (s, 1 H), 6.80 (d, *J* = 9 Hz, 2 H), 7.18 (d, *J* = 9 Hz, 2 H).

MS: *m*/*z* = 349 and 347 (M^+).

Anal. Calcd for $C_{17}H_{18}ClN_3O_3$: C, 58.78; H, 5.18; N, 12.10. Found: C, 58.76; H, 5.29; N, 12.02.

4h

Yield: 69%; viscous liquid.

UV (EtOH): λ_{max} (log ε) = 222 (2.12), 280 (2.96), 329 nm (2.19).

IR (KBr): ν = 2980, 1680, 1640, 1230 cm^{-1}.

^{1}H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.75 (s, 3 H), 3.35 (s, 3 H), 3.39 (s, 3 H), 3.81 (s, 2 H), 4.92 (s, 2 H), 5.36 (s, 1 H), 7.12–7.31 (m, 2 H), 7.58–7.64 (m, 1 H), 7.87–7.91 (m, 1 H).

MS: *m*/*z* = 358 (M^+).

Anal. Calcd for $C_{17}H_{18}N_4O_5$: C, 56.98; H, 5.02; N, 15.64. Found: C, 57.15; H, 5.11; N, 15.58.

4i

Yield: 70%; mp 74 °C.

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UV (EtOH): λ_{max} (log e) = 222 (3.50), 277 nm (3.45).

IR (KBr): ν = 2980, 2900, 1700, 1640, 1250 cm^{-1}.

^1H NMR ($CDCl_3$/TMS, 300 MHz): δ = 1.61 (s, 3 H), 2.72 (s, 3 H), 3.32 (s, 3 H), 3.36 (s, 3 H), 3.78 (s, 2 H), 4.67 (s, 2 H), 5.35 (s, 1 H), 6.83–6.91 (m, 4 H).

MS: *m*/*z* = 343 (M^+).

Anal. Calcd for $C_{18}H_{21}N_3O_4$: C, 62.97; H, 6.12; N, 12.24. Found: C, 63.03; H, 5.82; N, 12.13.

5-[(E)–Aryloxymethylidene]-1,3,8-trimethyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine-2,4(1H,3H)-diones 5a–i; General Procedure

Compounds **4a–i** (4 mmol) were refluxed in 1,2-dichlorobenzene for 17 h. The reaction mixture was cooled and chromatographed over silica gel. 1,2-Dichlorobenzene was eluted out with petroleum ether (bp 60–80 °C) and the rearranged products **5a–i** were obtained by eluting the column with EtOAc–benzene (1:9).

5a

Yield 70%, viscous liquid.

UV (EtOH): λ_{max} (log ε) = 267 (2.88), 314 nm (2.83).

IR (KBr): ν = 2920, 1660, 1610, 1200 cm^{-1}.

^1H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.73 (t, *J* = 6 Hz, 2 H), 2.77 (s, 3 H), 3.13 (t, *J* = 6 Hz, 2 H), 3.38 (s, 3 H), 3.45 (s, 3 H), 7.03–7.10 (m, 3 H), 7.27–7.31 (m, 2 H), 8.27 (s, 1 H).

^{13}C NMR ($CDCl_3$/TMS): d = 18.32 (C-6), 27.94 (CH_3), 33.09 (CH_3), 40.95 (N_8-CH_3), 49.28 (C-7), 95.97 (C-4a), 111.57 (C-5), 116.20 (C-12), 122.40 (C-14), 129.60 (C-13), 138.34 (C-9), 153.44 (C-2), 157.63 (C-8a, 11), 161.58 (C-4).

MS: *m*/*z* = 313 (M^+).

Anal. Calcd for $C_{17}H_{19}N_3O_3$: C, 65.17; H, 6.07; N, 13.41. Found: C, 65.26; H, 6.15; N, 13.37.

5b

Yield: 74%; mp 142 °C.

UV (EtOH): λ_{max} (log ε) = 267 (2.41), 317 nm (2.44).

IR (KBr): ν = 2960, 1700, 1620, 1250 cm^{-1}.

^1H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.27 (s, 3 H), 2.73–2.75 (m, 2 H), 2.77 (s, 3 H), 3.11–3.14 (m, 2 H), 3.36 (s, 3 H), 3.42 (s, 3 H), 6.92–7.15 (m, 4 H), 8.23 (s, 1 H).

MS: *m*/*z* = 327 (M^+).

Anal. Calcd for $C_{18}H_{21}N_3O_3$: C, 66.05; H, 6.42; N, 12.84. Found: C, 66.19; H, 6.31; N, 12.72.

5c

Yield: 72%; viscous liquid.

UV (EtOH): λ_{max} (log ε) = 224 (2.81), 282 (2.97), 317 nm (3.01).

IR (KBr): ν = 2920, 1690, 1640, 1240 cm^{-1}.

^1H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.27 (s, 3 H), 2.70 (t, *J* = 6 Hz, 2 H), 2.75 (s, 3 H), 3.10 (t, *J* = 6 Hz, 2 H), 3.35 (s, 3 H), 3.43 (s, 3 H), 6.93–6.99 (m, 2 H), 7.05–7.08 (m, 2 H), 8.20 (s, 1 H).

MS: *m*/*z* = 327 (M^+).

Anal. Calcd for $C_{18}H_{21}N_3O_3$: C, 66.05; H, 6.42; N, 12.84. Found: C, 66.29; H, 6.35; N, 12.70.

5d

Yield: 75%; mp 134 °C.

UV (EtOH): λ_{max} (log ε) = 209 (2.94) 266 (2.72), 316 nm (2.69).

IR (KBr): ν = 2900, 1680, 1620, 1280 cm^{-1}.

^1H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.32 (s, 6 H), 2.74 (t, *J* = 6 Hz, 2 H), 2.80 (s, 3 H), 3.15 (t, *J* = 6 Hz, 2 H), 3.41 (s, 3 H), 3.48 (s, 3 H), 6.62–6.73 (m, 3 H), 8.25 (s, 1 H).

MS: *m*/*z* = 341 (M^+).

Anal. Calcd for $C_{19}H_{23}N_3O_3$: C, 66.86; H, 6.74; N, 12.31. Found: C, 66.93; H, 6.66; N, 12.25.

5e

Yield: 73%; mp 162 °C.

UV (EtOH): λ_{max} (log ε) = 209 (3.06), 267 (2.98), 317 nm (2.92).

IR (KBr): ν = 2960, 1700, 1620, 1220 cm^{-1}.

^1H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.24 (s, 3 H), 2.30 (s, 3 H), 2.68–2.75 (m, 2 H), 2.77 (s, 3 H), 3.11–3.15 (m, 2 H), 3.37 (s, 3 H), 3.45 (s, 3 H), 6.94–6.96 (m, 3 H), 8.20 (s, 1 H).

MS: *m*/*z* = 341 (M^+).

Anal. Calcd for $C_{19}H_{23}N_3O_3$: C, 66.86; H, 6.74; N, 12.31. Found: C, 66.75; H, 6.60; N, 12.42.

5f

Yield: 68%; viscous liquid.

UV (EtOH): λ_{max} (log ε) = 211 (3.14), 312 nm (2.84).

IR (KBr): ν = 2900, 1690, 1630, 1250 cm^{-1}.

^1H NMR ($CDCl_3$/TMS, 100 MHz): δ = 2.64–2.72 (m, 2 H), 2.77 (s, 3 H), 3.05–3.24 (m, 2 H), 3.36 (s, 3 H), 3.44 (s, 3 H), 6.84–7.46 (m, 4 H), 8.28 (s, 1 H).

MS: *m*/*z* = 349 and 347 (M^+).

Anal. Calcd for $C_{17}H_{18}ClN_3O_3$: C, 58.78; H, 5.18; N, 12.10. Found: C, 58.80; H, 5.09; N, 12.12.

5g

Yield: 66%; viscous liquid.

UV (EtOH): λ_{max} (log ε) = 209 (3.05), 306 nm (2.60).

IR (KBr): ν = 2960, 1680, 1630, 1240 cm^{-1}.

^1H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.71 (t, *J* = 6 Hz, 2 H), 2.78 (s, 3 H), 3.13 (t, *J* = 6 Hz, 2 H), 3.35 (s, 3 H), 3.45 (s, 3 H), 6.99–7.02 (m, 2 H), 7.22–7.27 (m, 2 H), 8.21 (s, 1 H).

MS: *m*/*z* = 349 and 347 (M^+).

Anal.Calcd for $C_{17}H_{18}ClN_3O_3$: C, 58.78; H, 5.18; N, 12.10. Found: C, 58.85; H, 5.29; N, 12.14.

5h

Yield: 55%; mp 142 °C.

UV (EtOH): λ_{max} (log ε) = 312 nm (3.15).

IR (KBr): ν = 2940, 1690, 1630, 1250 cm^{-1}.

^1H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.70–2.75 (m, 2 H), 2.78 (s, 3 H), 3.12–3.16 (m, 2 H), 3.35 (s, 3 H), 3.43 (s, 3 H), 7.05–7.10 (m, 1 H), 7.31–7.34 (m, 1 H), 7.48–7.54 (m,1 H), 7.85–7.88 (m, 1 H), 8.30 (s, 1 H).

MS: *m*/*z* = 358 (M^+).

Anal. Calcd for $C_{17}H_{18}N_4O_5$: C, 56.98; H, 5.02; N, 15.64. Found: C, 57.05; H, 5.11; N, 15.71.

5i

Yield: 58%; viscous liquid.

UV (EtOH): λ_{max} (log e) = 226 (2.99), 273 nm (2.85).

IR (KBr): ν = 2960, 1700, 1635, 1230 cm^{-1}.

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^{1}H NMR ($CDCl_3$/TMS, 300 MHz): δ = 2.70–2.74 (m, 2 H), 2.77 (s, 3 H), 3.11–3.14 (m, 2 H), 3.37 (s, 3 H), 3.45 (s, 3 H), 3.77 (s, 3 H), 6.77–7.02 (m, 4 H), 8.18 (s, 1 H).

MS: *m*/*z* 343 (M^+).

Anal. Calcd for $C_{18}H_{21}N_3O_4$: C, 62.97; H, 6.12; N, 12.24. Found: C, 63.09; H, 6.05; N, 12.17.

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