Azoles and azolo-azines via 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile

Kamal M. Dawood*, Ahmad M. Farag and Hatem A. Abdel-Aziz

Department of Chemistry, Faculty of Science, University of Cairo, Giza, Egypt

3-(3-Methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**), a versatile synthon, was prepared and utilised in the synthesis of several azoles and fused azolo-azine derivatives.

Keywords: benzofurans, benzimidazoles, pyrazoles, triazines, nitrilimines, cycloaddition.

The benzofuran ring system is found as an integral part of various natural products.[1-3] In addition, benzofuran derivatives are potentially active antihyperglycemic,[4] antitumor,[5] cytotoxic,[6, 7] antifungal[8] and antiaromatase[8, 9] agents. Although the biologically active ethyl 3-methyl-2-benzofurancarboxylate (**1**)[10] has long been known, the more functionalised 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**) has not been reported so far.

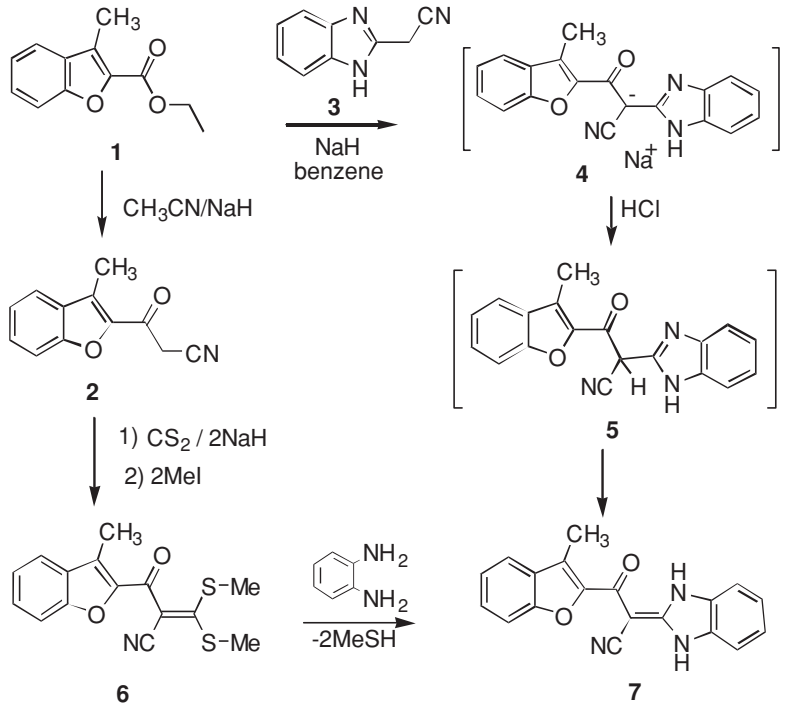
In connection with our endeavours on the synthesis of various substituted heterocyclic ring systems which could be adapted for the construction of libraries,[11-16] we report here on the preparation of compound **2** and its application to the synthesis of several heterocycles incorporating the 3-methylbenzofuran moiety that may open new avenues to biologically active benzofuran compounds.

To begin with, ethyl 3-methyl-2-benzofurancarboxylate (**1**) was prepared from phenol and ethyl acetoacetate according to the reported procedure,[10] and then utilised in the synthesis of the versatile, hitherto unreported, 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**) by refluxing equimolar amounts of the ester **1** and acetonitrile in the presence of sodium hydride in dry benzene (Scheme 1).

The structure of compound **2** was established on the basis of its elemental analysis, IR and ^{1}H NMR spectra. Its IR spectrum revealed two characteristic absorption bands at 2260 and 1682 cm^{-1} assignable to nitrile and carbonyl functions, respectively. The ^{1}H NMR spectrum of **2** displayed a singlet at δ 4.3 from the active methylene group in addition to the aromatic proton multiplet in the region δ 7.25–7.71.

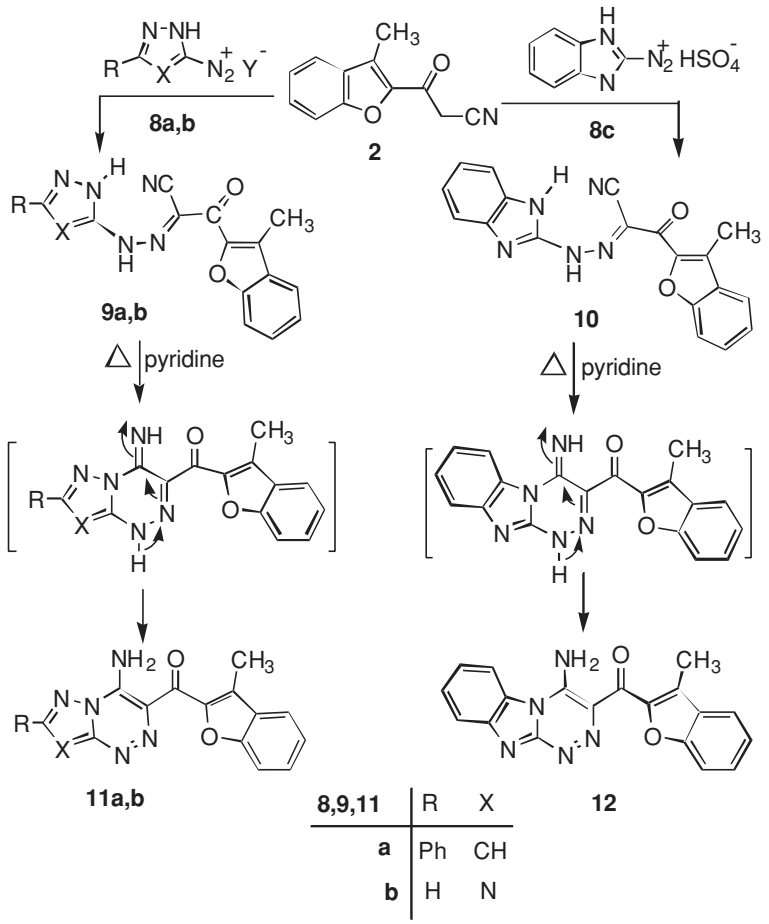
Further, treatment of ester **1** with an equimolar quantity of 2-cyanomethyl-1*H*-benzimidazole (**3**)[17] in the presence of sodium hydride in benzene under refluxing conditions, followed by neutralisation of the formed salt, resulted in a single product which analysed for $C_{19}H_{13}N_3O_2$. The structure of the product was assigned as 2-(1,3-dihydrobenzimidazol-2-ylidene)-3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**7**) on the basis of its spectral data (MS, IR and ^{1}H NMR). Its IR spectrum revealed two absorption bands at 3235 and 3180 cm^{-1} due to two NH groups and two bands at 2189 and 1652 cm^{-1} assignable to nitrile and carbonyl functions respectively. The ^{1}H NMR spectrum of the reaction product displayed a singlet signal at δ 13.07 due to two NH protons in addition to an aromatic multiplet in the region δ 7.28–7.76. The lack of an active methine proton signal in the ^{1}H NMR spectrum of the latter product indicates that it exists exclusively in the 1,3-dihydrobenzimidazol-2-ylidene structure **7**, and rules out the isomeric **5**.

The structure of compound **7** was further evidenced by its alternative synthesis shown in Scheme 1. Thus, treatment of 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**) with sodium hydride and carbon disulfide followed by methyl iodide afforded 2-bis(methylthio)methylene-3-(3-methyl-



Scheme 1

* Correspondent. E-mail: dr_dawood@yahoo.com

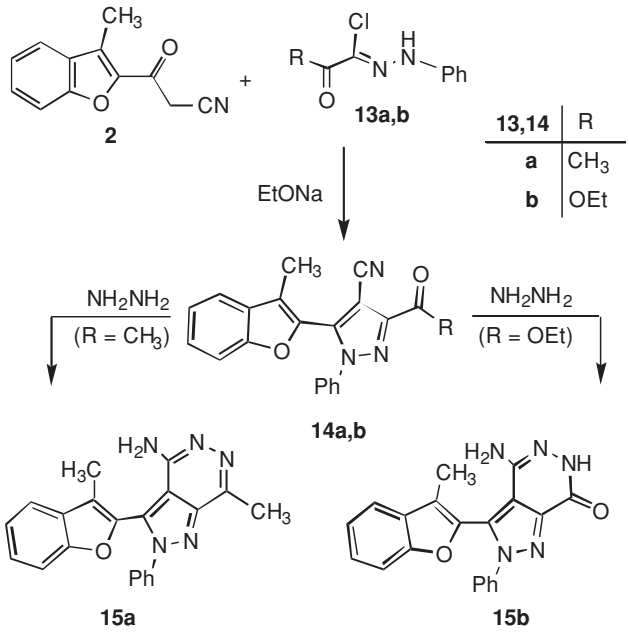


Scheme 2

benzofuran-2-yl)-3-oxopropanenitrile (**6**), which reacted with *o*-phenylenediamine in refluxing ethanol to afford in good yield a product identical in all respects (mp, mixed mp, IR and MS spectra) with compound **7**. The structure of compound **6** was established on the basis of its elemental analysis and spectral data (see Experimental section).

Next, the reactions of 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**3**) towards some heterocyclic diazonium salts were undertaken to synthesize bridgehead-nitrogen heterocycles incorporating the 3-methylbenzofuran moiety. It was found that compound **2** couples smoothly with the diazonium salts of 5-amino-3-phenylpyrazole (**8a**),[18] 5-amino-l,2,4-triazole (**8b**)[19] and 2-aminobenzimidazole (**8c**)[19, 20] to afford the corresponding hydrazones **9a**, **9b** and **10**, respectively (Scheme 2). The IR spectra of the isolated products showed, in each case, two absorption bands in the region 3425–3200 cm^{-1} corresponding to two NH groups in addition to nitrile and carbonyl functions around 2200 and 1650 cm^{-1}, respectively. Compounds **9a**, **9b** and **10** underwent intramolecular cyclisation upon boiling in pyridine to afford the corresponding fused heterocyclic systems: 4-amino-3-(3-methylbenzofuran-2-yl)carbonyl-7-phenylpyrazolo[5,1-*c*][1,2,4]triazine (**11a**), 4-amino-3-(3-methylbenzofuran-2-ylcarbonyl)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazine (**11b**), and 4-amino-3-(3-methylbenzofuran-2-yl)carbonyl-1,2,4-triazino[4,3-*a*]benzimidazole (**12**), respectively (Scheme 2). The lack of nitrile absorptions and the appearance of bands characteristic of the amino and carbonyl functions in the IR spectra of the reaction products supported the assigned structures **11a**,**b** and **12**.

The reaction of 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**) with hydrazonoyl chlorides **13a,b**[21, 22] in ethanolic sodium ethoxide solution furnished the pyrazole derivatives **14a,b**. Treatment of the latter products with hydrazine hydrate in refluxing ethanol afforded the pyrazolo[3,4-d]pyridazine derivatives **15a,b** (Scheme 3). The structures of the products **14a,b** and **15a,b** were substantiated from their elemental analyses and spectral data (cf. experimental part).



Scheme 3

Experimental

Melting points were measured with a Gallenkamp apparatus. IR spectra were recorded on a Shimadzu FT-IR 8101 PC infrared spectrophotometer. The ^{1}H and ^{13}C NMR spectra were determined in $CDCl_3$ or DMSO-d_6 at 300 MHz and 75 MHz, respectively, on a Varian Mercury VX 300 NMR spectrometer. Chemical shifts are related to that of the solvent. Mass spectra were measured on a GCMS-QP1000 EX spectrometer at 70 eV. Elemental analyses were carried out at the Microanalytical center of Cairo University.

Ethyl 3-methyl-2-benzofurancarboxylate (**1**)[10], 2-cyanomethyl-1*H*-benzimidazole (**3**),[17] the heterocyclic diazonium salts **8a**,[18] **8b**[19] and **8c**,[19,20] and the hydrazonoyl chlorides **13a**[21] and **13b**[22] were prepared as described in the literature procedures.

3-(3-Methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**): To ethyl 3-methyl-2-benzofurancarboxylate (**1**)[10] (20.04 g, 0.1 mol) and acetonitrile (4.1 ml, 0.1 mol) in dry benzene (250 ml) and dimethylformamide (10 ml), was added sodium hydride (4.8 g, 60%). The reaction mixture was refluxed for 4h, and then allowed to cool to room temperature. The solid formed was collected by filtration, washed with ether and dried. This material was dissolved in water and then neutralised with concentrated hydrochloric acid to pH 7. The precipitated product was collected by filtration, washed with water and dried. Recrystallisation from ethanol gave compound **2** (68% yield), m.p. 115–117 °C. IR (KBr): ν_{max}/cm^{-1} 2260 (C≡N), 1682 (C=O). ^{1}H NMR (DMSO-d_6): δ 2.54 (s, 3H, CH_3), 4.3 (s, 2H, CH_2), 7.25–7.71 (m, 4H, ArH). MS: *m/z* (%) 199 (M^+, 19.5), 159 (100), 131 (55), 51 (18.5). Calc. for $C_{12}H_9NO_2$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.26; H, 4.6; N, 6.9 %.

2-Bis(methylthio)methylene-3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**6**): To a stirred solution of sodium hydride (0.48 g, 20 mmol) in dimethylsulfoxide (20 ml), 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**) (1.99 g, 10 mmol) was added. The resulting mixture was stirred for 30 min, and then carbon disulfide (0.86 g, 10 mmol) was added. After 2h of stirring, methyl iodide (2.84 g, 20 mmol) was added and the stirring was continued for additional 4h. The resulting reaction mixture was then poured over crushed ice and the solid product was filtered off, washed with water, dried and finally recrystallised from ethanol to afford compound **6** (88% yield), m.p. 98–100 °C. IR (KBr): ν_{max}/cm^{-1} 2204 (C≡N), 1623 (C=O), 1566 (C=N). ^{1}H NMR ($CDCl_3$): δ 2.54 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 2.81 (s, 3H, CH_3), 7.29–7.68 (m, 4H, ArH). ^{13}C NMR: δ 8.0, 17.8, 104.2, 110.7, 114.5, 120.6, 122.4, 125.4, 127.1, 127.8, 144.9, 152.1, 175.1, 176.9. MS: (*m/z*, %) 304 (M^++1, 43), 303 (M^+, 100), 132 (57), 77 (44). Calc. for $C_{15}H_{13}NO_2S_2$: C, 59.38; H, 4.32; N, 4.62; S, 21.14. Found: C, 59.44; H, 4.29; N, 4.61; S, 21.18 %.

2-(1,3-Dihydrobenzimidazol-2-yl)-3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**7**): *Method A.* To a mixture of ethyl 3-methyl-2-benzofurancarboxylate (**1**) (20.04 g, 0.1 mol) and 1*H*-benzimidazole-2-acetonitrile (**3**)[24] (15.7 g, 0.1 mol) in dry benzene (250 ml) and dimethylformamide (10 ml) was added sodium hydride (4.8 g, 60%). The reaction mixture was refluxed for 4h, then allowed to cool. The solid that precipitated was collected by filtration, washed with ether and dried. The solid product was dissolved in water and the resulting solution was neutralised to pH 7 with concentrated hydrochloric acid. The precipitated solid was collected by filtration, washed with water and dried. Recrystallisation of the crude product from ethanol/DMF gave compound **7** (92% yield), M.p. >300 °C. IR (KBr): ν_{max}/cm^{-1} 3235, 3180 (2NH), 2189 (C≡N), 1652 (C=O). ^{1}H NMR (DMSO-d_6): δ 2.54 (s, 3H, CH_3), 7.28–7.49 (m, 4H, ArH), 7.58–7.76 (m, 4H, ArH), 13.07 (s, D_2O exchangeable, 2H, 2NH). MS: (*m/z*, %) 316 (M^++1, 21.7), 315 (M^+, 100), 300 (52), 183 (22), 132 (89), 77 (50). Calc. for $C_{19}H_{13}N_3O_2$: C, 72.37; H, 4.16; N, 13.33. Found: C, 72.36; H, 4.18; N, 13.30 %.

Method B. *o*-Phenylenediamine (0.11 g, 1 mmol) was added to a solution of bis(methylthio)methylene derivative (**6**) (0.30 g, 1 mmol) in ethanol (20 ml). The mixture was refluxed for 3h and then allowed to cool. The solid formed was filtered off, washed with ethanol and recrystallised from DMF/water to afford a product (87% yield) identical in all respects (TLC, IR spectrum) with that obtained by method A.

*Reaction of 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**) with heterocyclic diazonium salts. General procedure*

To a cold solution of 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**) (1.99 g, 10 mmol), in pyridine (50 ml), was added the appropriate heterocyclic diazonium salt of 5-amino-3-phenylpyrazole (**8a**),[18] 3-amino-l,2,4-triazole (**8b**)[19] or 2-aminobenzimidazole (**8c**)[19,20] (2 mmol) that were prepared according to literature procedures. The addition was carried out portionwise with stirring at 0–5°C over a period of 30 min. After complete addition, the reaction mixture was stirred for further 4h, then kept in an ice-chest for 12h, and finally diluted with water. The precipitated solid was collected, washed with water, dried and recrystallised from ethanol/DMF to afford the corresponding hydrazones **9a**, **9b** and **10** respectively.

3-(3-Methylbenzofuran-2-yl)-2-(3-phenyl-1H-pyrazol-5-ylhydrazono)-3-oxopropanenitrile (**9a**): Yield 68%, m.p. 196–198 °C. IR (KBr): ν_{max}/cm^{-1} 3425, 3310 (2NH), 2176 (C≡N), 1651 (C=O), 1528 (C=N): MS: (*m/z*, %) 370 (M^++1, 21.5), 369 (M^+,100), 266 (35), 211 (53), 159 (27), 116 (64), 77 (33). Calc. for $C_{21}H_{15}N_5O_2$: C, 68.28; H, 4.09; N, 18.96. Found: C, 68.27; H, 4.25; N, 19.02 %.

3-(3-Methylbenzofuran-2-yl)-2-(1H-1,2,4-triazol-5-ylhydrazono)-3-oxopropanenitrile (**9b**): Yield 69%, m.p. 180–182 °C. IR (KBr): ν_{max}/cm^{-1} 3340, 3136 (2NH), 2206 (C≡N), 1627 (C=O), 1560 (C=N). MS: (*m/z*, %) 295 (M^++1, 35.2), 294 (M^+, 26.4), 159 (100), 136 (62.6), 116 (34.7), 77 (40.0). Calc. for $C_{14}H_{10}N_6O_2$: C, 57.14; H, 3.43; N, 28.56. Found: C, 57.39; H, 3.51; N, 28.73 %.

3-(3-Methylbenzofuran-2-yl)-2-(1H-benzimidazol-2-ylhydrazono)-3-oxopropanenitrile (**10**): Yield 60%, m.p. 248–250 °C. IR (KBr): ν_{max}/cm^{-1} 3451, 3292 (2NH), 2204 (C≡N), 1683 (C=O), 1576 (C=N). MS: (*m/z*, %) 344 (M^++1, 100), 343 (M^+, 45.2), 184 (64.8) 159 (36), 116 (26), 77 (35). Calc. for $C_{19}H_{13}N_5O_2$: C, 66.47; H, 3.82; N, 20.40. Found: C, 66.71; H, 3.98; N, 20.51 %.

Cyclisation of the heterocyclic hydrazones **9a,b** *and* **10**. *General procedure*

A solution of the appropriate hydrazone **9a, 9b** or **10** (1 mmol) in pyridine (10 ml) was refluxed for 3h, then left to cool. The solid that formed was filtered off, washed with ethanol, dried and finally recrystallised from ethanol/DMF to afford the corresponding fused heterocycles **11a, 11b** and **12**, respectively.

4-Amino-3-(3-methylbenzofuran-2-yl)carbonyl-7-phenylpyrazolo[5,1-c][1,2,4]triazine (**11a**): Yield 74%, m.p. 260–262 °C. IR (KBr): ν_{max}/cm^{-1} 3250, 3140 (NH_2), 1636 (C=O). ^{1}H NMR (DMSO-d_6): δ 2.55 (s, 3H, CH_3), 7.20–7.51 (m, 5H, ArH), 7.59–7.76 (m, 4H, ArH), 8.58 (s, 1H, CH), 9.31 (br. s, D_2O exchangeable, 2H, NH_2). MS: (*m/z*, %) 370 (M^++1, 28.5), 369 (M^+, 100), 266 (34), 211 (25), 159 (67), 116 (25), 77 (57). Calc. for $C_{21}H_{15}N_5O_2$: C, 68.28; H, 4.09; N, 18.96. Found: C, 68.06; H, 3.86; N, 18.75 %.

4-Amino-3-(3-methylbenzofuran-2-yl)carbonyl[1,2,4]triazolo[5,1-c][1,2,4]triazine (**11b**): Yield 75%, m.p. 250–252 °C. IR (KBr): ν_{max}/cm^{-1} 3452, 3340 (NH_2), 1682 (C=O). ^{1}H NMR (DMSO-d_6): δ 2.57 (s, 3H, CH_3), 7.26–7.74 (m, 4H, ArH), 8.37 (s, 1H, CH), 8.95 (br. s, D_2O exchangeable, 2H, NH_2); MS: (*m/z*, %) 295 (M^++1, 36.4), 294 (M^+, 45), 159 (100), 136 (65), 116 (33), 77 (43). Calc. for $C_{14}H_{10}N_6O_2$: C, 57.14; H, 3.43; N, 28.56. Found: C, 57.02; H, 3.28; N, 28.66 %.

4-Amino-3-(3-methylbenzofuran-2-ylcarbonyl)[1,2,4]triazino[4,3-a]benzimidazole (**12**): Yield 66%, m.p. >300 °C. IR (KBr): ν_{max}/cm^{-1} 3450, 3340 (NH_2), 1682 (C=O). ^{1}H NMR (DMSO-d_6): δ 2.56 (s, 3H, CH_3), 6.90–7.42 (m, 4H, ArH), 7.49–7.82 (m, 4H, ArH), 9.45 (br. s, D_2O exchangeable, 2H, NH_2). MS: (*m/z*, %) 344 (M^++1, 37.2), 343 (M^+, 100), 184 (46), 159 (63), 116 (47), 77 (47). Calc. for $C_{19}H_{13}N_5O_2$: C, 66.47; H, 3.82; N, 20.40. Found: C, 66.24; H, 3.56; N, 20.25 %.

*Reaction of 3-(3-methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**) with hydrazonoyl chlorides* **13a,b**

3-(3-Methylbenzofuran-2-yl)-3-oxopropanenitrile (**2**) (1.99 g, 10 mmol) was added to a sodium ethoxide solution prepared from sodium metal (0.23 g, 10 mmol) and absolute ethanol (50 ml). After stirring for 10 min, the appropriate hydrazonoyl chloride **13a** or **13b** (10 mmol) was added and the stirring was continued, at room temperature, for 12h. The solid product was collected by filtration, washed with water, dried and finally recrystallised from ethanol to afford the corresponding pyrazole derivatives **14a,b**.

3-Acetyl-5-(3-methylbenzofuran-2-yl)-1-phenylpyrazole-4-carbonitrile (**14a**): Yield 72%, m.p. 120–122 °C. IR (KBr): ν_{max}/cm^{-1} 2230 (C≡N), 1697 (C=O). ^{1}H NMR (DMSO-d_6): δ 2.21 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 7.19–7.57 (m, 5H, ArH), 7.63–7.85 (m, 4H, ArH). MS: (*m/z*, %) 342 (M^++1, 16), 341 (M^+, 73), 195 (100), 105 (47), 77 (62). Calc. for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.3. Found: C, 74.05; H, 4.52; N, 12.18 %.

3-(Ethoxycarbonyl)-5-(3-methylbenzofuran-2-yl)-1-phenylpyrazole-4-carbonitrile (**14b**): Yield 75%, m.p. 138–140 °C. IR (KBr): ν_{max}/cm^{-1} 2237 (C≡N), 1713 (C=O). ^{1}H NMR (DMSO-d_6): δ 1.35 (t, 3H, CH_3), 2.59 (s, 3H, CH_3), 4.29 (q, 2H, CH_2), 7.26–7.55 (m, 5H, ArH), 7.61–7.81 (m, 4H, ArH); MS: (*m/z*, %) 372 (M^++1, 22.3), 371

(M^+, 100), 299 (41.1), 195 (17.7), 77 (54.4). Calc. for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.61; N, 11.31. Found: C, 70.86; H, 4.53; N, 11.17 %.

Reaction of **14a,b** *with hydrazine hydrate*

To compound **14a** or **14b** (2 mmol) in ethanol (10 ml) was added hydrazine hydrate (1 ml, 99%) and then the reaction mixture was heated for 8h. The precipitated product was filtered off, washed with ethanol, dried and finally crystallised from EtOH/DMF to afford the corresponding pyrazolo[3,4-d]pyridazine derivatives **15a** and **15b**, respectively.

4-Amino-7-methyl-3-(3-methylbenzofuran-2-yl)-2-phenyl-pyrazolo[3,4-d]pyridazine (**15a**): Yield 86%, m.p. 230–232 °C. IR (KBr): ν_{max}/cm^{-1} 3458, 3337 (NH_2). ^1H NMR (DMSO-d_6) δ 2.45 (s, 3H, CH_3), 2.53 (s, 3H, CH_3), 7.25–7.53 (m, 5H, ArH), 7.59–8.05 (m, 4H, ArH), 9.32 (s, D_2O exchangeable, 2H, NH_2). MS: (*m/z*, %) 356 (M^++1, 19.8), 355 (M^+, 100),131 (19.8), 116 (46.1), 77 (28.4). Calc. for $C_{21}H_{17}N_5O$: C, 70.97; H, 4.82; N, 19.71. Found: C, 71.08; H, 4.66; N, 19.60 %.

4-Amino-3-(3-methylbenzofuran-2-yl)-2-phenyl-7-oxo-6H-pyrazolo[3,4-d]pyridazine (**15b**): Yield 78%, m.p. 240–242 °C. IR (KBr): ν_{max}/cm^{-1} 3473, 3402, 3325 (NH, NH_2), 1667 (C=O). ^1H NMR (DMSO-d_6): δ 2.57 (s, 3H, CH_3), 7.23–7.57 (m, 5H, ArH), 7.63–7.88 (m, 4H, ArH), 9.32 (s, D_2O exchangeable, 2H, NH_2), 12.87 (s, D_2O exchangeable, 1H, NH). MS: (*m/z*, %) 358 (M^++1, 8.6), 357 (M^+, 100), 131 (43) 116 (31), 77 (22). Calc. for $C_{20}H_{15}N_5O_2$: C, 67.22; H, 4.23; N, 19.60. Found: C, 67.01; H, 4.37; N, 19.46 %.

Received 17 September 2004; accepted 14 March 2005
Paper 04/2771

References

1 J.A. Walker, K. Rossen, R.A. Reamer, R.P. Volante and P.J. Reider, *Tetrahedron Lett.* 1999, **40,** 4917.
2 A.G. Gonzalez, J.B. Barrera, A.C. Yanes, J.G. Diaz and E.M. Rodriguez, *Phytochemistry,* 1989, **28***,* 2520.
3 C.F. Carvalho and M. V. Sargent, *J. Chem. Soc., Perkin Trans. I,* 1984, 1605.
4 J.W. Ellingboe, T.R. Alessi, T.M. Dolak, T.T. Nguyen, J.D. Tomer, F. Guzzo, J.F. Bagli and M.L. McCaleb, *J. Med. Chem.* 1992**, 35**, 1176.
5 L. Pieters, S.V. Dyck, M. Gao, R. Bai, E. Hamel, A. Vlietinck and G. Lemiere, *J. Med. Chem.* 1999, **42,** 5475.
6 S.K. Wang and C.Y. Duh, *Planta Med.* 2001, **67***,* 555.
7 A.H. Banskota, Y. Tezuka, K. Midorikawa, K. Matsushige and S. Kadota, *J. Nat. Prod.* 2000, **63,** 1277.
8 F. Messina, M. Botta, F. Corelli and A. Paladino, *Tetrahedron Asymm.* 2000, **11**, 4895.
9 T.K. Vinh, M. Ahmadi, P.O.L. Delgado, S.F. Perez, H.M. Walters, H.J. Smith, P.J. Nicholls and C. Simons, *Bioorg. Med. Chem. Lett.* 1999, **9,** 2105.
10 W.R. Boehme, *Org. Synth.* 1963, **5**, 590.
11 A.M. Farag, K.M. Dawood and H.A. Elmenoufy, *Heteroatom Chem.,* 2004, **15**, 508.
12 K.M. Dawood, *Heteroatom Chem.,* 2004, **15**, 432.
13 K.M. Dawood, E.A. Ragab and A.M. Farag, *J. Chem. Res.* 2003*, (S),* 685 *(M),* 1151.
14 K.M. Dawood, M.A. Raslan and A.M. Farag, *Synth. Commun*. 2003*,* **33**, 4095.
15 A.M. Farag, K.M. Dawood and Z.E. Kandeel, *Tetrahedron,* 1997, **53***,* 161.
16 A.M. Farag, K.M. Dawood and Z.E. Kandeel, *Tetrahedron,* 1996, **52***,* 7893.
17 R.A.B. Copeland and A.R. Day, *J. Am. Chem. Soc.* 1943, **65,** 1072.
18 M.H. Elnagdy, M.R.H. Elmoghayar, D.H. Fleita, E.A.A. Hafez and S.M. Fahmy, *J. Org. Chem.* 1976, **41**, 3781.
19 A.M. Farag, *J. Chem. Res.* (*S*), 1995, 96.
20 R.N. Butler, *Chem. Rev.* 1975, **75**, 241.
21 W. Dieckmann and O. Platz, *Chem. Ber.* 1906**, 38**, 2989.
22 F. Hegarty, M.P. Cashoman and F.L. Scott, *Chem. Commun.,* 1971**, 13**, 884.