Multi Component Reactions under Increased Pressure: On the Mechanism of Formation of Pyridazino[5,4,3-de][1,6]naphthyridine Derivatives from Reaction of Malononitrile, Aldehyde and 2-Oxoglyoxalarylhydrazones in Q-Tubes

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Abstract: The considerable biological and medicinal activities of pyridazines has stimulated considerable research on efficient syntheses of these derivatives. In the last decade, microwave irradiation has generally been used for the energy source. As demonstrated in recent studies, pressure reactor “Q-tubes” may be used to accelerate several of these reactions in a more optimal and safer manner (compared to microwaves). In these studies there has been postulated a pathway for the formation of pyridazino[5,4,3-de][1,6]naphthyridine derivatives. In this paper we consider this pathway, and an alternate pathway, for several reactions. Contrary to the suggestion in these studies the pathway in which initial dimerization of malononitrile was postulated could be excluded based on chemical evidence. The reactions performed were the reaction of arylhydrazonals 1a,b with benzylidinemalononitrile which afforded in Q-tube the 3-acyl-4-aryl-1-phenyl-6-amino-1,4-dihydropyridazines, and the reaction of arylhydrazonals 1a,b, malononitrile 9 and aromatic aldehydes 10a-g in Q-tubes which afforded the tricyclic systems 12a-n whose structure could be established by X-ray crystal structure determination. In conclusion, we have added to the work of the recent studies by excluding a reaction pathway for one of their reaction products.

Keywords: X-ray; arylhydrazones; 2-amino-1,1,3-propenetricarbonitrile; pyridazines; rate enhancement under pressure

1. Introduction

The considerable biological and medicinal activities of pyridazines stimulated considerable research on efficient syntheses of these derivatives in past years [1-4]. Some time ago we reported synthesis of 2-amino-1,4-dihydropyridazine, isoelectronic derivative of 1,4-dihydropyrimidines of established biological activities [5-8], via 3+3 atom combination of 1a and 2 [9] (Scheme 1). Subsequent studies [10,11] however on this novel route revealed that it is of limited scope as reaction product proved dependent on the nature of reacting the aryl group in the aldehyde hydrazones and the sole product from reaction of aldehyde hydrazones 1a-c with α,β-functionally substituted cinnaminitriles. In recent article Abdelhamid et al. [12] have reported that the reaction of arylhydrazone 1f with α,β-unsaturated nitriles 2 form pyrazolo[4',3'-5,6]pyrimido[2,1-a]phthalazine-9-carbonitrile derivative 7, rather than the expected product 6 (Scheme 1).
Scheme 1: The reactivity of aryl hydrazones 1 towards α,β-functionally substituted cinnaminitriles.

We in the last decades have generally utilized microwaves irradiations as energy source [13-16]. However, we noted that microwaves technology is expensive to scale up [17]. The technique that renders the organic reaction under pressure, can be easily scaled up utilizing presser reactor “Q-tubes” to accelerate several reactions in a more optimal and safer manner, compared to Microwaves [18].

We reported on the efficient synthesis of benzo[c]chromen-6-one and phenanthridin-6(5H)-one derivatives in a four-component reaction in Q-Tube [19].

Recently, Moustafa et al. have developed a novel synthesis of tricyclic system 11 via reacting ethyl-3-oxo-2-(2-phenylhydrazono) pentanoate 8a with malononitrile 9 and aromatic aldehyde derivatives 10 in Q-Tube [20] (Scheme 2). Very recently Sadek and Elnagdi [21] reported the formation of 12 upon reacting arylhydrazonal with malononitrile and aromatic aldehydes in Q-tube but evidence for proposed structure looked debatable. In the present article, we report on the multicomponent reaction of aldehyde hydrazone 1, aromatic aldehydes and malononitrile, where we observed that under pressure in a Q-tube the reaction products different than those conducted by conventional heating as a result of apparent volume effect on the first step transition state of this multicomponent reaction (Scheme 2).
Scheme 2: novel synthesis of tricyclic system 11 via reacting ethyl-3-oxo-2-(2-phenylhydrazono) pentanoate 8a with malononitrile 9 and aromatic aldehyde derivatives 10 in Q-Tube

2. Results

Reacting 1a with 2a in Q-tube afforded 3. Compound 3 has also been obtained earlier by Elnagdi et al [9]. However reaction of 2-oxo-2-arylhydrazonals 1a,b with aromatic aldehydes 10a-g and malononitrile 9 afforded in dioxane in presence of piperidine in Q-Tube (cf. Fig.1) at 150 °C and 20 psi, the tricyclic system 12 is formed in 72%-85 % yield (Scheme 3, Table 1).

Scheme 3 A new reaction path for aldehyde hydrazone with malononitril and aldehydes.

Table 1: Synthesis of pyridazino[5,4,3-de][1,6]naphthyridine derivatives 12a-n.

<table>
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<tr>
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<tr>
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Fig. 1: X-ray crystallography of compound 12a [22].

Fig. 2: X-ray crystallography of compound 12m [23].
Fig. 3: X-ray crystallography of compound 12n [24].

The structure of the reaction products could be established to be pyridazino[5,4,3-de][1,6]naphthyridine derivatives 12a-n via X-ray crystal structure determination of products 12a, 12m and 12n (Fig. 1-3).

3. Discussion

Two mechanistic pathways seem possible (Scheme 4). Initial dimerization of malononitrile to yield 13 dimer, that then condense with the acyl carbonyl yielding 14 that cyclize to form 15 (rout A), as has been suggested by Moustafa et al. [20] could be readily eliminated. As in our hand arylhydrazonals 1a, b did not condense with malononitrile dimer 13 under a variety of rustic conditions.

Moustafa et al. [20] also reported that the dimer 13 alone reacts with their arylhydrazone 1a,b yielding pyridazino[5,4,3-de][1,6]naphthyridine derivatives, not condensed with pyridazine derivatives. Thus, it is almost certain that the initial step leading to formation of 12 is the condensation of malononitrile 9 with acyl carbonyl 18. The product 19 can then either cyclize into 20 then 21 (rout C) or condense aromatic aldehyde to give 22 then 23(rout D), neither rout (C, D) can be completely ruled out. Although we believe that aromatic aldehyde condenses initially with 19 then subsequent reaction leading to 22 and then react with malononitrile 9 to form 23 which cyclize to the final product 12 that taking place in rout D (Scheme 4).
Scheme 4: A suggested mechanism for the formation of pyridazino[5,4,3-de][1,6]naphthyridine derivatives 12a-n.

4. Experimental Section

4.1 General

Q-tube assisted reactions were performed in a Q-tube safe pressure reactor from Q Labtech, equipped with a cap/sleeve, pressure adapter (120 psi), needle adapter/needle, borosilicate glass tube, Teflon septum, and catch bottle. All reactions were monitored by using TLC with 1:1 ethyl acetate-petroleum ether as eluent and were carried out until starting materials were completely consumed. Melting points are reported uncorrected and were determined with a Sanyo (Gallaenkamp) instrument. Infrared spectra were recorded using KBr pellets and a Jasco FT–IR 6300 instrument and
absorption bands are reported in cm⁻¹. ¹H- and ¹³C-NMR spectra were determined by using a Bruker DPX instrument at 400 MHz or 600 MHz for ¹H-NMR and 100 MHz for ¹³C-NMR and either CDCl₃ or DMSO-d₆ solutions with TMS as internal standards. Chemical shifts are reported in ppm. Mass spectra and accurate mass measurements were made using a GCMS DFS Thermo spectrometer with the EI (70 EV) mode. X-ray crystallographic structure determinations were performed by using Rigaku Rapid II and Bruker X8 Prospector single crystal X-ray Diffractometers. All X-ray crystal structure data can be obtained free of charge from the Cambridge Crystallographic Data Centre [21-24] via www.ccdc.cam.ac.uk.

4.2 General Procedures for Q-Tube-Assisted Synthesis of 12a-n

2-oxo-2-arylhydrazonals (1a,b) (0.01 mol), aromatic aldehydes (13a-g) (0.01 mol) and malononitrile (14) (0.02 mol) in presence of piperidine (1 mL) and dioxin (20 mL) as solvent were sequentially added in a 35 mL Q-tube pressure tube, furnished by Q Labtech. A Teflon septum was placed on the top of the tube, and an appropriate cap was used. The mixture was heated in an oil bath at 150 °C. After about 60 min, the reaction mixture was monitored by TLC. The mixture was cooled and poured into ice-water. The solid was collected by filtration and purified by column chromatography utilizing appropriate suitable solvents mixture to give crystals of compounds 12a-n.

8-Amino-1,5-diphenyl-1H-pyridazino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12a)

Dark yellow crystals, Yield 75%; mp. 314-315 ºC; Anal. Calcd for C₂₃H₁₈N₆ (396.06): C, 66.59; H, 3.30; N, 21.8. Found: C, 66.70; H, 3.35; N, 21.20. EI-HRMS: m/z = 396.08 (MH⁺); C₂₃H₁₈N₆ requires: m/z = 396.08 (MH⁺); δ = 162.1, 160.0, 154.6, 151.0, 141.7, 138.7, 136.7, 133.4, 130.3, 129.1 (2C), 128.9 (2C), 128.2, 126.6 (2C), 124.6 (2C), 118.0, 109.1, 104.6, 56.0. MS: m/z (%) 396.1 (M⁺, 100), 368 (10), 198 (10), 166 (5), 77 (5).

8-amino-5-(4-chlorophenyl)-1-phenyl-1H-pyridazino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12b)

Green crystals, yield 75%; mp. 340-341 ºC; Anal. Calcd for C₂₃H₁₆ClN₆ (376.14): C, 73.39; H, 3.79; N, 22.33. Found: C, 73.34; H, 4.30; N, 22.28. EI-HRMS: m/z = 376.14 (MH⁺); C₂₃H₁₆ClN₆ requires: m/z = 376.14 (MH⁺); δ = 162.2, 160.0, 154.6, 151.1, 141.7, 138.8, 138.5, 132.4, 131.4, 130.6, 129.9 (2C), 128.8, 128.2, 127.4 (2C), 126.4 (2C), 116.8, 108.9, 108.8, 73.1. MS: m/z (%) 376.1 (M⁺, 100), 361 (15), 334 (5), 198 (10), 166 (5), 77 (5).

8-amino-5-(3-chlorophenyl)-1-phenyl-1H-pyridazino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12c)

Faint green crystals, yield 77%; mp. 340-341 ºC; Anal. Calcd for C₂₃H₁₆N₆ (376.14): C, 73.39; H, 4.28; N, 22.33. Found: C, 73.34; H, 4.30; N, 22.28. EI-HRMS: m/z = 376.14 (MH⁺); C₂₃H₁₆N₆ requires: m/z = 376.14 (MH⁺); δ = 162.3, 160.0, 154.6, 151.1, 141.7, 138.8, 138.5, 132.4, 131.4, 130.6, 129.9 (2C), 128.8, 128.2, 127.4 (2C), 126.4 (2C), 116.8, 108.9, 108.8, 73.1. MS: m/z (%) 376.1 (M⁺, 100), 361 (15), 334 (5), 198 (10), 166 (5), 77 (5).

8-amino-1-phenyl-5-p-tolyl-1H-pyridazino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12d)

Faint green crystals, yield 77%; mp. 340-341 ºC; Anal. Calcd for C₂₃H₁₆N₆ (376.14): C, 73.39; H, 4.28; N, 22.33. Found: C, 73.34; H, 4.30; N, 22.28. EI-HRMS: m/z = 376.14 (MH⁺); C₂₃H₁₆N₆ requires: m/z = 376.14 (MH⁺); δ = 162.3, 160.0, 154.6, 151.1, 141.7, 138.8, 138.5, 132.4, 131.4, 130.6, 129.9 (2C), 128.8, 128.2, 127.4 (2C), 126.4 (2C), 116.8, 108.9, 108.8, 73.1. MS: m/z (%) 376.1 (M⁺, 100), 361 (15), 334 (5), 198 (10), 166 (5), 77 (5).
8-amino-1-phenyl-5-m-tolyl-1H-pyrazidino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12e)

Green crystals, yield 73%; mp. 280-281 °C; Anal. Calcd for C_{23}H_{16}N_{6} (376.14): C, 73.39; H, 4.28; N, 22.33. Found: C, 73.38; H, 4.27; N, 22.31. EI-HRMS: m/z = 376.14 (M+); C_{23}H_{16}N_{6} requires: m/z = 376.14 (M+); IR: 3450, 3338 (NH_{2}), 2197 (CN); ^1H NMR (400 MHz, DMSO-d_6): δ = 2.43 (s, 3H, CH_{3}), 7.07 (br, 2H, NH_{2}, D_{2}O exchangeable), 7.18 (s, 1H, CH), 7.34-7.66 (m, 9H, Ph-H, CH), 8.40 (s, 1H, CH); ^13C NMR (100 MHz, DMSO-d_6): δ = 162.2, 161.2, 154.4, 150.9, 141.7, 140.2, 138.8, 135.1, 133.2, 129.4 (2C), 128.8 (2C), 128.1, 127.1 (2C), 126.3 (2C), 116.9, 108.7, 104.2, 73.3, 20.9. MS: m/z (%) 376.2 (M^+, 100), 348 (10), 188 (10), 77 (5).

8-amino-5-(4-nitrophenyl)-1-phenyl-1H-pyrazidino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12f)

Dark brown crystals, yield 82%; mp. 397-398 °C; Anal. Calcd for C_{23}H_{16}ClN_{6} (410.1): C, 64.86; H, 3.22; N, 24.07. Found: C, 64.75; H, 3.10; N, 24.12. EI-HRMS: m/z = 407.11 (M+); C_{23}H_{16}ClO_{7}N_{6} requires: m/z = 407.11 (M+); IR: 3433, 3334 (NH_{2}), 2199 (CN); ^1H NMR (400 MHz, DMSO-d_6): δ = 7.18 (br, 2H, NH_{2}, D_{2}O exchangeable), 7.48-8.48 (m, 10H, Ph-H, CH), 9.20 (s, 1H, CH). MS: m/z (%) 407.2 (M^+, 100), 361 (20), 334 (10), 180 (10), 77 (5).

8-amino-5-(furan-2-yl)-1-phenyl-1H-pyrazidino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12g)

Green crystals, yield 73%; mp. 345-346 °C; Anal. Calcd for C_{23}H_{16}N_{6} (352.11): C, 68.18; H, 3.43; N, 23.85. Found: C, 68.21; H, 3.52; N, 23.77. EI-HRMS: m/z = 352.10 (M+); C_{23}H_{16}O_{7}N_{6} requires: m/z = 352.11 (M+); IR: 3460, 3329 (NH_{2}), 2203 (CN); ^1H NMR (400 MHz, DMSO-d_6): δ = 6.74-6.75 (m, 1H, furayl-H), 7.05 (br, 2H, NH_{2}, D_{2}O exchangeable), 7.24-7.97 (m, 8H, Ph-H, furyl-H, CH), 8.42 (s, 1H, CH); ^13C NMR (100 MHz, DMSO-d_6): δ = 154.6, 153.2, 152.7, 150.8, 145.6, 141.7, 138.6, 133.2, 128.2 (2C), 128.2, 126.3 (2C), 116.8, 112.7, 11.8, 108.6, 102.7, 73.0. MS: m/z (%) 352.1 (M^+, 100), 324 (5), 176 (10), 77 (5).

8-amino-4-methyl-1,5-diphenyl-1H-pyrazidino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12h)

Yellow crystals, yield 83%; mp. 364-365 °C; Anal. Calcd for C_{23}H_{16}N_{6} (376.14): C, 73.39; H, 4.28; N, 22.33. Found: C, 73.35; H, 4.15; N, 22.41. EI-HRMS: m/z = 376.14 (M+); C_{23}H_{16}N_{6} requires: m/z = 376.14 (M+); IR: 3482, 3341 (NH_{2}), 2198 (CN); ^1H NMR (400 MHz, DMSO-d_6): δ = 2.34 (s, 3H, CH_{3}), 6.95 (br, 2H, NH_{2}, D_{2}O exchangeable), 7.45-7.66 (m, 10H, Ph-H, CH), 8.56 (s, 1H, CH); ^13C NMR (100 MHz, DMSO-d_6): δ = 164.5, 161.6, 152.3, 150.6, 141.8, 140.0, 136.9, 131.0, 129.0 (2C), 128.8 (2C), 128.5, 128.2, 128.0 (2C), 126.3 (2C), 117.1, 114.1, 108.9, 72.6, 13.9. MS: m/z (%) 376.2 (M^+, 100), 368 (10), 348 (5), 255 (5), 188 (10), 97 (10), 57 (5).

8-amino-5-(4-chlorophenyl)-4-methyl-1-phenyl-1H-pyrazidino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12i)

Dark yellow crystals, yield 78%; mp. 345-346 °C; Anal. Calcd for C_{23}H_{16}ClN_{6} (410.1): C, 67.24; H, 3.68; N, 20.45. Found: C, 67.27; H, 3.56; N, 20.45. EI-HRMS: m/z = 410.10 (M+); C_{23}H_{16}ClN_{6} requires: m/z = 410.1 (M+); IR: 3479, 3329 (NH_{2}), 2201 (CN); ^1H NMR (400 MHz, DMSO-d_6): δ = 2.35 (s, 3H, CH_{3}), 6.90 (br, 2H, NH_{2}, D_{2}O exchangeable), 7.45-7.66 (m, 9H, Ph-H, CH), 8.58 (s, 1H, CH); ^13C NMR (100 MHz, DMSO-d_6): δ = 163.8, 162.1, 156.4, 151.1, 142.3, 139.4, 137.3, 134.0, 132.5, 131.7, 131.3 (2C), 129.3 (2C), 128.6 (2C), 126.7 (2C), 117.2, 114.8, 109.7, 73.5, 14.3. MS: m/z (%) 410.1 (M^+, 100), 374 (10), 346 (5), 255 (5), 205 (5), 187 (10), 173 (5), 97 (5), 77 (5).
8-amino-4-methyl-1-phenyl-5-p-tolyl-1H-pyridazino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12k)

Dark orange crystals, Yield 80%; mp. 370-371 ºC; Anal. Calcd for C_{24}H_{18}N_{6} (390.16): C, 73.83; H, 4.65; N, 21.52. Found: C, 73.88; H, 4.59; N, 21.60. EI-HRMS: m/z = 390.15 (MH+); C_{24}H_{18}N_{6} requires: m/z = 390.16 (MH+); IR: 3426, 3320 (NH2), 2206 (CN); 1H NMR (400 MHz, DMSO-d6): δ = 2.36 (s, 3H, CH3), 2.41 (s, 3H, CH3), 6.93 (br, 2H, NH2, D2O exchangeable), 7.34-7.67 (m, 9H, Ph-H, CH), 8.56 (s, 1H, CH); 13C NMR (100 MHz, DMSO-d6): δ = 163.9, 161.6, 152.4, 150.7, 141.8, 140.2, 137.2, 129.0 (2C), 128.8 (2C), 128.6 (2C), 127.1, 126.3 (2C), 129.1, 124.5, 119.1, 114.8, 109.7, 72.6, 20.8, 14.0. MS: m/z (%) 390.2 (M+, 100), 375 (5), 269 (5), 187 (5), 72.6, 20.8, 14.0. MS: m/z (%) 390.2 (M+, 100), 375 (5), 269 (5), 187 (5), 72.6, 20.8, 14.0.

8-amino-4-methyl-1-phenyl-5-m-tolyl-1H-pyridazino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12l)

Yellow crystals, yield 72%; mp. 284-285 ºC; Anal. Calcd for C_{24}H_{18}N_{6} (390.16): C, 73.83; H, 4.65; N, 21.52. Found: C, 73.81; H, 4.68; N, 21.55. EI-HRMS: m/z = 390.15 (MH+); C_{24}H_{18}N_{6} requires: m/z = 390.16 (MH+); IR: 3489, 3336 (NH2), 2200 (CN); 1H NMR (400 MHz, DMSO-d6): δ = 2.08 (s, 3H, CH3), 2.11 (s, 3H, CH3), 6.96 (br, 2H, NH2, D2O exchangeable), 7.19-7.66 (m, 9H, Ph-H, CH), 8.53 (s, 1H, CH); 13C NMR (100 MHz, DMSO-d6): δ = 165.5, 161.5, 152.4, 150.7, 141.8, 139.8, 136.9, 134.8, 130.6, 130.0, 128.9 (2C), 128.2 (2C), 126.3 (2C), 125.6 (2C), 117.1, 114.7, 109.0, 72.6, 19.0, 13.0. MS: m/z (%) 390.2 (M+, 50), 375 (100), 346 (5), 255 (5), 195 (5), 187 (15), 173 (10), 129 (5), 77 (5).

8-amino-4-methyl-5-(4-nitrophenyl)-1-phenyl-1H-pyridazino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12m)

Dark yellow crystals, yield 82%; mp. 368-369 ºC; Anal. Calcd for C_{23}H_{15}N_{7}O_{2} (421.13): C, 65.55; H, 3.59; N, 23.27. Found: C, 65.59; H, 3.63; N, 23.31. EI-HRMS: m/z = 421.15 (MH+); C_{23}H_{15}O_{2}N_{7} requires: m/z = 421.15 (MH+); IR: 3464, 3350 (NH2), 2198 (CN); 1H NMR (400 MHz, DMSO-d6): δ = 2.37 (s, 3H, CH3), 6.82 (br, 2H, NH2, D2O exchangeable), 7.47-8.38 (m, 9H, Ph-H, CH), 8.58 (s, 1H, CH). MS: m/z (%) 421.2 (M+, 100), 390 (15), 374 (25), 348 (10), 255 (5), 187 (10), 77 (5).

8-amino-5-(furan-2-yl)-4-methyl-1-phenyl-1H-pyridazino[5,4,3-de][1,6]naphthyridine-7-carbonitrile (12n)

Dark green crystals, yield 86%; mp. 368-369 ºC; Anal. Calcd for C_{21}H_{14}N_{6}O (366.12): C, 68.84; H, 3.85; N, 22.94. Found: C, 68.89; H, 3.78; N, 22.88. EI-HRMS: m/z = 366.12 (MH+); C_{21}H_{14}O_{1}N_{6} requires: m/z = 366.12 (MH+); IR: 3470, 3330 (NH2), 2203 (CN); 1H NMR (400 MHz, DMSO-d6): δ = 2.50 (s, 3H, CH3), 6.72-6.73 (m, 1H, furyl-H), 6.91 (br, 2H, NH2, D2O exchangeable), 7.47-8.38 (m, 9H, Ph-H, CH), 8.58 (s, 1H, CH). MS: m/z (%) 366.1 (M+, 100), 337 (5), 311 (5), 183 (5), 77 (10).

5. Conclusions

Under pressure MCRs change their sequence and initial steps change sequence as a result of preference of formation of products of least activation volume. Reactions under pressure can be more easily and much less expensively scaled up on it is thus recommend to expand this technique.

Ethics approval and consent to participate

The authors approve the ethics and consent to participate

Consent for publication

The authors approve publication.

Availability of data and material

The data and material are available in the Supplementary material and manuscript. Supplementary material is attached as PDF format and submitted along with the manuscript.

Competing interests
The authors declare that they have no competing interests.

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Authors’ contributions
The main part of the work was carried out by Majdah A. AL-Johani and Sameera M. Mousally, with the direct supervision of Khadijah M. Al-Zaydi and Norah F. Alqahtani. Conceptually the work was designed by Mohamed H. Elnagdi, Khadijah M. Al-Zaydi and Norah F. Alqahtani. All authors read and approved the final manuscript.

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References


22. A single crystal of compound 12a was obtained by slow evaporation from a mixture of ethanol:DMF (2:1). The crystal structure was solved and refined using maxus (nonius, Deflt and MacScience, Japan). Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1434604 Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union, Road, Cambridge CB2 1EZ, UK. [fax: 144 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

23. A single crystal of compound 12m was obtained by slow evaporation from a mixture of ethanol:DMF (2:1). The crystal structure was solved and refined using maxus (nonius, Deflt and MacScience, Japan). Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as...
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24. A single crystal of compound 12n was obtained by slow evaporation from a mixture of ethanol:DMF (2:1). The crystal structure was solved and refined using maxus (nonius, Delft and MacScience, Japan). Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1493165 Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union, Road, Cambridge CB2 1EZ, UK. [Fax: 144 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].