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Utility of 2-cyano-3-phenyl-2-propenoyl chloride as Michael's acceptor in heterocyclic synthesis with mono- and bi-dentate nucleophiles

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ABSTRACT

(*E*) 2-Cyano-3-phenyl-2-propenoyl chloride reacts with nitrogen, oxygen and sulphur mono- and bi-dentate nucleophilic reagents to give the amide derivatives, the ester derivatives, as well as some heterocyclic systems, namely quinazolinone, pyridopyrimidine and benzothiazepine. Cyclization of some obtained amides affords the benzoxazinones, quinazolinone, whereas that of other amides yields oxadiazole and benzoxazole, respectively.

1. Introduction

The recent pharmaceutical applications of 2-propenoyl amides [1], 2-propenoates [2,3], and other heterocyclic skeletons, like benzoxazinones [4,5], quinazolinones [6], benzoxazoles [7-9], oxadiazoles [10] have stimulated the authors to synthesize new derivatives of these classes of compounds hoping to obtain structures with possibly enhanced potency.

In continuation of our ongoing program in the synthesis of biologically active heterocyclic systems from simple readily obtainable materials [11-21], the present work investigates the reactivity of high functionality 2-cyano-3-phenyl-2-propenoyl chloride [22] (**1**) with different mono- and bi-dentate nucleophiles aiming to obtain new derivatives with anticipated biological activities.

2. Experimental

Melting points reported have been measured on a Stuart Scientific melting point apparatus and are uncorrected. The IR spectra were recorded on Pye Unicam SP 1200 spectrophotometer using KBr wafer technique. ^{1}H NMR spectra were determined on a Varian FT-200, and a Bruker AC-200 MHz spectrometer using TMS as internal standard. All chemical shifts (δ) are expressed in ppm. All the NH or OH protons disappeared on addition of D_2O. The mass spectra were determined using MP model MS-5988 and Shimadzu single focusing mass spectrophotometer (70 eV). Compound **1** has been synthesized according to Jaafar *et al.* method [22]. The conduction time of all reactions and the purity of the products were monitored using thin-layer chromatography (TLC) technique.

2.1. N-[2-Cyano-3-phenyl-2-propenoyl]benzylamine (2)

To a solution of propenoyl chloride (**1**) (1.9 g; 10 mmol) in dry benzene (30 mL) in presence of triethylamine (1.38 mL; 10 mmol), benzylamine (1.08 mL; 10 mmol) was added and the reaction mixture was stirred at room temperature for an hour. The solid formed was collected, washed with water several times, dried and crystallized from benzene to yield **2** as colourless crystals (Scheme 1). Yield: 60%. M.p.: 135-137 °C. FT-IR (KBr, cm^{-1}): 3337 ν(NH), 2220 ν(CN), 1663 ν(C=O) (amide). ^{1}H NMR (300 MHz, DMSO-d_6): 4.44 (d, 2H, *J* = 20 Hz, C*H*$_2$-NH), 7.24-7.95 (m, 10H, Ar-*H*), 8.21 (s, 1H, =C*H*), 8.97 (t, 1H, *J* = 20 Hz, N*H*-CH$_2$). MS (EI, m/z): 262 (M$^{\cdot+}$). Anal. Calcd. for $C_{17}H_{14}N_2O$: C, 77.86; H, 5.34; N, 10.68. Found: C, 77.54; H, 5.66; N, 10.29%.

2.2. N-(4-methoxyphenyl)2-cyano-3-phenyl-2-propenoyl amide (3)

To a solution of **1** (1.9 g; 10 mmol) in dry benzene (30 mL) in presence of triethylamine (1.38 mL; 10 mmol), *p*-anisidine (1.22 g; 10 mmol) was added. The reaction mixture was stirred at room temperature for an hour. The semisolid produced was collected, washed with water several times, and then triturated with methyl alcohol. The solid separated was collected, dried and crystallized from methanol to give **3** as yellow crystals (Scheme 1). Yield: 60%. M.p.: 155-157 °C. FT-IR (KBr, cm^{-1}): 3312 ν(NH), 2220 ν(CN), 1676 ν(C=O) (amide).

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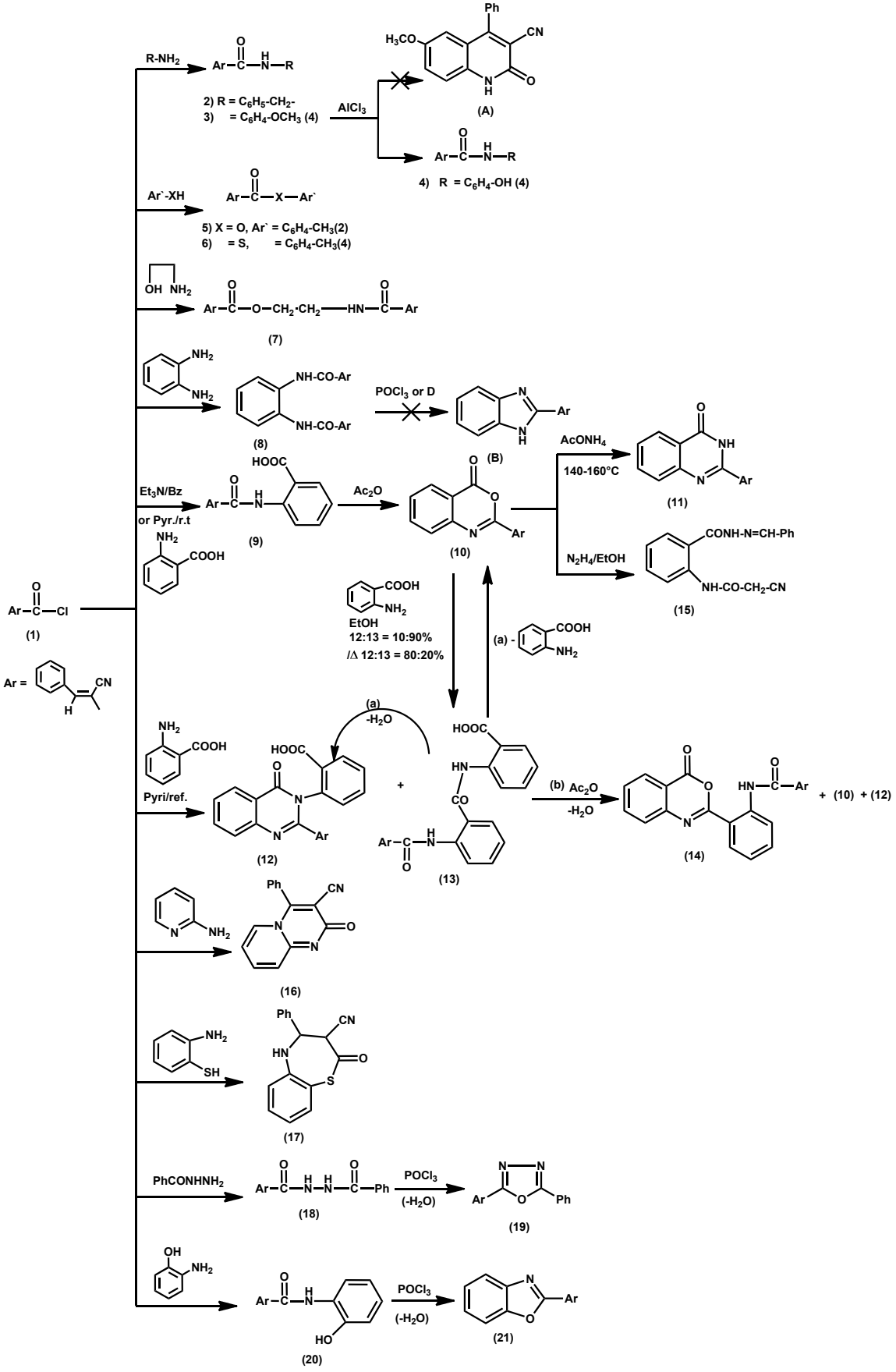


Scheme 1

^{1}H NMR (300 MHz, DMSO-d_6): 3.75 (s, 3H, OC*H*$_3$), 6.91-7.94 (m, 9 H, Ar-*H*), 8.25 (s, 1H, =C*H*), 10.25 (s, 1H, N*H*). MS (EI, m/z): 278(M$^{\cdot+}$). Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.38; H, 5.03; N, 10.07. Found: C, 73.11; H, 5.41; N, 10.32%.

2.3. N-(4-hydroxyphenyl) 2-cyano-3-phenyl-2-propenoyl amide (4)

A mixture of **3** (1.4 g, 5 mmol) and anhydrous aluminium chloride (1.33 g, 10 mmol) in dry benzene or chlorobenzene (50 mL) was stirred at room temperature for three hours, then refluxed for 24 hours and left overnight. The reaction mixture was poured onto cold dilute HCl. The organic solvent was removed by steam distillation and the residue was extracted by diethyl ether (3 x 50 mL), and then dried over anhydrous $MgSO_4$. The diethyl ether was removed by distillation and the residue was crystallized from methanol to give **4** as green crystals (Scheme 1). Yield: 90-95%. M.p.: 195-196 ^{o}C. FT-IR (KBr, cm^{-1}): 3338, 3258 ν(NH), 2222 ν(CN), 1653 ν(C=O) (amide). ^{1}H NMR (300 MHz, DMSO-d_6): 6.75-7.96 (m, 9 H, Ar-*H*), 8.22 (s, 1H, =C*H*), 9.36 (s, 1H, N*H*), 10.14 (s, 1H, O*H*). MS (EI, m/z): 264 (M$^+$). Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.54; N, 10.61. Found: C, 73.00; H, 4.42; N, 10.31%.

2.4. General procedure to synthesize compounds 5, 6, 7, 8, 9, 17, 18 and 20

To a solution of propenoyl chloride (**1**) (1.9 g; 10 mmol) in dry benzene (30 mL) containing triethylamine (1.38 mL; 10 mmol), *o*-cresol, *p*-thiocresol, ethanolamine, *o*-phenylene diamine, anthranilic acid, 2-aminothiophenol, benzoyl hydrazine and/or 2-aminophenol (10 mmol) was added and the reaction mixture was stirred at room temperature for 1 h. The triethylamine hydrochloride was filtered off and most of the solvent was distilled off. The solid that separated out was collected by suction and recrystallized from the appropriate solvent to afford the desired product (Scheme 1).

2-Methyphenyl 2-cyano-3-phenyl-2-propenoate (**5**): Compound **5** crystallized from benzene to give green crystals. Yield: 85%. M.p.: 101-103 ^{o}C. FT-IR (KBr, cm^{-1}): 2220 ν(CN), 1734 ν(C=O) (ester). ^{1}H NMR (300 MHz, DMSO-d_6): 2.20 (s, 3H, C*H*$_3$), 7.27-8.15 (m, 9 H, Ar-*H*), 8.64 (s, 1H, =C*H*). MS (EI, m/z): 263 (M$^{\cdot+}$). Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.56; H, 4.94; N, 5.32. Found: C, 77.24; H, 4.82; N, 5.54%.

S-4-Methyphenyl 2-cyano-3-phenyl-2-propenthioate (**6**): Compound **6** crystallized from benzene to give yellow crystals. Yield: 90%. M.p.: 110-112 ^{o}C. FT-IR (KBr, cm^{-1}): 2216 ν(CN), 1662 ν(C=O) (thioester). ^{1}H NMR (300 MHz, DMSO-d_6): 2.37 (s, 3H, C*H*$_3$), 7.32- 8.09 (m, 9 H, Ar-*H*), 8.40 (s, 1H, =C*H*). MS (EI, m/z): 279 (M$^{\cdot+}$). Anal. Calcd. for $C_{17}H_{13}NOS$: C, 73.11; H, 4.65; N, 5.01. Found: C, 73.26; H, 4.52; N, 5.28%.

2-N-(2`-Cyano-3`-phenyl-2`-propenoyl)-1-O-(2`-cyano-3`-phenyl-2`-propenoyl)ethanolamine (**7**): Compound **7** crystallized from *n*-butanol to give yellow crystals. Yield: 60%. M.p.: 212-214 ^{o}C. FT-IR (KBr, cm^{-1}): 3442 ν(NH), 2208 ν(CN), 1726 ν(C=O) (ester), 1684 ν(C=O) (amide). ^{1}H NMR (300 MHz, DMSO-d_6): 3.59 (q, 2H, C*H*$_2$-NH), 4.40 (t, 2H, C*H*$_2$-O), 7.54-8.05 (m, 10H, Ar-*H*), 8.44 (s, 1H, =C*H*), 8.70 (s, 1H, =C*H*), 8.87 (t, 1H, J = 20Hz, N*H*-CH$_2$). MS (EI, m/z (%)): 371 (M$^{\cdot+}$). Anal. Calcd. for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.58; N, 11.32. Found: C, 70.77; H, 4.33; N, 11.67%.

(2E,2'E)-N,N'-(1,2-phenylene)bis(2-cyano-3-phenylacryl amide) (**8**): Compound **8** crystallized from *n*-butanol to give yellow crystals. Yield: 62%. M.p.: 215-218 ^{o}C. FT-IR (KBr, cm^{-1}): 3298 ν(NH), 2216 ν(CN), 1672 ν(C=O) (amide). ^{1}H NMR (300 MHz, DMSO-d_6): 7.32-7.98 (m, 14 H, Ar-*H*), 8.36 (s, 2H, 2 x =C*H*), 9.92 (s, br, 2H, 2xN*H*). MS (EI, m/z): 418 (M$^{\cdot+}$). Anal. Calcd. for $C_{26}H_{18}N_4O_2$: C, 73.23; H, 4.22; N, 15.02. Found: C, 72.81; H, 4.17; N, 15.07%.

2-N-(2-Cyano-3-phenyl-2-propenoyl)aminobenzoic acid (**9**): Compound **9** crystallized from benzene/EtOH to give colourless crystals. Yield: 85%. M.p.: 248-250 ^{o}C. FT-IR (KBr, cm^{-1}): 2848, 3167 ν(NH) and ν(OH), 2208 ν(CN), 1674 ν(C=O). ^{1}H NMR (300 MHz, DMSO-d_6): 7.27-8.62 (m, 10 H, =C*H*, Ar-*H*), 11.33 (s, 1H, CO-N*H*), 12.23 (s, 1H, COO*H*). MS (EI, m/z): 292 (M$^{\cdot+}$). Anal. Calcd. for $C_{17}H_{12}N_2O_3$: C, 69.86; H, 4.11; N, 9.58. Found: C, 70.17; H, 4.01; N, 9.79%.

2-oxo-4-phenyl-2,3,4,5-tetrahydrobenzo[b][1,4]thiazepine-3-carbonitrile (**17**): Compound **17** crystallized from dioxane to give yellow crystals. Yield: 50%. M.p.: 222-224 ^{o}C. FT-IR (KBr, cm^{-1}): 3190 ν(NH), 2247 ν(CN), 1672 ν(C=O) (thiazapinone). ^{1}H NMR (300 MHz, DMSO-d_6): 4.58 (d, 1H, *J* = 22 Hz, -C*H*-CN), 5.16 (d, 1H, *J* = 7 Hz, Ph-C*H*-CH-CN), 7.22-7.69 (m, 9H, Ar-*H*), 10.52 (s, 1H, N*H*). MS (EI, m/z): 280 (M$^{\cdot+}$). Anal. Calcd. for $C_{16}H_{12}N_2OS$: C, 69.06; H, 3.59; N, 10.07. Found: C, 69.38; H, 3.40; N, 10.39%.

N`-(2-cyano-3-phenyl-2-propenoyl)benzohydrazide (**18**): Compound **18** crystallized from benzene/ethanol to give colourless crystals. Yield: 65%. M.p.: 201-203 ^{o}C. FT-IR (KBr, cm^{-1}): 3210 ν(NH), 2208 ν(CN), 1679 ν(C=O) (amide). ^{1}H NMR (300 MHz, DMSO-d_6): 7.52-7.98 (m, 10H, Ar-*H*), 8.27 (s, 1H, =C*H*), 10.57 (s, 2H, 2 x N*H*). MS (EI, m/z): 291 (M$^{\cdot+}$). Anal. Calcd. for $C_{17}H_{13}N_3O_2$: C, 70.10; H, 4.46; N, 14.43. Found: C, 69.81; H, 4.55; N, 14.74%.

2-N-(2`-Cyano-3`-phenyl-2`-propenoyl)aminophenol (**20**): Compound **20** crystallized from benzene to give yellow crystals. Yield: 50%. M.p.: 208-210 ^{o}C. FT-IR (KBr, cm^{-1}): 3368, 3201 ν(OH) and ν(NH), 2211 ν(CN), 1663 ν(C=O) (amide). ^{1}H NMR (300 MHz, DMSO-d_6): 6.81-8.01(m, 9H, Ar-*H*), 8.35 (s, 1H, =C*H*), 9.29 (br s, 1H, N*H*), 10.02 (s, 1H, O*H*). MS (EI, m/z): 264 (M$^{\cdot+}$). Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.54; N, 10.61. Found: C, 72.69; H, 4.84; N, 10.95%.

2.5. 2-[1-Cyano-2-phenyl-ethen-1-yl]-(4H)-3,1-benzoxazin-4-one (10)

A mixture of benzoic acid derivative **9** (3 g) and freshly distilled acetic anhydride (10 mL) was heated on water bath for an hour. The solid separated out at room temperature was collected, washed with dry petroleum ether 40-60°C, dried and crystallized from light petroleum (80-100 ^{o}C) to give **10** as yellow crystals (Scheme 1). Yield: 88%. M.p.: 190-192 ^{o}C. FT-IR (KBr, cm^{-1}): 2227 ν(CN), 1765 ν(C=O) (oxazinone). ^{1}H NMR (300 MHz, DMSO-d_6): 7.60-8.19 (m, 9 H, Ar-*H*), 8.46 (s, 1H, =C*H*). MS (EI, m/z): 274 (M$^{\cdot+}$). Anal. Calcd. for $C_{17}H_{10}N_2O_2$: C, 74.45; H, 3.64; N, 10.21. Found: C, 74.66; H, 3.25; N, 9.87%.

2.6. 2-(1-Cyano-2-phenyl-ethen-1-yl)-quinazolin-4(3H)-one (11)

A mixture of benzoxazinone **10** (0.9 g; 3 mmol) and ammonium acetate (1 g; 12 mmol) was heated without solvent at 160-170 ^{o}C for four hours. The solid mass was triturated with warm water. The solid separated was filtered, washed with water several times, dried and crystallized from dioxane to yield **11** as yellow crystals (Scheme 1). Yield: 60%. M.p.: 301-303 ^{o}C. FT-IR (KBr, cm^{-1}): 3183 ν(NH), 2228 ν(CN), 1676 ν(C=O) (quinazolinone). ^{1}H NMR (300 MHz, DMSO-d_6): 7.55-8.16 (m, 10 H, =CH, Ar-*H*), 8.50 (s, 1H, N*H*). MS (EI, m/z): 273 (M$^{\cdot+}$). Anal. Calcd. for $C_{17}H_{11}N_3O$: C, 74.72; H, 4.02; N, 15.38. Found: C, 75.11; H, 3.84; N, 15.68%.

2.7. 2-(1-Cyano-2-phenyl-ethen-1-yl)-3-(2-carboxyphenyl) quinazolin-4-one (12) and (E)-2-(2-(2-cyano-3-phenyl acrylamido)benzamido)benzoic acid (13)

A mixture of **1** (1.9 g; 10 mmol) and anthranilic acid (1.36 g, 10 mmol) in dry pyridine (30 mL) was refluxed for two hours. After cooling the mixture was acidified with cold dilute HCl. The

precipitate formed was collected, washed with water, dried and triturated by ethanol then fractionally crystallized to afford quinazolinone **12** and benzamide derivative **13** (Scheme 1).

Compound **12** crystallized from light petroleum (80-100 °C) to give yellow crystals. Yield: 65%. M.p.: 190-192 °C. FT-IR (KBr, cm^{-1}): 3750, 3315 ν(OH) and ν(NH), 2213 ν(CN), 1693 ν(C=O) (acid), 1660 ν(C=O) (cyclic amide). ^{1}H NMR (300 MHz, DMSO-d_6): 7.24-8.59 (m, 14 H, =C*H*, Ar-*H*), 12.09 (s, 1H, O*H*). MS (EI, m/z): 393 ($M^{+\cdot}$). Anal. Calcd. for $C_{24}H_{15}N_3O_3$: C, 73.28; H, 3.84; N, 10.68. Found: C, 73.01; H, 4.00; N, 10.90%.

Compound **13** crystallized from benzene/ethanol to give brown crystals. Yield: 15%. M.p.: 220-223 °C. FT-IR (KBr, cm^{-1}): 3340, 2640 ν(OH) and ν(NH), 2210 ν(CN), 1681 ν(C=O). ^{1}H NMR (300 MHz, DMSO-d_6): 7.22 -8.62 (m, 14H, =C*H*, Ar-*H*), 11.63 (s, 1H, N*H*), 12.07 (s, 1H, N*H*), 12.22 (s, 1H, COO*H*). MS (EI, m/z): 411 ($M^{+\cdot}$). Anal. Calcd. for $C_{24}H_{17}N_3O_4$: C, 70.07; H, 4.17; N, 10.21. Found: C, 70.31; H, 3.92; N, 10.00%.

2.8. Conversion of benzoxazinone (10) into (12) and (13)

Procedure (I) in ethanol: A mixture of benzoxazinone **10** (1.49 g; 5 mmol) and anthranilic acid (0.9 g; 5 mmol) in ethanol (50 mL) was refluxed for 3 h. The solvent was distilled off and the residue was fractionally crystallized to give **12** in 10% yield and **13** in 90% yield (Scheme 1).

Procedure (II) heating without solvent: The same previous mixture was heated at 140-160 °C without solvent for 1 h. After cooling, the residue was fractionally crystallized to give **12** and **13** in 80% and 20% yield, respectively (Scheme 1).

2.9. 2-[2-N-(2-Cyano-3-phenyl-2-propenoyl)amino]phenyl-4H-benzo[d][1,3]oxazin-4-one (14), (10) and (12)

A mixture of benzamide derivative (**13**) (2 g) and acetic anhydride (30 mL) was heated on water bath for two hours, and then poured into crushed ice. The solid separated was collected, washed with water, dried and fractionally crystallized to give a mixture of **10**, **12** and **14** in 5, 25, 45% yields, respectively (Scheme 1).

Compound **14** was crystallized from dioxane to give pale yellow crystals. Yield: 45%. M.p.: 271-274 °C. FT-IR (KBr, cm^{-1}): 3172 ν(NH), 2208 ν(CN), 1763 ν(C=O) (oxazinone), 1695 ν(C=O) (amide). ^{1}H NMR (300 MHz, DMSO-d_6): 7.03-8.10 (m, 13 H, Ar-*H*), 8.21 (s, 1H, CN-C=C*H*), 10.23 (s, 1H, N*H*). MS (EI, m/z): 393 ($M^{+\cdot}$). Anal. Calcd. for $C_{24}H_{15}N_3O_3$: C, 73.28; H, 3.84; N, 10.68. Found: C, 73.42; H, 3.61; N, 10.55%.

2.10. N-[2-(2-benzylidenehydrazinecarbonyl)phenyl]-2-cyanoacetamide (15)

A mixture of benzoxazinone **10** (1.49 g; 5 mmol) and hydrazine hydrate (0.1 mL, 5 mmol) in ethanol (50 mL) was refluxed for 3 h. The solid separated after concentration was collected and crystallized from ethanol to yield **15** as pale yellow crystals (Scheme 1). Yield: 55%. M.p.: 140-142 °C. FT-IR (KBr, cm^{-1}): 3240, 3192 ν(NH), 2212 ν(CN), 1696 ν(C=O) (amide). ^{1}H NMR (300 MHz, DMSO-d_6): 3.91 (s, 2H, CH_2-CN), 7.30-8.49 (m, 10 H, =C*H*, Ar-*H*), 11.49 (br s, 1H, 2N*H*). MS (EI, m/z): 306 ($M^{+\cdot}$). Anal. Calcd. for $C_{17}H_{14}N_4O_2$: C, 66.60; H, 4.60; N, 18.28. Found: C, 66.33; H, 4.72; N, 18.01%.

2.11. 2-oxo-4-phenyl-2H-pyrido[1,2-a]pyrimidine-3-carbonitrile (16)

To a solution of **1** (1.9 g; 10 mmol) in dry benzene (30 mL) in presence of triethylamine (1.38 mL; 10 mmol), 2-aminopyridine (0.9 g; 10 mmol) was added. The reaction mixture was stirred at room temperature for 1 h. The semisolid produced was collected, washed with water several times, and then triturated with methyl alcohol. The solid separated was collected, dried and crystallized from methanol to afford **16** as colourless crystals. Yield: 40%. M.p.: 203-205 °C. FT-IR (KBr, cm^{-1}): 2218 ν(CN), 1705 ν(C=O) (cyclic amide). ^{1}H NMR (300 MHz, DMSO-d_6): 7.59-9.80 (m, 9 H, Ar-*H*). MS (EI, m/z): 247 ($M^{+\cdot}$). Anal. Calcd. for $C_{15}H_9N_3O$: C, 72.87; H, 3.64; N, 17.01. Found: C, 72.43; H, 3.71; N, 17.23%.

2.12. 2-(1-Cyano-2-phenyl-ethen-1-yl)-5-phenyl-1,3,4-oxadiazole (19)

A solution of (**18**) (1 g) in phosphorous oxychloride (20 mL) was heated on water bath for 4 h. The reaction mixture was left to cool, and then poured with stirring into crushed ice. The solid separated out was filtered off, washed with water several times, dried and crystallized from ethanol to yield **19** as colourless crystals (Scheme 1). Yield: 40%. M.p.: 168-170 °C. FT-IR (KBr, cm^{-1}): 2222 ν(CN). ^{1}H NMR (300 MHz, DMSO-d_6): 7.62-8.15 (m, 10H, Ar-*H*), 8.53 (s, 1H, =C*H*). MS (EI, m/z): 273 ($M^{+\cdot}$). Anal. Calcd. for $C_{17}H_{11}N_3O$: C, 74.72; H, 4.02; N, 15.38. Found: C, 74.98; H, 4.22; N, 15.46%.

2.13. 2-(1-Cyano-2-phenyl-ethen-1-yl)benzo[d]oxazole (21)

A solution of **20** (1 g) in phosphorous oxychloride (20 mL) was heated on water bath for 8 h. The reaction mixture was left to cool, and then poured into crushed ice. The solid, which separated out, was filtered, washed with water several times, dried and crystallized from benzene to afford 21 as yellow crystals (Scheme 1). Yield: 40%. M.p.: 140-142 °C. FT-IR (KBr, cm^{-1}): 2226 ν(CN). ^{1}H NMR (300 MHz, DMSO- DMSO-d_6): 7.47-8.03 (m, 9 H, Ar-*H*), 8.52 (s, 1H, =C*H*). MS (EI, m/z): 246 ($M^{+\cdot}$). Anal. Calcd. for $C_{16}H_{10}N_2O$: C, 78.04; H, 4.06; N, 11.38. Found: C, 78.11; H, 3.77; N, 11.51%.

3. Results and discussions

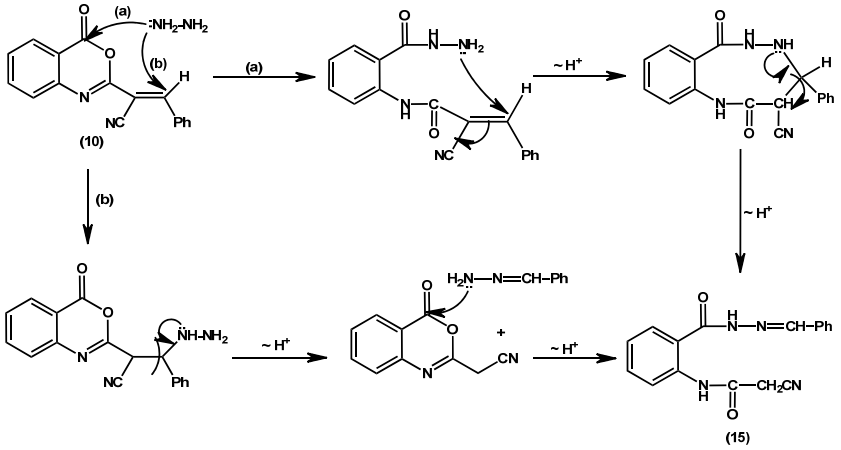
Condensation of **1** with benzylamine or *p*-anisidine in presence of triethylamine afforded the corresponding 2-propenoylamides (**2** and **3**). Treatment of **3** with anhydrous aluminium chloride in benzene or chlorobenzene gave the corresponding unexpected demethylated derivative (**4**) instead of the expected quinolinone derivative [23] (A) (Scheme 1).

Esterification of **1** with *o*-cresol and *p*-thiocresol yielded the ester and thioester (**5** and **6**) (Scheme 1). On the other hand, condensation of **1** with ethanolamine gave the disubstituted derivative (**7**).

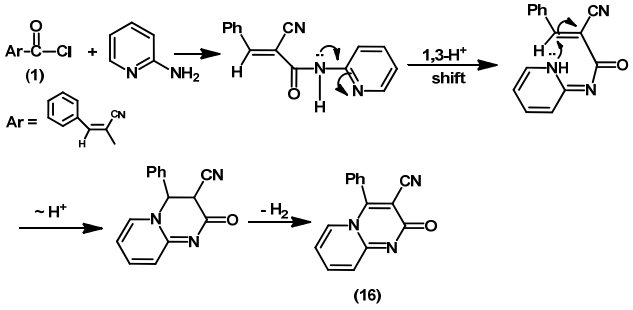
Furthermore, reaction of **1** with *o*- phenylenediamine afforded the corresponding diamide (**8**) which, on treatment with $POCl_3$ or heating at its melting point, failed to give the expected benzimidazole derivative (B) [18] (Scheme 1).

The condensation product of reaction of **1** with anthranilic acid depends upon both the base used and reaction conditions. In presence of triethylamine or pyridine at room temperature, the authors obtained the amide (**9**), which upon treatment with acetic anhydride underwent cyclization to the benzoxazinone derivative (**10**) that upon heating with ammonium acetate at 140-160 °C without solvent afforded the corresponding quinazolinone derivative (**11**) (Scheme 1).

On the other hand, in presence of pyridine at refluxing temperature, a mixture of quinazolinone derivative (**12**) and benzamide derivative (**13**) was obtained. The reaction probably proceeded *via* the formation of benzoxazinone (**10**) followed by further addition of anthranilic acid molecule to give (**13**) which underwent cyclization under the reaction conditions to afford the quinazolinone (**12**) (Scheme 1, route a).



Scheme 2



Scheme 3

The previous pathway was confirmed by reaction of benzoxazinone (**10**) with anthranilic acid in ethanol to yield a mixture of **12**:**13** in 10:90% yield, respectively, while upon heating compound **10** with anthranilic acid at 140-150 °C in absence of solvent, the mixture **12**:**13** was obtained in 80:20 % yield, respectively (Scheme 1).

Furthermore, refluxing benzamide derivative (**13**) in freshly distilled acetic anhydride yielded a mixture of benzoxazinone derivative (**14**) besides benzoxazinone (**10**) and quinazolinone (**12**) in 45:5:25% yield *via* the available cyclization in route (a) or (b) to give **12** and **14** and/or unexpected addition *via* route (a) with subsequent cleavage of anthranilic acid moiety to give **10** (Scheme 1).

Hydrazinolysis of benzoxazinone (**10**) with hydrazine hydrate in refluxing ethanol afforded the hydrazide derivative **15** (Scheme 1), which probably produced according to the plausible mechanism shown in Scheme 2.

With 2-aminopyridine, acid chloride (**1**) gave the fused bicyclic system pyrido[1,2-a] pyrimidine derivative (**16**) (Scheme 1). The formation of pyridopyrimidine **16** can be interpreted as shown in (Scheme 3) through normal substitution by tetrahedral mechanism on the carbonyl functionality of compound **1** followed by 1,3-proton shift and addition to α,β-unsaturated nitrile with subsequent dehydrogenation [24] under the reaction conditions, according to the pathway shown in Scheme 3.

Reaction of chloride (**1**) with 2-aminothiophenol gave the benzo-1,5-thiazepinone derivative (**17**) (Scheme 1) whereas the treatment of **1** with benzoylhydrazine afforded the corresponding hydrazide derivative (**18**) which on heating with $POCl_3$ gave the oxadiazole derivative **19**.

With 2-aminophenol, the isolated product was the amide derivative (**20**) which was dehydrated under the effect of $POCl_3$ to give the benzoxazole derivative.

4. Conclusion

*(E)*2-Cyano-3-phenyl-2-propenoyl chloride could be utilized in the synthesis of some heterocyclic systems like benzoxazinone, quinazolinone, pyridopyrimidine, benzothiazepine, oxadiazole and benzoxazole *via* 2-propenoylamides as intermediates.

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References

[1]. Li, Y. L.; Xu, W. F. *Bioorgan. Med. Chem.* **2004**, *12(19)*, 5171-5180.

[2]. Sousa, J. B.; Calheiros, R.; Rio, V.; Borges, F.; Marques, M. P. M. *J. Mol. Struc.* **2006**, *783(1-3)*, 122-135.

[3]. Schwaiger, S.; Cervellati, R.; Seger, C.; Ellmerer, E. P.; About, N.; Renimel, I.; Godenir, C.; André, P.; Gafner, F.; Stuppner, H. *Tetrahedron* **2005**, *61(19)*, 4621-4630.

[4]. Wu, C. C.; Wang, T. W.; Wang, W. Y.; Hsieh, P. W.; Wu, Y. C. *Eur. J. Pharm. Sci.* **2005**, *527(1-3)*, 37-43.

[5]. Rieu, J. P.; Duflos, A.; Tristani, J. C.; Patoiseau, J. F.; Tisne-Versailles, J.; Bessac, A. M.; Bonnafous, R.; Marty, A.; Verscheure, Y.; Bigg, D. C. H. *Eur. J. Med. Chem.* **1993**, *28(9)*, 683-691.

[6]. Blackburn, C.; LaMarche, M. J.; Brown, J.; Che, J. L.; Cullis, C. A.; Lai, S.; Magurie, M.; Marsilje, T.; Geddes, B.; Govek, E.; Kadambi, V.; Doherty, C.; Dayton, B.; Brodjian, S.; Marsh, K. C.; Collins, C. A.; Kym, P. R. *Bioorgan. Med. Chem. Lett.* **2006**, *16(10)*, 2621-2627.

[7]. Rida, S. M.; Ashour, F. A.; El-Hawash, S. A. M.; El-Semary, M. M.; Badr, M. H.; Shalaby, M. A. *Eur. J. Med. Chem.* **2005**, *40(9)*, 949-959.

[8]. Lavergne, O.; Fernandes, A-C.; Bréhu, L.; Sidhu, A.; Brézak, M-C.; Prévost, G.; Ducomnun, B.; Contour-Galceru, M. O. *Bioorgan. Med. Chem. Lett.* **2006**, *16(1)*, 171-175.

[9]. Lopez-Tudanca, P. L.; Labeaga, L.; Innerarity, A.; Alonsocires, L.; Tapia, I.; Mosquera, R.; Orjales, A. *Bioorgan. Med. Chem.* **2003**, *11(13)*, 2709-2714.

[10]. Palmer, J. T.; Hirschbein, B. L.; Cheung, H.; McCarter, J.; Janc, J. W.; Yu, Z. W.; Wesolowski, G. *Bioorgan. Med. Chem. Lett.* **2006**, *16(11)*, 2909-2914.
[11]. Madkour, H. M. F.; Shiba, S. A.; Sayed, H. M.; Hamed, A. A. *Sulfur Lett.* **2001**, *24(4)*, 151-179.
[12]. Madkour, H. M. F.; Farag, A. A.; Ramses, S. Sh.; Ibrahiem, N. A. A. *Phosphorus Sulfur* **2006**, *181*, 255-265.
[13]. Nofal, Z. M.; El-Zahar, M. I.; Salem, M. A. I.; Madkour, H. M. F. *Egypt. J. Chem.* **2005**, *48(5)*, 587-604.
[14]. Nofal, Z. M.; Fahmy, H. H.; Madkour, H. M. F.; Zareaa, E. S.; Hassan, S. A. *Egypt. J. Pharm.* **2006**, *5(1),* 45-60.
[15]. Madkour, H. M. F.; Mahmoud, M. R.; Sakr A. M.; Habashy, M. M. *Sci. Pharm.* **2001**, *69*, 33-52.
[16]. Madkour, H. M. F.; Salem M. A. I.; Soliman, E. A.; Mahmoud, N. F. H. *Phosphorus Sulfur* **2001**, *170*, 15-27.
[17]. Salem, M. A. I.; Madkour, H. M. F.; Soliman, E. A.; Mahmoud, N. F. H. *Heterocycles* **2000**, *53(5)* , 1129-1143.
[18]. Shiba, S. A. *Phosphorus Sulfur* **1996**, *114*, 29-37.
[19]. Shiba, S. A.; Fahmy, A. F. M.; Abdel-Hamid, H. A.; Massoud, M. S. *Egypt. J. Chem.* **1993**, 36, 409-418.
[20]. Abdel-Hamid, H. A.; Fahmy, A. F.; Shiba, S. A.; El-Hawary, N. A. *Egypt. J. Chem.* **1993**, *36*, 167-175.
[21]. Shiba, S. A. *Arch. Pharm.* **1998**, *331*, 91-96.
[22]. Jaafar, I.; Francis, G.; Danion-Bougot, R.; Danion, D. *Synthesis* **1994**, *1*, 56-60.
[23]. Wang, T. C.; Chen, Y. L.; Lee, K. H.; Tzeng, C. C. *Tetrahedron Lett.* **1996**, *37(35)*, 6369-6370.
[24]. March, J. Advanced Organic Chemistry, 3rd edition, John Wiley & Sons. Interscience Pub. , New York p 1053, **1985**.