Enaminones as building blocks in heterocyclic synthesis. Synthesis of polyfunctionally substituted 3-azolylpyridines and azolylazoloazines by thermal and microwave heating

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2-Azolyl-3-enaminones (**Ia–e)** react with ethyl cyanoacetate to yield 2-pyridones or 2-aminopyridines depending on the reaction conditions. The reaction of **Ia** with benzoylacetonitrile afforded a pyridine derivative. Condensation of heteroaromatic aminoazoles with **Ia–e** afforded azolopyrimidines. HMBC and NOE difference experiments assisted the assignment of structures to the reaction products.

Keywords: enaminones, benzotriazoles, benzimidazoles, pyrazoles, 2-pyridones, aminopyridines, fused pyrimidines, 1,2,4-triazoles, microwave heating

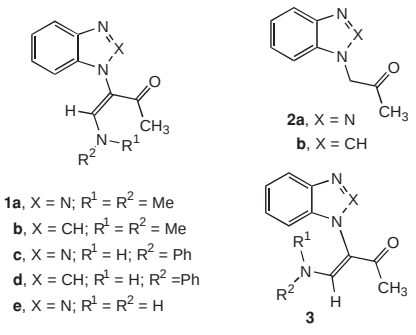
Enaminones are versatile reagents and their chemistry has in the past received considerable attention.[1] Despite this extensive interest, their behaviour towards nucleophiles under microwave heating has not, to our knowledge, been investigated. Solventless reactions by microwave heating have recently received interest because of their "green" value.[2-4] The reaction of enaminones with active methylenes and with aminoazoles has recently been utilised for the synthesis of pyridines and azolopyrimidines.[5,6] In conjunction with our interest in the synthesis of poly-functionally substituted heteroaromatics as potential agrochemicals, pharmaceuticals and/or dye intermediates,[7-10] we report here on the utility of enaminones **Ia–e** for synthesis of azolylpyridines and azolylazoloazines. Our trials to extend the range of the azolyl moiety in the produced products are also described. Being considered as a good leaving group, termed "poor halides", benzotriazoles has been extensively utilized as auxiliaries.[11-14] Moreover, whenever possible reactions were conducted by both conventional and microwave heating, and the outcome of the reactions are compared.

Results and discussion

Compound **1a** was prepared from reaction of **2a** with dimethylformamide dimethylacetal (DMFDMA) following a recently reported procedure.[15] We find that a much better yield of this product can be obtained on heating **2a** with DMFDMA for 45 seconds in a domestic microwave oven. Compound **1a** was converted into **1c** when heated with aniline in a domestic microwave oven at full power. This procedure produces much better yield than conventional heating with aniline in ethanolic solution. Microwave heating of **1a** with ammonium acetate for two minutes in a domestic microwave oven at full power produced **1e**. We failed to obtain **1e** by conventional heating with NH_4OAc in acetic acid. Compound **1b** was also prepared by heating **2b** with DMFDMA in xylene for 6h. This condensation reaction could not be effected by microwave heating.

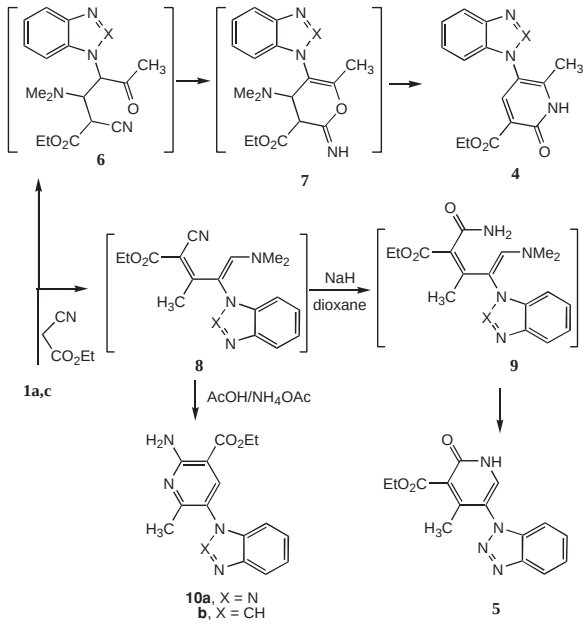
Although **1a–e** may also exist in the *Z* form (**3**), NOE difference experiments indicated that they exist solely in the *E* form as irradiation of the olefinic proton at δ 8.10 ppm enhanced the benzotriazole H-7 signal. In contrast, compound **1e** exists, at least in DMSO solution, as an equilibrium mixture of both *E* and *Z* form, in which the *E* form predominated (76%) as indicated from ^{1}H NMR (*cf.* Scheme 1).

Compounds **1a** reacted with ethyl cyanoacetate (ECA) in refluxing dioxane in the presence of sodium hydride to yield products that may be formulated as **4** or the isomeric **5**. The formation of **4** may proceed via initial Michael addition of ECA across the activated double bond yielding adduct **6** that



Scheme 1

is then converted into **7** and then rearrangement and elimination of $NHMe_2$ into **4**. On the other hand, formation of **5** may occur, proceeding via the intermediacy of condensation products **8** and **9** (*cf.* Scheme 2). Enaminones has been established in the past to react with active methylenes in either way depending on the reaction conditions.[16,17] We assign structure **5** to the reaction product, based on HMBC which indicated cross peaks for the pyridone H-4 and cyano function. The behaviour of **1a** toward ECA resembles previously reported behaviour toward malononitrile and cyanothioacetamide.[15]



Scheme 2

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In contrast to the observed formation of **5** on heating **1a** with ECA in the presence of sodium hydride, **1a,b** reacted with ECA in acetic acid in the presence of ammonium acetate to yield the aminopyridine derivatives **10a,b** (Scheme 2). Trials to conduct this reaction in a domestic microwave oven failed. Support for the structure assignment of **10b** was obtained from HMBC which showed that the pyridine H-4 at δ_H 8.08 ppm had cross peaks with the ester carbonyl signal at δ_C 166.6, pyridine C-2 at δ_C 161.5 and pyridine C-6 at δ_C 159.3 ppm.

Compounds **1a** and **1c** reacted with benzoylacetonitrile (**11**) to yield pyridine derivatives that may be formulated as **12** or the isomeric **13** (Scheme 3). The structure **12** was established based on HMBC in which pyridine H-4 at δ_H 8.16 had cross peaks with the CN carbon at δ_C 116.95 ppm. The behaviour of **1a-d** toward **11** thus finds a parallel in its observed behaviour toward malononitrile and cyanothioacetate.

Trials to prepare **12** by reaction of 2-cyano-3-dimethylaminoacrylonitrile **14** with benzotriazolylacetone **2a** resulted only in the formation of **1a** (Scheme 3). The reaction of **1a** with 3-methylpyrazol-5-amine has been reported recently.[15]

Reaction of compounds **1a–c** with 2-aminobenzimidazole **15** yielded the benzimidazopyrimidines **16a,b**. Structure **16a** is supported by NOE difference experiments that indicated proximity of the benzimidazole H-7 and methyl functions.

Similarly, 3-aminopyrazole **17** reacted with **1a,b** to yield **18a,b.** Attempts to prepare **18** via condensation of **17** with DMFDMA, under conditions described recently[15] for reacting **2a** with 5-methyl-3-aminopyrazole, failed.

Compounds **1a,c** also reacted with 3-amino-l,2,4-triazole **19** to yield products that may be formulated as **20** or the isomeric **21**. NOE difference experiments favoured structure **20**, since irradiating the methyl signal at δ_H 2.68 enhanced both the triazole singlet at δ 8.93 and the benzotriazole H-7 at δ 8.71.

Compounds **16a**, **18a**, and **20** were also obtained in better yields on reacting **15**, **17**, and **19** with **1a** in absence of solvent in a domestic microwave oven (*cf.* Scheme 4).

Attempts to replace the benzotriazole moiety in the products described here by nucleophiles under a variety of conditions failed. One may thus conclude that carbanions and amines react initially across the activated enaminone double bond.

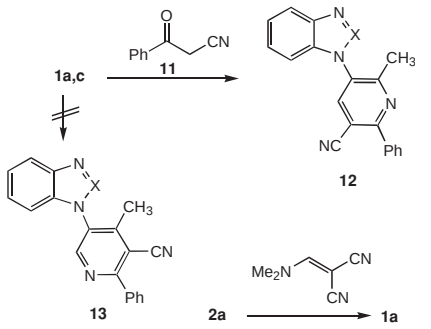
Moreover, microwave heating provides a rapid and environmentally clean way of preparing polyfunctionally substituted heteroaromatics from enaminones with yields equivalent to or better than those obtained by conventional heating in solvent. Although microwave heating in domestic oven failed to make some transformations, others can only be conducted in the microwave oven. It may also be stated that the ease of replacement of the benzotriazole moiety in a heteroaromatic system is very different from the replacement of halogens.

Experimental

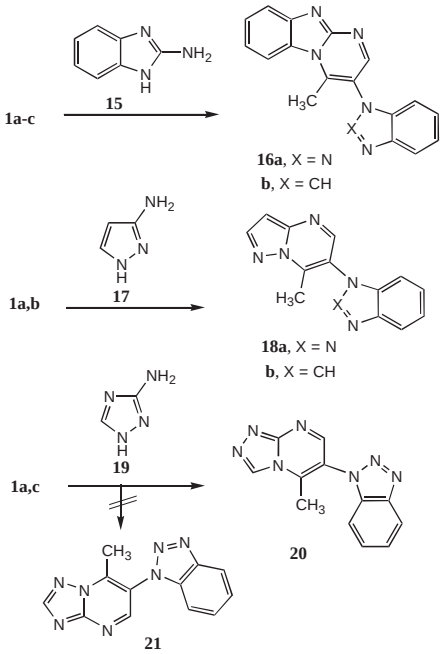
IR spectra were recorded in KBr with a Pye Unicam SP 1100 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian EM-390 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6 as solvent using TMS as internal standard; chemical shifts are reported in δ units (ppm). Mass spectra were measured on MS 30 and MS 9 (AEI) at 70 eV in EI mode. Microanalyses were performed on LECO CHNS-932. Microwave heating was conducted in a microwave oven DAEWOO model II (KOR-8667).

Compounds **2a,b** were prepared following published procedure.[18,19]

3-Benzotriazol-1-yl)-4-dimethylaminobut-3-en-2-one (**1a**): *Method A, microwave heating*. A mixture of **2a** (1.75g, 10 mmol) and DMFDMA (1.19 g, 10 mmol) was heated in a microwave at full power for 45 seconds. The solid product so formed was collected by filtration and crystallised from toluene. Compound **1a** (1.48 g, 64%) formed yellow crystals, m.p. 156 °C. IR: ν_{max}/cm^{-1} 1655 (CO), ^{1}H NMR (DMSO-d_6): δ 1.66 (s, 3H, CH_3), 2.04 (s, 3H, NCH_3), 3.17 (s, 3H, NCH_3), 7.40–7.57 (m, 3H, benzotriazolyl H-4, H-5, H-6), 7.94 (s, 1H, CH), 8.10 (d, 1H, benzotriazolyl H-7). MS: *m/z* 230 [M$^+$]. Found C, 62.59; H, 5.95; N, 24.31. $C_{12}H_{14}N_4O$ (230.26) requires C, 62.59; H, 6.12; N, 24.33 %.



Scheme 3



Scheme 4

Method B, thermal reaction. Reaction of **2a** with DMFDMA for 6h using the published procedure[20] gave **1a** (54%).

3-(3H-Benzimidazol-1-yl)-4-dimethylamino-but-3-en-2-one (**1b**): DMFDMA (1.19 g 10 mmol) was added to a suspension of compound **2b** (1.74 g 10 mmol) in xylene (20 ml). The reaction mixture was refluxed for 6h. The solvent was then evaporated under vacuum and the residue was left at room temperature. The solid product so formed was crystallised from xylene. Compound **1b** formed buff crystals (1.46 g, 64%), m.p. 142 °C, IR: ν_{max}/cm^{-1} 3074 (CH), 1648 (CO), ^{1}H NMR (DMSO-d_6): δ 1.77 (s, 3H, CH_3), 2.29 (s, 3H, NCH_3), 3.13 (s, 3H, NCH_3), 7.28–7.38 (3H, H-4, H-5, H-6), 7.84 (s, 1H, H-2), 7.87 (m, 1H; H-7) and 7.92 (s; 1H, propene H-4). MS: *m/z* 229 [M$^+$]. Found C, 68.30; H, 6.80; N 18.54. $C_{13}H_{15}N_3O$ (229.28) requires C, 68.10; H, 6.59; N, 18.31 %.

General procedures for the preparation of **1c,d**: *Method A: thermal reaction.* Compound **1a** or **1b** (10 mmol) and aniline (0.93 g, 10 mmol) were refluxed in ethanol (20 ml) for 2h, then poured onto water. The solid product was collected by filtration and crystallised from ethanol.

3-(Benzotriazol-1-yl)-4-phenylamino-but-3-en-2-one (**1c**): yellow crystals (1.47 g, 53%), m.p. 170 °C. IR: ν_{max}/cm^{-1} 3433, (NH), 1657 (CO); ^{1}H NMR ($CDCl_3$): δ 1.83 (s, 2.28 H, CH_3), 2.08 (s, 0.72 H), 7.1–8.45 (Ar-H and propene H), 11.87 (d, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 196.5 (CO), 146.1, 144.95, 139.3. 135.7, 130.3, 128.6, 125.5, 124.7, 120.6, 117.5, 110.1,109.6, 25.5. MS: *m/z* 278 [M$^+$]. Found C, 69.11; H, 5.07; N, 20.19. $C_{16}H_{14}N_4O$ (278.31) requires C, 69.05; H, 5.07; N, 20.13 %.

3-(Benzimidazol-1-yl)-4-phenyIamino-but-3-en-2-one (**1d**): buff crystals (1.02 g, 37%), m.p. 219 °C. IR: ν_{max}/cm^{-1} 3166 (NH), 3064, (CH), 1631 cm^{-1} (CO), ^{1}H NMR (DMSO-d_6): δ 2.30 (s, 3H, CH_3),

7.04–8.42 (9 arom. H). 9.31 (d, 1H, propene H), 11.6 (d, 1H, NH). MS: *m/z* 277 [M^+]. Found C, 73.27; H, 5.35; N, 15.23. $C_{17}H_{15}N_3O$ (277.32) requires C, 73.62; H, 5.45; N, 15.15 %.

Method B: microwave heating. **1a** (2.30 g, 10 mmol) and aniline (0.93 g, 10 mmol) were heated in a microwave oven at full power for 2 minutes. After cooling, the solid product was crystallised from ethanol to give **1c (**1.98 g, 71%).

4-Amino-3-(benzotriazol-1-yl)-but-3-en-2-one (**1e**): A mixture of **1a** (2.30 g, 10 mmol), acetic acid (1ml) and ammonium acetate (3g) was heated in a microwave oven at full power for 30 seconds, then poured onto water and neutralized with aqueous ammonia. The solid product so formed was collected and crystallised from ethanol. **1e** formed yellow crystals (1.84 g, 91%), m.p. 202 °C. IR: ν_{max}/cm^{-1} 3324 and 3153 (2NH), 1662 (CO); ^1H NMR ($CDCl_3$): δ 1.73 (s. 3H, CH_3), 5.83 (br, 1H, NH), 7.14–7.56 (m, 5H, benzotriazolyl H-4, H-5, H-6 propene H-4, NH) and 8.10 (d, 1H; *J* 8Hz, benzotriazolyl H-7). MS: *m/z* 202 [M^+]. Found C, 59.40; H, 5.06; N, 27.57. $C_{10}H_{10}N_4O$ (202.21) requires C, 59.39; H, 4.98; N, 27.70 %.

5-(Benzotriazol-I-yl)-6-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid ethyl ester (**5**): A solution of ECA (1.13 g 10 mmol) in dioxane, (20 ml) containing sodium hydride (0.40 g) was treated with **1a** (2.30 g 10 mmol). The reaction mixture was refluxed for 5h. The solvent was evaporated under reduced pressure. The remaining product was triturated with water and then neutralised with hydrochloric acid. The solid product was collected by filtration and crystallised from ethanol. Compound **5** formed yellow crystals (18.9 g. 64%), m.p. 234 °C. IR: ν_{max}/cm^{-1} 3064 (NH); 1731 (CO) ester, 1649 (CO); ^1H NMR ($CDCl_3$): δ 1.32 (s, 3H, CH_3); 2.29 (t, 3H, CH_3); 4.35 (q, 2H, OCH_2CH_3), 7.3–7.5 (m, 3H; (benzotriazolyl H-4; H-5, H-6); 8.15 (m, 1H (benzotriazolyl H-7), 7.23 (s, 1H, pyridyl H-6). MS: *m/z* 298 [M^+]. Found C, 60.18; H, 4.82; N, 18.61. $C_{15}H_{14}N_4O_3$ (298.28) requires C, 60.40; H, 4.73; N, 18.78 %.

General procedure for the preparation of **10a,b** *and* **12**. Each of **1a–c** (10 mmol) were added to ECA or benzoylacetonitrile (10 mmol) in acetic acid (4 ml) and ammonium acetate (2g). The reaction mixture was refluxed for 3h, then poured into water and neutralised with aqueous ammonia. The solid product so formed was collected by filtration and crystallised from ethanol : DMF (3 : 1 by volume).

2-Amino-5-(benzotriazol-1-yl)-6-methylnicotinic acid ethyl ester (**10a**): buff crystals (1.59 g, 53%), m.p. 178 °C. IR: ν_{max}/cm^{-1} 3424 and 3278 (2NH), 1695 (CO) ester; 1624 (CO); ^1H NMR ($CDCl_3$): δ 1.35 (t, 3H, *J* = 8Hz, CH_3), 2.17 (s, 3H, CH_3), 4.35 (q, 2H, *J* = 8Hz, CH_2), 5.8 (2H, NH_2), 7.28–7.58 (m, 3H, benzotriazolyl H-4, H-5, H-6), 8.14 (s, 1H, pyridyl H-6), 8.19 (m, 1H, benzotriazolyl H-7). ^{13}C NMR ($CDCl_3$): δ 166.6 (CO), 161.1, 159.7, 146.05, 139.2, 134.6, 128.7, 124.7, 121.6, 120.7, 110.1, 104.7, 61.65 (CH_2), 21.3 (CH_3), 14.6 ($COCH_3$). MS: *m/z* 297 [M^+]. Found C, 60.65; H, 5.21; N, 23.70. $C_{15}H_{15}N_5O_2$ (297.31) requires C, 60.54; H, 5.08; N, 23.55 %.

2-Amino-5-(benzimidazol-1-yl)-6-methylnicotinic acid ethyl ester (**10b**): buff crystals (1.28 g, 43%), m.p. 242 °C. IR: ν_{max}/cm^{-1} 3485 and 3361 (2NH), 3068, (CH) and 1693 (CO); ^1H NMR ($CDCl_3$): δ 1.36 (t, 3H, CH_3), 2.17 (s, 3H, CH_3), 4.35 (q, 2H, CH_2, *J* = 8Hz), 5.5–6.4 (br, 2H, NH_2); 7.15–7.39 (m, 3H, benzimidazolyl H-4; H-5, H-6), 7.9 (m, benzimidazolyl H-7), 8.08 (s, 1H, pyridyl H-4). ^{13}C NMR (100 MHz, $CDCl_3$): 166.6 (CO), 161.5, 159.3, 143.7, 143.65, 139.6, 135., 124.2, 123.2, 121.0, 120.85, 110.5, 104.9, 61.6 (CH_2), 21.1 (CH_3), 14.6 ($COCH_3$). MS: *m/z* 296 [M^+]. Found C, 64.83; H, 5.41; N, 18.92. $C_{16}H_{16}N_4O_2$ (296.31) requires C, 64.85; H, 5.44; N, 18.90%.

5-(Benzotriazol-1-yl)-4-methyl-2-phenylnicotinonitrile (**12**): white crystals (2.24 g, 72%), m.p. 170 °C. IR: ν_{max}/cm^{-1} 2232 cm^{-1} (CN);. ^1H NMR ($CDCl_3$): δ 2.59 (s, 3H, CH_3). 7.43–8.07 (m, 8H, Ph and benzotriazolyl H-4, H-5, H-6), 8.16 (s, 1H, pyridyl H-4), 8.24 (d, *J* = 8Hz, benzotriazolyl H-7), ^{13}C NMR ($CDCl_3$): δ 161.6, 160.2, 146.3, 139.7, 136.7. 133.9. 131.3, 130.4, 129.6, 129.5, 129.4, 125.3, 121.2, 116.95, 109.7, 106.0, 22.5. MS; *m/z* 311 [M^+]. Found C, 73.23; H, 4.30; N, 22.58. $C_{19}H_{13}N_5$ (311.34) requires C, 73.29; H, 4.20; N, 22.49 %.

General procedure for the reactions of ***1a–c*** *with heterocyclic aromatic amines: Method A, thermal reaction.* Compounds **1a–c** (10 mmol) were separately added to amines **15, 17** or **19** (10 mmol) in acetic acid (10 ml) containing ammonium acetate (2 g). The reaction mixture was refluxed for 4h, then poured onto water and neutralised with aqueous ammonia. The solid product was filtered off and crystallised from DMF.

3-(Benzotriazol-1-yl)-4-methylpyrimido[1,2-a]benzimidazole (**16a**): orange crystals (2.0 g, 67%) m.p. 308 °C. ^1H NMR ($CDCl_3$): δ 2.92 (s, 3H, CH_3), 7.28–8.28 (m, 8H, benzotriazolyl and benzoimidazolyl H); 8.82 (s, 1H, H-2). MS: *m/z* 300 [M^+]. Found C. 67.76; H, 4.19; N, 27.98. $C_{17}H_{12}N_6$ (300.32) requires C, 67.98; H, 4.02; N, 27.98 %.

3-(Benzimidazol-1-yl)-4-methylpyrimido[1,2-a]benzimidazole (**16b**): brown crystals (1.96g, 66%), m.p. 302–304 °C. ^1H NMR ($CDCl_3$): δ 2.89 (s, 3H, CH_3), 7.21-8.17 (m, 8H, benzimidazolyl H), 8.75 (s, 1H, benzimidazolyl H-2). MS: *m/z* 299 [M^+]. Found C, 71.76; H, 4.41; N, 23.10. $C_{18}H_{13}N_5$ (299.33) requires C, 72.22; H, 4.37; N, 23.39 %.

1-(7-Methylpyrazolo[1,5-a]pyridin-6-yl]-1H-benzotriazole (**18a**): yellow crystals (1.58 g, 63%), m.p. 205–207 °C. ^1H NMR ($CDCl_3$): δ 2.7 (s, 3H, CH_3); 6.92 (d, 1H, pyrazolopyrimidine H-3), 7.40–7.63 (m, 3H, benzotriazolyl H-4, H-5, H-6), 8.23 (d, 1H, *J* = 8 Hz, benzotriazolyl H-7); 8.34 (d, 1H, *J* = 4 Hz, pyrazolopyrimidine H-2), 8.56 (s, 1H, pyrazolopyrimidine H-5); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.6, 147.0, 146.9, 146.2, 145.1, 134.4, 129.5, 125.2, 121.0, 118.2, 109.6, 99.05, 13.6. MS: *m/z* 250 [M^+]. Found C, 62.35; H, 4.07; N, 33.96. $C_{13}H_{10}N_6$ (250.26) requires C, 62.39; H, 4.02; N, 33.58 %.

6-(Benzimidazol-1-yl)-7-methylpyrazolo[1,5-a]pyrimidine (**18b**): colourless crystals (1.90 g, 76%), m.p. 88 °C. ^1H NMR ($CDCl_3$): δ 2.68 (s, 3H, CH_3); 6.92 (d, *J* = 2.4 Hz, pyrazolopyrimidine H-3), 7.28–7.97 (benzotriazolyl H), 8.07 (s, 1H, pyrazolopyrimidine H-5); 8.32 (d, 1H, *J* = 2.4 Hz, pyrazolopyrimidine H-2), 8.5 (s, 1H, benzimidazole H-2). MS: *m/z* 49 [M^+]. Found C, 67.38; H, 4.46; N, 28.01. $C_{14}H_{11}N_5$ (249.27) requires C, 67.45; H. 4.44; N, 28.09 %.

6-(Benzotriazol-1-yl)-5-methyl[1,2,4]triazolo[4,3-a]pyrimidine (**20**): orange crystals (1.52 g, 61%), m.p. 203–205 °C, ^1H NMR ($CDCl_3$): δ 2.82 (s, 3H, CH_3); 7.28–8.27 (m, 4H, benzotriazolyl H), 8.70 (s, 1H, triazolopyrimidine H-6), 8.9 (triazolopyrimidine H-2). MS: *m/z* 251 {[M^+]. Found C, 57.37; H, 3.69; N, 39.78. $C_{12}H_9N_7$ (251.25) requires C, 57.36; H, 3.61; N, 39.02%.

Method B, microwave heating: Compound **1a** (10 mmol) and ammonium acetate (5 g) were added to **15**, **17** and **19** (10 mmol) in acetic acid (4ml). The mixture was heated in a microwave oven at full power. The heating times were 30, 45 and 60 seconds respectively. The mixture was then poured into water and neutralised with aqueous ammonia. The solid product was collected by filtration and crystallised from DMF to give **16a** (2.48 g, 83%), **18a** (1.93 g, 77%) and **20** (2.02 g, 80%).

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References

1 A. Elassar and A.A. Elkhair, *Tetrahedron*, 2003, **59**, 8463.
2 A.S. Matlack *Introduction to Green Chemistry* Marcel Dekker Inc., New York, Basel, 2001.
3 P. Lidstrom, J. Fiemey, B. Wathey and J. Western**,** *Tetrahedron*, 2001, **57**, 9225.
4 S. Caddick, *Tetrahedron*, 2001, **51**, 10403.
5 A. El-Enzy, B. Al-Saleh and M.H. Elnagdi, *J. Chem. Res.* 1997, *(S), 4; (M)*, 110.
6 M.A. Al-Shiekh, A.M. Salah El-Din, E.A. Hafez and M.H. Elnagdi, *J. Chem. Res.*, 2004, 174.
7 M.A. Megid, M.H. Elnagdi and A.M. Negm, *J. Heterocycl. Chem.*, 2002, **39**, 105.
8 N. Al-Awadi, M.H. Elnagdi, Y.A. Ibrahim, K. Kaul and A. Kumar, *Tetrahedron*, 2001, **57**, 609.
9 M.M.A. Khalik, S.M. Agamy and M.H. Elnagdi, *Synthesis*, 2001, 1861.
10 B. Al-Saleh, N. Al-Awadi, H. Al-Kandari, M.M.A. Khalik and M.H. Elnagdi, *J. Chem. Res.*, 2001, *(S)*, 16; *(M)*, 0201.
11 A.R. Katritzky, X. Lan, J.Z. Yang and O.V. Denisko, *Chem. Rev.*, 1998, **98**, 409.
12 A.R. Katritzky, *J. Heterocycl. Chem.*, 1999**, 36,** 1501.
13 A.R. Katritzky, S. Zhang, M. Wang, H.C. Kolbad and P.J. Steel, *J. Heterocycl. Chem.*, 2002**, 39,** 759.
14 A.R. Katritzky, G. Qui, Q.H. Long, H.Y. Head and P.J. Steel, *J. Org. Chem.*, 2000, **69,** 9201.
15 F. Al-Omran, *J. Heterocycl. Chem.*, 2000, **37**,1219.
16 F. Al-Omran, N. Al-Awadi, M.M.A. Khalik, K. Kaul, A.A. El-Khair and M.H. Elnagdi, *J. Chem. Res.*, 1997, *(S), 84; (M)* 601.
17 S. Al-Mousawi, K.S. George and M.H. Elnagdi, *Pharmazie*, 1999, **54**, 571.
18 A.R. Katritzky and J Wu, *Synthesis*, 1994, 1861.
19 A.R. Katritzky and J.V. Shcherbakov, *J. Heterocyclic Chem.*, 1996, **33**, 2031.
20 B. Al-Saleh. M.M. Abdel-Khalik, E. Darwich, O.A. Saleh and M.H. Elnagdi, *Heteroatom Chem.*, 2002, **13**, 141.