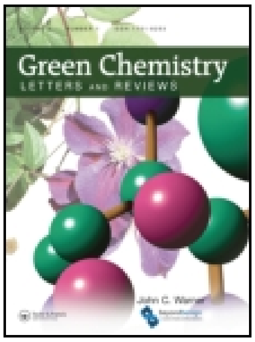

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RESEARCH LETTER

Arylhydrazononitriles as precursors to 2-substituted 1,2,3-triazoles and 4-amino-5-cyano-pyrazole derivatives utilizing microwave and ultrasound irradiation

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Cyanoacetamides **3a–d** were prepared by reacting ethyl cyanoacetate with primary aliphatic amines **2a–d**. The formed cyanoacetamides **3a–d** were coupled with aromatic diazonium salts to give the corresponding arylhydrazones **4a–i** which were used as precursors to title triazoles and pyrazoles by reacting with hydroxylamine and chloroacetonitrile. Yields of products formed by conventional heating are compared with those of microwave and ultrasound irradiation

Keywords: green synthetic approaches; 2-arylhydrazononitriles; X-ray crystal structure determination; 4-amino-5-cyano-pyrazoles; 1,2,3-triazoles

Introduction

Recently, many papers have been published dealing with 2-arylhydrazononitriles as precursors to heteroaromatics (*1–6*). Elnagdi et al. (*7–10*) have reported efficient synthetic approaches to functionally substituted pyrazoles and 1,2,3-triazoles utilizing arylhydrazononitrile precursors. In the light of our recent interest in adopting green synthetic methodologies for the synthesis of functionally substituted heteroaromatics utilizing microwave (Mw) heating and ultrasound (Us) irradiation (*11–25*), we aim in this work to report on the synthesis and utility of arylhydrazononitrile as precursors to 1,2,3-traizoles **7**, **10**, and pyrazole derivatives **13**.

Results and discussion

Ethyl cyanoacetate (*1*) was reacted with a variety of aliphatic amines **2a–d** under Mw heating or Us activation to yield cyanoacetamides **3a–d** (Scheme 1).

Compounds **3a–d** were coupled readily with aromatic diazonium salts to yield the corresponding arylhydrazononitriles **4a–i**, in 67–95% yields (Scheme 2). The structures of compounds **4a–i** were established on the basis of their elemental analyses and spectral data. ^{1}H NMR spectra of compounds **4a–i** showed a singlet signal in region 11.10–14.97 ppm corresponding to the hydrazone (NH) proton. The structure assigned to compounds **4a–i** could be unequivocally established by single crystal X-ray diffraction of compound **4c** (*26*), as shown in Figure 1.

Parallel to the recent literature data (*7,8,27–29*), compounds **4a–i** reacted with hydroxylamine hydrochloride in the presence of sodium acetate to yield the amidoximes **5a–h**. It has been found that the reaction completion time was 1 h in refluxing ethanol and 2–5 min under Mw heating. The structures of the new amidoximes **5a–h** have been elucidated by elemental analyses and spectroscopic measurements. For example, the ^{1}H NMR spectra of compound **5a** revealed the presence of (NH_2) protons at δ6.52 ppm and a broad singlet signal at δ14.21 ppm corresponding to (OH) proton. The IR spectra of compound **5a** showed absorption bands at $\nu = 3587$, 3456, and 3420 cm^{-1} due to OH and NH_2 groups, respectively.

Upon heating **5** in dimethylformamide (DMF) at reflux temperature for 1 h or under Mw irradiation for 2–5 min or by utilizing Us irradiation for 1 h at 40°C, this compound gave solid products whose structures were assumed to be **6**, **7**, or **8** (Scheme 3).

The structure of isoxazoles **6** was readily ruled out for the reaction products on the basis of spectral data. Thus, the presence of an amide carbonyl absorption in region $\nu = 1642–1658$ cm^{-1} in the IR spectra of the reaction products allowed us to discard the possible structure **6**. Moreover, ^{13}C NMR spectra of the reaction products confirmed the presence of a CO carbon at $\delta \approx 164$ ppm. If the reaction product was

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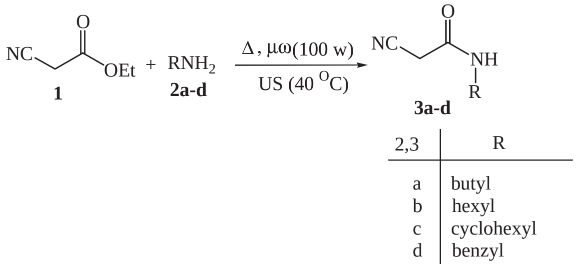


Scheme 1. Synthesis of cyanoacetamides.

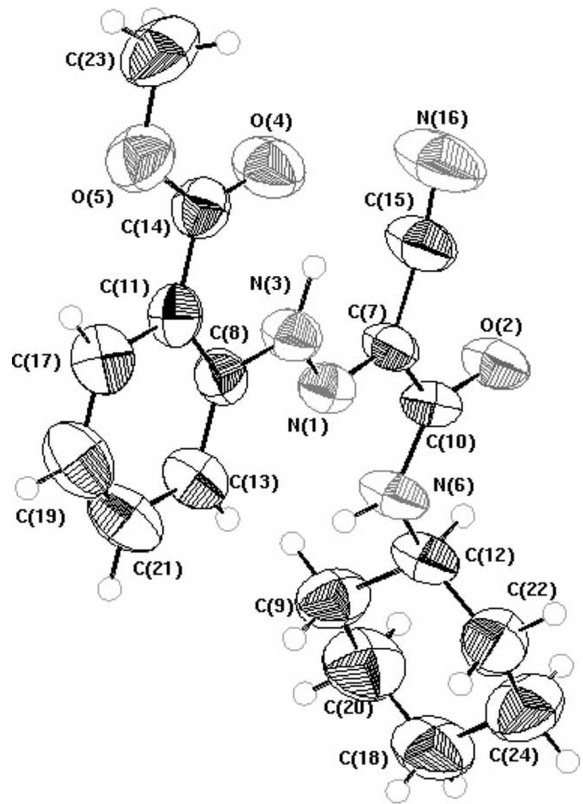


Figure 1. X-ray crystal structure of **4c**.

the isomer **6**, it would be difficult to assign this signal. Elemental analysis and spectral data could not unequivocally differentiate the two isomers **7** and **8**. Therefore, the 1,2,3-triazolo[4,5-*d*]pyrimidines **10** was prepared to chemically verify the structure of **7**. Reaction of aminotriazoles **7** with dimethylformamide dimethylacetal (DMF DMA), under different reaction conditions, gave the ring-closed 1,2,3-triazolo[4,5-*d*]pyrimidines **10**, via the intermediate **9** (Scheme 3). It is difficult to obtain these reaction products **10** with the isomer **8**.

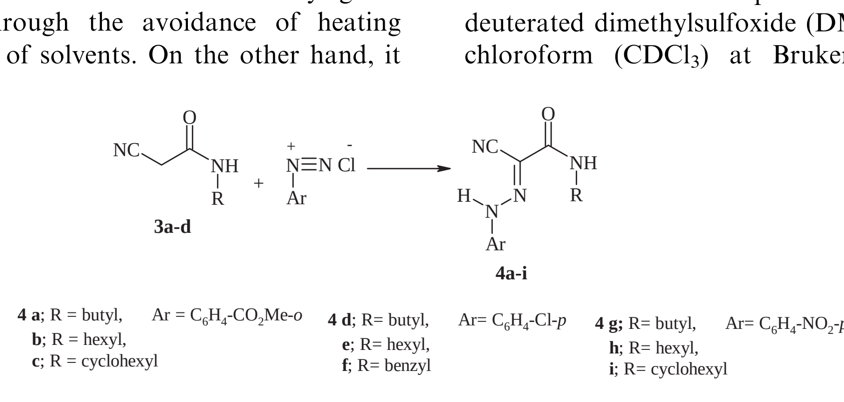
Recently, Elnagdi et al. (*2,7,30*) have reported that refluxing 2-arylhydrazononitriles with functionally substituted alkyl halides afforded 4-aminopyrazole derivatives. Now, compound **4** was next reacted with chloroacetonitrile, under conventional heating, Mw irradiation, and sonication, to afford the 4-aminopyrazoles **13**, via the acyclic non-isolable intermediate **12** (Scheme 4). The identity of compounds **13** was supported by correct elemental analyses and mass spectra as well as the IR and NMR spectra which were compatible with assigned structures (see Section "Experimental"). The reaction times and yields of the products formed via traditional methods were compared with those of Mw and Us irradiation (see Table 1).

In conclusion, we have shown that the synthesis of 2-aryl-1,2,3-triazoles and 4-aminopyrazoles from arylhydrazononitriles is better conducted by green methodologies through the avoidance of heating and excessive use of solvents. On the other hand, it should be noted that reactions occur at different temperatures with these techniques and therefore strict comparisons will require a balance between effectiveness and energy costs.

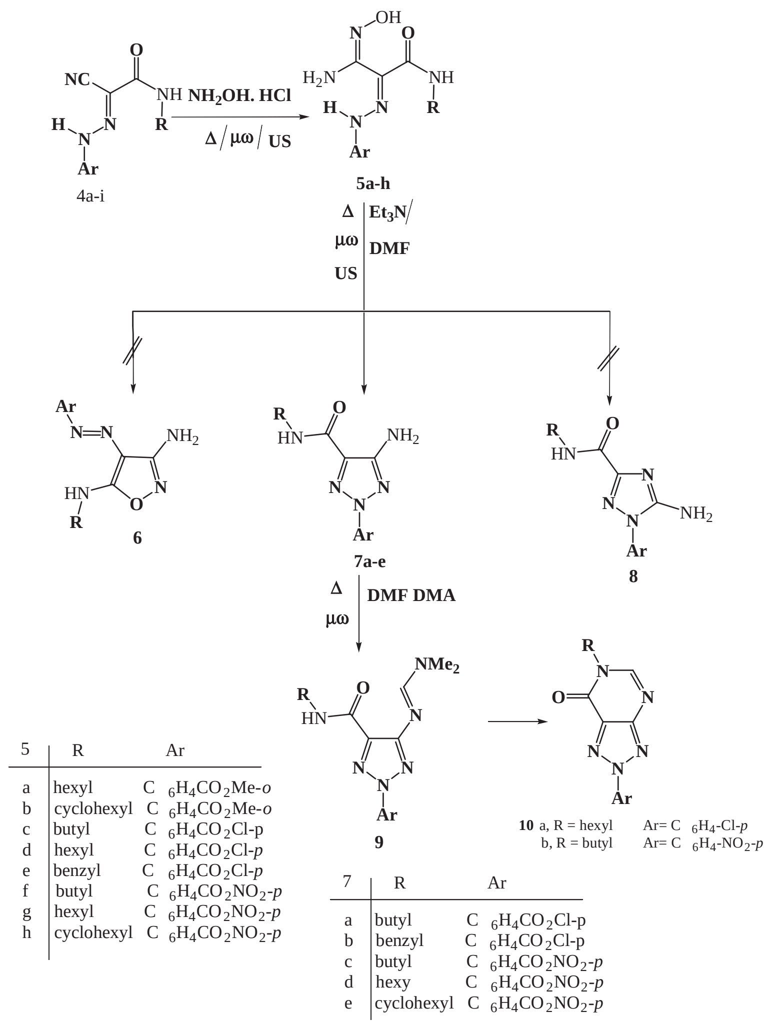
Experimental

General

All melting points were measured on a Gallenkamp electrothermal melting point apparatus and are uncorrected. The IR absorption spectra were measured on a Nicolet Magna 520FT IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in deuterated dimethylsulfoxide (DMSO) or deuterated chloroform ($CDCl_3$) at Bruker DPX 400 MHz



Scheme 2. Synthesis of 2-arylhydrazononitrile derivatives.

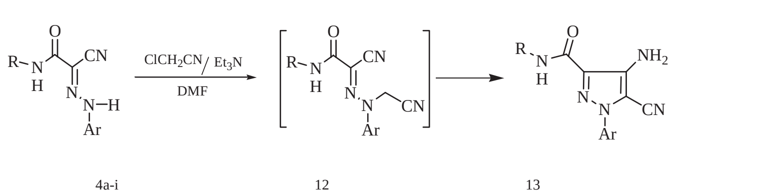


5	R	Ar
a	hexyl	$C_6H_4CO_2Me$-*o*
b	cyclohexyl	$C_6H_4CO_2Me$-*o*
c	butyl	$C_6H_4CO_2Cl$-p
d	hexyl	$C_6H_4CO_2Cl$-*p*
e	benzyl	$C_6H_4CO_2Cl$-*p*
f	butyl	$C_6H_4CO_2NO_2$-*p*
g	hexyl	$C_6H_4CO_2NO_2$-*p*
h	cyclohexyl	$C_6H_4CO_2NO_2$-*p*

7	R	Ar
a	butyl	$C_6H_4CO_2Cl$-p
b	benzyl	$C_6H_4CO_2Cl$-p
c	butyl	$C_6H_4CO_2NO_2$-*p*
d	hexy	$C_6H_4CO_2NO_2$-*p*
e	cyclohexyl	$C_6H_4CO_2NO_2$-*p*

Scheme 3. Synthesis of 5-amino-1,2,3-triazole and 1,2,3-triazolo[4,5-d]pyrimidin-7-one derivatives.

spectrometer using tetramethylsilane (TMS) as an internal reference. Mass spectra were performed on a Shimadzu GCMS-QP 1000 EX mass spectrometer at 70 eV. Mw irradiation was carried out using the commercial Mw oven (SGO 1000 W). A thermocouple used to monitor the temperature inside the Mw vessel during the reactions found that the temperature was approximately 105–110°C. Us irradiation was carried out with a microprocessor controlled-2004, high intensity ultrasonic processor with temperature controller (750 W). The ultrasonic frequency of the cleaning bath used was equal to 25



13	R	Ar
a	cyclohexyl	$C_6H_4CO_2Me$-*o*
b	butyl	C_6H_4Cl-*p*
c	hexyl	C_6H_4Cl-*p*
d	benzyl	C_6H_4Cl-*p*
e	hexyl	$C_6H_4NO_2$-*p*

Scheme 4. Synthesis of pyrazole derivatives.

Table 1. Yield as well as reaction times by the three methodologies are compared.

No.	Time			Yield%		
	Δ	Mw	Us	Δ	Mw	Us
3a	3 h	4 min	7 min	67	89	74
3b	4 h	3 min	10 min	90	91	88
3c	2 h	2 min	5 min	83	90	80
3d	1 h	1 min	2 min	89	93	90
5a	1 h	2 min	30 min	40	80	72
5b	1 h	5 min	30 min	37	74	70
5c	1 h	4 min	30 min	48	80	76
5d	1 h	3 min	30 min	35	35	66
5e	1 h	2 min	30 min	40	75	78
5f	1 h	3 min	30 min	44	89	81
5g	1 h	5 min	30 min	48	80	77
5h	1 h	3 min	30 min	39	79	78
7a	1 h	2 min	1 h	40	60	58
7b	1 h	2 min	1 h	44	73	70
7c	1 h	3 min	1 h	45	77	68
7d	1 h	2 min	1 h	43	79	71
7e	1 h	4 min	1 h	40	66	56
10a	7 h	2 min	–	47	90	–
10b	7 h	2 min	–	46	88	–
13a	1 h	2 min	1 h	60	77	73
13b	1 h	2 min	1 h	55	84	78
13c	1 h	2 min	1 h	59	79	70
13d	1 h	2 min	1 h	58	89	84
13e	1 h	2 min	1 h	54	80	78

KHz. The reaction temperature was stabilized at 35–40°C even after more than 1 h by addition or removal of water in ultrasonic bath to keep the required temperature. Elemental analyses were measured by means of Perkin Elmer 2400 CHN elemental analyzer flowchart. X-ray crystallography was carried out on a Kappa CCD Enraf Nonius FR 590 diffractometer, at National Research Center, Dokki, Cairo, Egypt.

*General procedure for the preparation of N-substituted-2-cyano-acetamide **3a–d***

Method I (Δ). Equimolar amounts (0.1 mol) of both ethyl cyanoacetate and the aliphatic amines **2a–d** were stirred at room temperature for 1–4 h and the resulting solid product was re-crystallized from ethanol.

Method II (μω). A mixture of ethyl cyanoacetate (0.1 mol) and the appropriate amount of aliphatic amines **2a–d** (0.1 mol) was placed in the Mw oven and irradiated at 460 W for 1–4 min. Then, the reaction mixture was left to cool to room temperature. The solid product so-formed was filtered and re-crystallized from ethanol.

Method III (Us). Equimolar amounts (0.1 mol) of both ethyl cyanoacetate and the aliphatic amines **2a–d** were mixed and heated under Us irradiation at 40°C for 2–10 min, and then left to cool to room temperature. The solid product so-formed was filtered and re-crystallized from ethanol.

*N-Butyl-2-cyanoacetamide (**3a**).* Orange crystals from ethanol; mp 72°C; IR ν_{max} cm^{-1}: 3299 (NH), 2954 (CH aliphatic), 2258 (CN), and 1653 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 0.85 (t, 3H, CH_3, $J = 7$ Hz), 1.27 (m, 2H, CH_2, $J = 7$ Hz), 1.38 (m, 2H, CH_2, $J = 7$ Hz), 3.06 (q, 2H, CH_2, $J = 7$ Hz), 3.56 (s, 2H, CH_2CN), and 8.18 (br s, 1H, NH) ppm; ^{13}C NMR; (DMSO-d_6); δ = 14.02, 20.00, 25.76, 31.40 (butyl carbons), 39.27 (CH_2CN), 116.71 (CN), and 162.39 (C=O) ppm; MS: 141 [$M^+ + 1$]. Analysis calculated for $C_7H_{12}N_2O$ (140.19): C, 59.98; H, 8.63; and N, 19.98. found: C, 59.90; H, 8.70; and N, 19.92.

*2-Cyano-N-hexyl-acetamide (**3b**).* Yellow crystals from ethanol; mp 67°C; IR ν_{max} cm^{-1}: 3299 (NH), 2932 (CH aliphatic), 2260 (CN), and 1645 (C=O); ^{1}H NMR; ($CDCl_3$); δ = 0.81 (t, 3H, CH_3, $J = 6$ Hz), 1.24 (m, 6H, 3CH_2), 1.45 (m, 2H, CH_2, $J = 7$ Hz), 3.17 (q, 2H, CH_2, $J = 7$ Hz), 3.42 (s, 2H, CH_2CN), and 7.17 (s, 1H, NH) ppm; ^{13}C NMR; ($CDCl_3$); δ = 13.99, 22.54, 26.04, 26.55, 29.11, 31.43 (hexyl carbons), 40.45 (CH_2CN), 115.22 (CN), and 162.03 (C=O) ppm; MS: 169 [$M^+ + 1$]. Analysis calculated for $C_9H_{16}N_2O$ (168.24): C, 64.25; H, 9.59; and N,16.65. Found: C, 64.20; H, 9.61; and N, 16.69.

*2-Cyano-N-cyclohexyl-acetamide (**3c**).* Colorless crystals from ethanol; mp 136°C; IR ν_{max} cm^{-1}: 3272 (NH), 2933 (CH aliphatic), 2261 (CN), and 1628 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 1.12 − 1.68 (m, 6H, 3CH_2), 1.70–2.03 (m, 4H, 2CH_2), 3.46–3.54 (m, 1H, CH), 3.22 (s, 2H, CH_2CN), and 8.14 (d, 1H, NH, $J = 7$ Hz) ppm; ^{13}C NMR; (DMSO-d_6); δ = 24.35, 24.87, 25.62, 25.84, 30.91, 32.60 (cyclohexyl carbons), 48.73 (CH_2CN), 116.73 (CN), and 161.51 (C=O) ppm; MS: 166 [M^+]. Analysis calculated for $C_9H_{14}N_2O$ (166.22): C, 65.05; H, 8.49; and N, 16.85. Found: C, 65.10; H, 8.36; and N, 16.89.

*N-Benzyl-2-cyano-acetamide (**3d**).* Brown crystals from ethanol; mp 124°C; IR ν_{max} cm^{-1}: 3295 (NH), 3091 (CH aromatic), 2923 (CH aliphatic), 2220 (CN), and 1640 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 3.71 (s, 2H, CH_2CN), 4.30 (d, 2H, $PhCH_2$, $J = 5$ Hz), 7.29–7.34 (m, 5H, ph–H), and 8.74 (t, 1H, NH, $J = 7$ Hz) ppm; MS: 174 [M^+]. Analysis calculated for

$C_{10}H_{10}N_2O$ (174.20): C, 68.95; H, 5.79; and N, 16.08. Found: C, 68.90; H, 5.67; and N, 16.20.

*Preparation of arylhydrazone derivatives **4a–i***

A cold solution of aryldiazonium salt (10 mmol) was prepared by adding a solution of sodium nitrite (1g into 10 mL H_2O) to a cold solution of arylamine hydrochloride or arylamine nitrate (10 mmol) with stirring. The resulting solution of the aryldiazonium was then added to a cold solution of *N*-substituted-2-cyanoacetamides **3a–d** (0.1mol) in ethanol (50 mL) containing sodium acetate (1 g into 10 mL H_2O). The mixture was stirred at room temperature for 1 h and the solid product so-formed was collected by filtration and re-crystallized from ethanol.

*2-[N′-(Butylcarbamoyl-cyano-methylene)-hydrazino]-benzoic acid methyl ester (**4a**).* Yellow crystals from ethanol; yield 70%, mp 166°C; IR ν_{max} cm^{-1}: 3388 (NH), 3026 (CH aromatic), 2953 (CH aliphatic), 2214 (CN), 1696 (C=O ester), and 1668 (C=O amide); 1H NMR; (DMSO-d_6); δ = 0.89 (t, 3H, CH_3, J = 7 Hz), 1.31 (m, 2H, CH_2, J = 7 Hz), 1.49 (m, 2H, CH_2, J = 7 Hz), 3.23 (q, 2H, CH_2, J = 7 Hz), 3.91 (s, 3H, ester CH_3), 7.20 (t, 1H, Ar H, J = 7 Hz), 7.69 (t, 1H, Ar H, J = 7 Hz), 7.98 (d, 1H, Ar H, J = 8 Hz), 8.16 (d, 1H, Ar H, J = 8 Hz), 8.58 (t, 1H, NH, J = 5 Hz), and 12.28 (s, 1H, NH) ppm; 13C NMR; (DMSO-d_6); δ = 14.26, 20.15, 31.92 (butyl carbons), 53.33 (ester CH_3), 111.18, 112.99, 113.53, 123.60, 131.23, 135.51 (C6H_4COOCH_3-*o*), 116.54 (CN), 143.67 (C=N–NH), and 159.97, 168.15 (2C=O) ppm; MS: 301 [M+–1]. Analysis calculated for C15H18N4O3 (302.34): C, 59.59; H, 6.00; and N, 18.53. Found: C, 59.68; H, 6.35; and N, 18.43.

*2-[N′-(Cyano-hexylcarbamoyl-methylene)-hydrazino]-benzoic acid methyl ester (**4b**).* Yellow crystals from ethanol; yield 67%, mp 140°C; IR ν_{max} cm^{-1}: 3391 (NH), 3023 (CH aromatic), 2951 (CH aliphatic), 2215 (CN), 1697 (C=O ester), and 1670 (C=O amide); ^{1}H NMR; (DMSO-d_6); δ = 0.83 (t, 3H, CH_3CH_2, J = 6 Hz), 1.24 (m, 6H, 3CH_2), 1.48 (m, 2H, CH_2, J = 7 Hz), 3.17 (q, 2H, CH_2, J = 7 Hz), 3.88 (s, 3H, ester CH_3), 7.16 (t, 1H, Ar H, J = 7 Hz), 7.63 (t, 1H, Ar H, J = 7 Hz), 7.95 (d, 1H, Ar H, J = 8 Hz), 8.12 (d, 1H, Ar H, J = 8 Hz), 8.50 (t, 1H, NH, J = 5 Hz), and 14.97 (s, 1H, NH) ppm; MS: 330 [M^+]. Analysis calculated for $C_{17}H_{22}N_4O_3$ (330.39): C, 61.80; H, 6.71; and N, 16.96. Found: C, 61.74; H, 6.98; and N, 16.79.

*2-[N′-(Cyano-cyclohexylcarbamoyl-methylene)-hydrazino]-benzoic acid methyl ester (**4c**).* Orange crystals from ethanol; yield 77%, mp 166°C; IR ν_{max} cm^{-1}: 3290 (NH), 3032 (CH aromatic), 2935 (CH aliphatic), 2210 (CN), 1720 (C=O ester), and 1689 (C=O amide); ^{1}H NMR; (DMSO-d_6); δ = 1.09–1.62 (m, 6H, 3CH_2), 1.78–2.11 (m, 4H, 2CH_2), 3.62–3.88 (m, 1H, cyclohexyl CH), 3.91 (s, 3H, $COOCH_3$), 7.01 (d, 1H, NH, J = 7 Hz), 7.20 (t, 1H, Ar H, J = 7 Hz), 7.70 (t, 1H, Ar H, J = 7 Hz), 7.79 (d, 1H, Ar H, J = 8 Hz), 8.13 (d, 1H, Ar H, J = 8 Hz), and 12.28 (s, 1H, NH) ppm; ^{13}C NMR; (DMSO-d_6); δ = 25.58, 25.73, 32.76, 49.01 (cyclohexyl carbons), 53.33 (ester CH_3), 111.24, 113.23, 113.54, 123.61, 131.22, 135.48 ($C_6H_4COOCH_3$-*o*), 116.66 (CN), 143.62 (C=N–NH), and 159.17, 168.15 (2C=O) ppm; MS: 327[M^+–1]. Analysis calculated for $C_{17}H_{20}N_4O_3$ (328.37): C, 62.18; H, 6.14; and N, 17.06. Found: C, 62.26; H, 6.32; and N, 17.00.

*N′-Butyl-2-[(4-chlorophenyl)-hydrazono]-2-cyano-acetamide (**4d**).* Brown crystals from ethanol; yield 90%, mp 185°C; IR ν_{max} cm^{-1}: 3380 (2NH), 3086 (CH aromatic), 2927 (CH aliphatic), 2211 (CN), and 1646 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 0.86 (t, 3H, CH_3, J = 7 Hz), 1.28 (m, 2H, CH_2, J = 7 Hz), 1.45 (m, 2H, CH_2, J = 7 Hz), 3.19 (q, 2H, CH_2, J = 7 Hz), 7.35 (d, 2H, Ar H, J = 8 Hz), 7.63 (d, 2H, Ar H, J = 8 Hz), 8.26 (t, 1H, NH, J = 5 Hz), and 13.90 (s, 1H, NH) ppm; MS: 277[M^+–1]. Analysis calculated for $C_{13}H_{15}ClN_4O$ (278.74): C, 56.02; H, 5.42; and N, 20.10. Found: C, 56.15; H, 5.58; and N, 20.22.

*2-[(4-Chlorophenyl)-hydrazono]-2-cyano-N-hexyl-acetamide (**4e**).* Orange crystals from ethanol; yield 85%, mp 176°C; IR ν_{max} cm^{-1}: 3391 (NH), 3089 (CH aromatic), 2939 (CH aliphatic), 2212 (CN), and 1654 (C=O); ^{1}H NMR; ($CDCl_3$); δ = 0.60 (t, 3H, CH_3, J = 6 Hz), 1.30 (m, 6H, 3CH_2), 2.29 (m, 2H, CH_2, J = 7 Hz), 3.05 (q, 2H, CH_2, J = 7 Hz), 6.90 (t, 1H, NH, J = 5 Hz), 6.98 (dd, 2H, Ar H, J = 8 Hz), 7.18 (d, 2H, Ar H, J = 8 Hz), and 11.10 (s, 1H, NH) ppm; ^{13}C NMR; ($CDCl_3$); δ = 13.93, 22.36, 26.42, 29.53, 31.30 (hexyl carbons), 108.74, 128.83, 129.02, 140.75 (C_6H_4–Cl-*p*), 117.06 (CN), 157.30 (C=N–NH), and 160.56 (C=O) ppm; MS: 306 [M^+]. Analysis calculated for $C_{15}H_{19}ClN_4O$ (306.80): C, 58.73; H, 6.24; and N, 18.26. Found: C, 58.51; H, 6.15; and N, 18.40.

*N′-Benzyl-2-[(4-chlorophenyl)-hydrazono]-2-cyano-acetamide (**4f**).* Yellow crystals from ethanol; yield 85%, mp 129°C; IR ν_{max} cm^{-1}: 3336 (NH), 3032 (CH aromatic), 2928 (CH aliphatic), 2218 (CN), and 1643 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 4.29 (d, 2H, CH_2ph, J = 5 Hz), 7.23–7.36 (m, 5H, Ph–H), 7.41 (d, 2H, Ar–H, J = 8 Hz), 7.70 (d, 2H, Ar–H, J = 8 Hz), 9.12 (t, 1H, NH, J = 5 Hz), and 13.83 (s, 1H, NH) ppm; ^{13}C NMR; (DMSO-d_6); δ = 43.02 (CH_2ph), 107.22, 108.91, 111.87, 127.58 (C_6H_4Cl-*p*), 116.75 (CN), 127.95, 128.82, 128.91, 139.10 (phenyl carbons), 141.72 (C = N–NH), and 162.73 (C = O) ppm; MS: 311 [M^+–1]. Analysis calculated for $C_{16}H_{13}ClN_4O$ (312.76): C, 61.45; H, 4.19; and N, 17.91. Found: C, 61.65; H, 4.29; and N, 17.85.

*N′-Butyl-2-cyano-2-[(4-nitrophenyl)-hydrazono]-acetamide (**4g**)*. Orange crystals from ethanol; yield 89%, mp 144°C; IR ν_{max} cm^{-1}: 3242 (NH), 3072 (CH aromatic), 2957 (CH aliphatic), 2220 (CN), and 1660 (C = O); ^1H NMR; ($CDCl_3$); δ = 0.77 (t, 3H, CH_3, *J* = 7 Hz), 1.22 (m, 2H, CH_2, *J* = 7 Hz), 1.41 (m, 2H, CH_2, *J* = 7 Hz), 3.22 (q, 2H, CH_2, *J* = 7 Hz), 7.06 (t, 1H, NH, *J* = 5 Hz), 7.44 (d, 2H, Ar H, *J* = 8 Hz), 8.03 (d, 2H, Ar H, *J* = 8 Hz), and 11.60 (s, 1H, NH) ppm; ^{13}C NMR; ($CDCl_3$); δ = 13.78, 20.04, 31.11, 31.68 (butyl carbons), 110.57, 112.10, 123.37, 125.32, 134.72, 143.27 (C_6H_4–NO_2-*p*), 115.58 (CN), 147.42 (C = N–NH), and 160.04 (C = O) ppm; MS: 288 [M^+–1]. Analysis calculated for $C_{13}H_{15}N_5O_3$ (289.30): C, 53.97; H, 5.23; and N, 24.21. Found: C, 53.83; H, 5.42; and N, 24.22.

*2-Cyano-N-hexyl-2-[(4-nitrophenyl)-hydrazono]-acetamide (**4h**)*. Brown crystals from ethanol; yield 92%, mp 186°C; IR ν_{max} cm^{-1}: 3369 (NH), 3091 (CH aromatic), 2929 (CH aliphatic), 2218 (CN), and 1656 (C = O); ^1H NMR; (DMSO-d_6); δ = 0.84 (t, 3H, CH_3, *J* = 6 Hz), 1.26 (m, 6H, $3CH_2$), 1.49 (m, 2H, CH_2, *J* = 7 Hz), 3.21 (q, 2H, CH_2, *J* = 7 Hz), 7.80 (d, 2H, Ar H, *J* = 8 Hz), 8.19 (d, 2H, Ar H, *J* = 8 Hz), 8.50 (t, 1H, NH, *J* = 5 Hz), and 13.88 (s, 1H, NH) ppm; ^{13}C NMR; (DMSO-d_6); δ = 14.44, 22.59, 26.65, 29.74, 31.59 (hexyl carbons), 111.33, 112.51, 125.74, 143.13 (C_6H_4–NO_2-*p*), 116.32 (CN), 148.32 (C = N–NH), and 160.26 (C = O) ppm; MS: 316 [M^+–1]. Analysis calculated for $C_{15}H_{19}N_5O_3$ (317.35): C, 56.77; H, 6.03; and N, 22.07. Found: C, 56.69; H, 6.15; and N, 22.31.

*2-Cyano-N-cyclohexyl-2-[(4-nitrophenyl)-hydrazono]-acetamide (**4i**)*. Brown crystals from ethanol; yield 88%, mp 212°C; IR ν_{max} cm^{-1}: 3313 (NH), 3020 (CH aromatic), 2931 (CH aliphatic), 2214 (CN), and 1651 (C = O); ^1H NMR; (DMSO-d_6); δ = 1.09–410 (m, 11H, cyclohexyl H), 7.58 (d, 2H, Ar H, *J* = 8 Hz), 8.07 (d, 2H, Ar H, *J* = 8 Hz), 8.24 (d, 1H, NH, *J* = 7 Hz), and 13.71 (s, 1H, NH) ppm; MS: 314 [M^+–1]. Analysis calculated for $C_{15}H_{17}N_5O_3$ (315.33): C, 57.14; H, 5.43; and N, 22.21. Found: C, 57.26; H, 5.18; and N, 22.11.

*Preparation of **5a–h***

Method I (Δ). To a solution of hydroxylamine hydrochloride (0.1 mol) and hydrazono-2-cyanoacetamide derivatives **4a–i** (0.1 mol) in ethanol (50 mL), anhydrous sodium acetate (0.1 mol) was added and the reaction mixture was refluxed for 1 h. After concentration and cooling to room temperature, the solid product so-formed was filtered and re-crystallized from ethanol.

Method II (μω). A mixture of hydroxylamine hydrochloride (0.1 mol), hydrazono-2-cyanoacetamide derivatives **4a–i** (0.1 mol), anhydrous sodium acetate, and drops of ethanol was irradiated under Mw irradiation at 460 W for 1–5 min, until no starting materials were present (monitored by TLC) in 1-min intervals. The reaction mixture was left to cool to room temperature. The solid product so-formed was filtered and re-crystallized from ethanol.

Method III (Us). To a solution of hydroxylamine hydrochloride (0.1 mol) and hydrazono-2-cyanoacetamide derivatives **4a–i** (0.1 mol) in ethanol (50 mL), anhydrous sodium acetate (0.1 mol) was added and the reaction mixture was irradiated under Us irradiation at 40°C for 30 min, until no starting materials were present (monitored by TLC). The solid product so-formed was filtered and re-crystallized from ethanol.

*2-{N-[Hexylcarbamoyl-(N-hydroxycarbamimidoyl)-methylene]-hydrazino}-benzoic acid methyl ester (**5a**)*. Yellow crystals from ethanol; mp 130°C; IR ν_{max} cm^{-1}: 3587 (br OH), 3456, 3420 (NH_2), 3379 (br 2NH), 3097 (CH aromatic), 2955 (CH aliphatic), 1701 (C = O ester), and 1651 (C = O amide); ^1H NMR; ($CDCl_3$); δ = 0.87 (t, 3H, CH_3, *J* = 6 Hz), 1.35 (m, 6H, $3CH_2$), 1.59 (m, 2H, CH_2, *J* = 7 Hz), 3.34 (q, 2H, CH_2, *J* = 7 Hz), 3.87 (s, 3H, ester CH_3), 6.52 (s, 2H, NH_2), 6.98 (t, 1H, NH, *J* = 5 Hz), 7.16 (t, 1H, Ar H, *J* = 7 Hz), 7.50 (t, 1H, Ar H, *J* = 7 Hz), 7.70 (d, 1H, Ar H, *J* = 8 Hz), 7.96 (d, 1H, Ar H, *J* = 8 Hz), 13.88 (s, 1H, NH), and 14.21 (s, 1H, OH) ppm; ^{13}C NMR; ($CDCl_3$); δ = 14.10, 22.68, 26.76, 29.68, 31.56, 39.48 (hexyl carbons), 52.33 (ester CH_3), 113.98, 114.65, 121.31, 122.23, 131.34, 134.29 ($C_6H_4COOCH_3$-*o*), 145.30 (C = N–NH), 151.35 (C = N–OH), 165.70 (HN–C = O), and 167.29 ($COOCH_3$) ppm; MS: 363 [M^+]. Analysis calculated for $C_{17}H_{25}N_5O_4$ (363.42): C, 56.19; H, 6.93; and N, 19.27. Found: C, 56.31; H, 6.45; and N, 19.55.

*2-{N-[Cyclohexylcarbamoyl-(N-hydroxycarbamimidoyl)-methylene]-hydrazino}-benzoic acid methyl ester (**5b**)*. Brown crystals from ethanol; mp 134°C; IR

ν_{max} cm^{-1}: 3520 (br OH), 3423, 3401 (NH_2), 3279 (NH), 3088 (CH aromatic), 2933 (CH aliphatic), and 1650 (2C = O); MS: 361 [M^+]. Analysis calculated for $C_{17}H_{23}N_5O_4$ (361.40): C, 56.50; H, 6.41; and N, 19.38. Found: C, 56.36; H, 6.70; and N, 19.25.

*N-Butyl-2-[(4-chlorophenyl)-hydrazono]-2-(N-hydroxycarbamimidoyl)-acetamide (**5c**).* Orange crystals from ethanol; mp 86°C; IR ν_{max} cm^{-1}: 3568 (OH), 3498, 3471 (NH_2), 3379, 3356 (NH), 3047 (CH aromatic), 2958 (CH aliphatic), and 1643 (C = O); ^{1}H NMR; (DMSO-d_6); δ = 0.89 (t, 3H, CH_3, J = 7 Hz), 1.30 (m, 2H, CH_2, J = 7 Hz), 1.46 (m, 2H, CH_2, J = 7 Hz), 3.21 (q, 2H, CH_2, J = 7 Hz), 6.72 (s, 2H, NH_2), 7.29 (d, 2H, Ar H, J = 8 Hz), 7.44 (d, 2H, Ar H, J = 8 Hz), 8.32 (t, 1H, NH, J = 5 Hz), 10.11 (s, 1H, NH), and 13.48 (s, 1H, OH) ppm; ^{13}C NMR; (DMSO-d_6); δ = 14.20, 19.10, 20.24, 20.29 (butyl carbons), 116.21, 122.76, 126.39, 129.73 (C_6H_4–Cl-p), 142.50 (C = N–NH), 151.05 (C = N–OH), and 163.85 (C = O) ppm; MS: 310 [M^+–1]. Analysis calculated for $C_{13}H_{18}ClN_5O_2$ (311.77): C, 50.08; H, 5.82; and N, 22.46. Found: C, 50.45; H, 5.75; and N, 22.36.

*2-[(4-Chlorophenyl)-hydrazono]-N-hexyl-2-(N-hydroxycarbamimidoyl)-acetamide (**5d**).* Colorless crystals from ethanol; mp 82°C; IR ν_{max} cm^{-1}: 3585 (br OH), 3470, 3434 (NH_2), 3392 (NH), 3085 (CH aromatic), 2918 (CH aliphatic), and 1636 (C = O); ^{1}H NMR; (DMSO-d_6); δ = 0.84 (t, 3H, CH_3, J = 6 Hz), 1.05 (m, 6H, $3CH_2$), 1.43 (quintet, 2H, CH_2, J = 7 Hz), 3.17 (t, 2H, CH_2, J = 7 Hz), 6.66 (s, 2H, NH_2), 7.26 (d, 2H, Ar H, J = 8 Hz), 7.39 (d, 2H, Ar H, J = 8 Hz), 8.22 (t, 1H, NH, J = 5 Hz), 13.36 (s, 1H, NH), and 13.52 (s, 1H, OH) ppm; MS: 338 [M^+–1]. Analysis calculated for $C_{15}H_{22}N_5O_2Cl$ (339.83): C, 53.02; H, 6.53; and N, 20.61. Found: C, 53.31; H, 6.45; and N, 20.55.

*N-Benzyl-2-[(4-chlorophenyl)-hydrazono]-2-(N-hydroxycarbamimidoyl)-acetamide (**5e**).* Yellow crystals from ethanol; mp 135°C; IR ν_{max} cm^{-1}: 3580 (OH), 3483, 3432 (NH_2), 3390 (NH), 3091 (CH aromatic), 2923 (CH aliphatic), and 1640 (C = O); ^{1}H NMR; ($CDCl_3$); δ = 4.51 (d, 2H, CH_2ph, J = 5 Hz), 6.65 (s, 2H, NH_2), 7.31–7.80 (m, 9H, Ar–H), 9.62 (t, 1H, NH, J = 5 Hz), 13.10 (s, 1H, NH), and 13.98 (s, 1H, OH) ppm; MS: 344 [M^+–1]. Analysis calculated for $C_{16}H_{16}N_5O_2Cl$ (345.79): C, 55.58; H, 4.66; and N, 20.25. Found: C, 55.70; H, 4.52; and N, 20.16.

*N-Butyl-2-(N-hydroxycarbamimidoyl)-2-[(4-nitrophenyl)-hydrazono]-acetamide (**5f**).* Brown crystals from ethanol; mp185°C; IR ν_{max} cm^{-1}: 3535 (OH), 3471, 3451 (NH_2), 3391 (NH), 3052 (CH aromatic), 2918 (CH aliphatic), and 1643 (C = O); ^{1}H NMR; (DMSO-d_6); δ = 0.87 (t, 3H, CH_3, J = 7 Hz), 1.32 (m, 2H, CH_2, J = 7 Hz), 1.45 (m, 2H, CH_2, J = 7 Hz), 3.20 (q, 2H, CH_2, J = 7 Hz), 6.62 (s, 2H, NH_2), 7.57 (d, 2H, Ar H, J = 8 Hz), 8.16 (d, 2H, Ar H, J = 8 Hz), 9.41 (t, 1H, NH, J = 5 Hz), 13.10 (s, 1H, NH), and 13.65 (s, 1H, OH) ppm; MS: 322 [M^+]. Analysis calculated for $C_{13}H_{18}N_6O_4$ (322.33): C, 48.44; H, 5.63; and N, 26.07. Found: C, 48.22; H, 5.75; and N, 26.15.

*N-Hexyl-2-(N-hydroxycarbamimidoyl)-2-[(4-nitrophenyl)-hydrazono]-acetamide (**5g**).* Brown crystals from ethanol; mp 195°C; IR ν_{max} cm^{-1}: 3548 (OH), 3491, 3442 (NH_2), 3385 (NH), 3049 (CH aromatic), 2922 (CH aliphatic), and 1653 (C = O); MS: 350 [M^+]. Analysis calculated for $C_{15}H_{22}N_6O_4$ (350.38): C, 51.42; H, 6.33; N, 23.99. Found: C, 51.56; H, 6.29; and N, 23.81.

*N-Cyclohexyl-2-(N-hydroxycarbamimidoyl)-2-[(4-nitrophenyl)-hydrazono]-acetamide (**5h**).* Brown crystals from ethanol; mp 282°C; IR ν_{max} cm^{-1}: 3501 (br OH), 3454, 3398 (NH_2), 3242 (NH), 3103 (CH aromatic), 2925 (CH aliphatic), and 1644 (C = O); ^{1}H NMR; (DMSO-d_6); δ = 1.11–1.65 (m, 6H, $3CH_2$), 1.78–2.12 (m, 4H, $2CH_2$), 3.61–3.89 (m, 1H, cyclohexyl CH), 6.62 (s, 2H, NH_2), 7.59 (d, 2H, Ar H, J = 8 Hz), 8.05 (d, 2H, Ar H, J = 8 Hz), 9.52 (d, 1H, NH, J = 7 Hz), 13.23 (s, 1H, NH), and 13.56 (s, 1H, OH) ppm; MS: 348 [M^+]. Analysis calculated for $C_{15}H_{20}N_6O_4$ (348.36): C, 51.72; H, 5.79; and N, 24.12. Found: C, 51.61; H, 5.50; and N, 24.38.

*Preparation of triazole compounds **7a–e***

Method I (Δ). To a solution of compounds **5c** and **5e–h** (0.1 mol) in DMF (10 mL), triethylamine (0.1 mol) was added. The reaction mixture was heated under reflux for 1 h. Then, it was left to cool to room temperature. The solid product so-formed was filtered and re-crystallized from ethanol.

Method II (μω). A mixture of compounds **5c** and **5e–h** (0.1 mol) and triethylamine (0.1 mol) was placed in a tightly closed tube and subjected to a Mw irradiation for 1–5 min until completion of the reaction (monitored by TLC). The reaction mixture was left to cool to room temperature. The solid product so-formed was filtered and re-crystallized from ethanol.

Method III (Us). Triethylamine (0.1 mol) was added to a solution of compounds **5c** and **5e–h** (0.1 mol) in

DMF (10 mL). The reaction mixture was irradiated under Us irradiation at 40°C for 1 h. Then, it was left to cool to room temperature. The solid product so-formed was filtered and re-crystallized from ethanol.

*5-Amino-2-(4-chlorophenyl)-2H-[1,2,3]triazole-4-carboxylic acid butyl amide (**7a**)*. Yellow crystals from ethanol; mp120°C; IR ν_{max} cm^{-1}: 3474, 3431 (NH_2), 3335 (NH), 3080 (CH aromatic), 2930 (CH aliphatic), and 1648 (C=O); ^{1}H NMR; ($CDCl_3$); δ = 0.93 (t, 3H, CH_3, $J=7$ Hz), 1.39 (m, 2H, CH_2, $J=7$ Hz), 1.57 (m, 2H, CH_2, $J=7$ Hz), 3.34 (q, 2H, CH_2, $J=7$ Hz), 6.69 (s, 2H, NH_2), 7.08 (d, 2H, Ar H, $J=8$ Hz), 7.26 (d, 2H, Ar H, $J=8$ Hz), and 9.28 (t, 1H, NH, $J=5$ Hz) ppm; ^{13}C NMR; ($CDCl_3$); δ = 13.87, 20.26, 31.34, 38.81 (butyl carbons), 115.44, 119.34, 128.06, 129.48 (C_6H_4–Cl-*p*), 141.46, 153.50 (triazole carbons), and 165.67 (C=O) ppm; MS: 293 [M^+]. Analysis calculated for $C_{13}H_{16}ClN_5O$ (293.76): C, 53.15; H, 5.49; N, 23.84. Found: C, 53.26; H, 5.35; and N, 23.80.

*5-Amino-2-(4-chlorophenyl)-2H-[1,2,3]triazole-4-carboxylic acid benzyl amide (**7b**)*. Brown crystals from ethanol; mp 137°C; IR ν_{max} cm^{-1}: 3461, 3430 (NH_2), 3221 (NH), 3021 (CH aromatic), 2920 (CH aliphatic), and 1642 (C=O); ^{1}H NMR; ($CDCl_3$); δ = 5.21 (d, 2H, CH_2ph, $J=5$ Hz), 6.67 (s, 2H, NH_2), 7.31–7.83 (m, 9H, Ar–H), and 7.97 (t, 1H, NH, $J=5$ Hz) ppm; MS: 327 [M^+]. Analysis calculated for $C_{16}H_{14}ClN_5O$ (327.78): C, 58.63; H, 4.31; and N, 21.37. Found: C, 58.60; H, 4.47; and N, 21.41.

*5-Amino-2-(4-nitrophenyl)-2H-[1,2,3]triazole-4-carboxylic acid butyl amide (**7c**)*. Brown crystals from ethanol; mp103°C; IR ν_{max} cm^{-1}: 3484, 3452 (NH_2), 3325 (NH), 3099 (CH aromatic), 2990 (CH aliphatic), and 1658 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 0.93 (t, 3H, CH_3, $J=7$ Hz), 1.35 (m, 2H, CH_2, $J=7$ Hz), 1.56 (m, 2H, CH_2, $J=7$ Hz), 3.41 (q, 2H, CH_2, $J=7$ Hz), 6.68 (s, 2H, NH_2), 7.19 (d, 2H, Ar H, $J=8$ Hz), 7.51 (d, 2H, Ar H, $J=8$ Hz), and 9.31 (t, 1H, NH, $J=5$ Hz) ppm; MS: 304 [M^+]. Analysis calculated for $C_{13}H_{16}N_6O_3$ (304.31): C, 51.31; H, 5.30; and N, 27.62. Found: C, 51.24; H, 5.42; and N, 27.51.

*5-Amino-2-(4-nitrophenyl)-2H-[1,2,3]triazole-4-carboxylic acid hexyl amide (**7d**)*. Brown crystals from ethanol; mp 176°C; IR ν_{max} cm^{-1}: 3492, 3386 (NH_2), 3344 (NH), 3053 (CH aromatic), 2920 (CH aliphatic), and 1653 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 0.84 (t, 3H, CH_3, $J=6$ Hz), 1.27 (m, 6H, 3CH_2), 1.48 (m, 2H, CH_2, $J=7$ Hz), 3.19 (t, 2H, CH_2, $J=7$ Hz), 6.18 (s, 2H, NH_2), 7.58 (d, 2H, Ar H, $J=8$ Hz), 8.12 (d, 2H, Ar H, $J=8$ Hz), and 9.40 (t, 1H, NH, $J=5$ Hz) ppm; MS: 332 [M^+]. Analysis calculated for $C_{15}H_{20}N_6O_3$ (332.37): C, 54.21; H, 6.07; and N, 25.29. Found: C, 54.29; H, 6.16; and N, 25.32.

*5-Amino-2-(4-nitrophenyl)-2H-[1,2,3]triazole-4-carboxylic acid cyclohexyl amide (**7e**)*. Brown crystals from ethanol; mp167°C; IR ν_{max} cm^{-1}: 3479, 3448 (NH_2), 3367 (NH), 3078 (CH aromatic), 2924 (CH aliphatic), and 1651 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 1.07–1.67 (m, 6H, 3CH_2), 1.71–2.86 (m, 4H, 2CH_2), 2.93–3.80 (m, 1H, cyclohexyl CH), 7.20–8.28 (m, 4H, Ar–H), 6.70 (s, 2H, NH_2), and 9.32 (d, 1H, NH, $J=7$ Hz) ppm; ^{13}C NMR; (DMSO-d_6); δ = 24.59, 25.62, 29.75, 32.48 (cyclohexyl carbons), 113.56, 125.01, 125.33, 125.96 (C_6H_4–NO_2-*p*), 142.38, 147.92 (triazole carbons), and 162.33 (C=O) ppm; MS: 330 [M^+]. Analysis calculated for $C_{15}H_{18}N_6O_3$ (330.35): C, 54.54; H, 5.49; and N, 25.44. Found: C, 54.39; H, 5.35; and N, 25.20.

*General method to reaction of triazole compounds **7a–e** with dimethylformamide dimethylacetal (DMF DMA)*

Method I (Δ). To a solution of compounds **7a–e** (0.1 mol) in dry xylene (20 mL), DMF DMA (0.1 mol) was added. The reaction mixture was refluxed for 30 min. Then it was left to cool to room temperature, and poured into ice-cold water. The solid product so-formed was filtered and re-crystallized from ethanol.

Method II (μω). A mixture of compounds **7a–e** (0.1 mol) and of DMF DMA (0.1 mol) was placed in a tightly closed tube, and subjected to a Mw irradiation for 2–5 min until completion of the reaction (monitored by TLC). The reaction mixture was left to cool to room temperature, and then poured into ice-cold water. The solid product so-formed was filtered and re-crystallized from ethanol.

*2-(4-Chlorophenyl)-6-hexyl-2,6-dihydro-[1,2,3]triazolo-[4,5-d]pyrimidin-7-one (**10a**)*. Yellow crystals from ethanol; mp 78°C; IR ν_{max} cm^{-1}: 3089 (CH aromatic), 2925 (CH aliphatic), and 1645 (C=O); ^{1}H NMR; ($CDCl_3$); δ = 0.91 (t, 3H, CH_3, $J=6$ Hz), 1.29 (m, 6H, 3CH_2), 1.47 (m, 2H, CH_2, $J=7$ Hz), 3.29 (t, 2H, CH_2, $J=7$ Hz), 7.05 (s, 1H, pyrimidine CH), 7.32 (d, 2H, Ar, H, $J=8$ Hz), and 7.61 (d, 2H, Ar, H, $J=8$ Hz) ppm; MS: 331 [M^+]. Analysis calculated for $C_{16}H_{18}ClN_5O$ (331.81): C, 57.92; H, 5.47; and N, 21.11. Found: C, 57.75; H, 5.25; and N, 21.47.

*6-Butyl-2-(4-nitrophenyl)-2,6-dihydro-[1,2,3]triazolo-[4,5-d]pyrimidin-7-one (**10b**)*. Brown crystals from ethanol; mp 190°C; IR ν_{max} cm^{-1}: 3092 (CH aromatic), 2939 (CH aliphatic), and 1670 (C=O);

^{1}H NMR; ($CDCl_3$); δ = 0.89 (t, 3H, CH_3, J = 6 Hz), 1.40 (m, 2H, CH_2, J = 7 Hz), 1.66 (m, 2H, CH_2, J = 7 Hz), 3.49 (q, 2H, CH_2, J = 7 Hz), 7.15 (s, 1H, pyrimidine CH), 7.31 (d, 2H, Ar, H, J = 8 Hz), and 7.65 (d, 2H, Ar, H, J = 8 Hz) ppm; MS: 314 [M^+]. Analysis calculated for $C_{14}H_{14}N_6O_3$ (314.31): C, 53.50; H, 4.49; and N, 26.74. Found: C, 53.72; H, 4.64; and N, 26.59.

*Preparation of pyrazole compounds **13a–e***

Method I (Δ). To a solution of compounds **4a–i** (0.1 mol) in triethylamine (20 mL) and chloroacetonitrile (0.1 mol) were refluxed for 30 min. The reaction mixture was left to cool to room temperature, and then poured into ice-cold water. The solid product so-formed was filtered and re-crystallized from ethanol.

Method II (μω). To a mixture of compounds **4a–i** (0.1 mol) and chloroacetonitrile (0.1 mol), a few drops from triethylamine were added, then the mixture was placed in a tightly closed tube and subjected to a Mw irradiation for 2 min until completion of the reaction (monitored by TLC). The reaction mixture was left to cool to room temperature, and then poured into ice-cold water. The solid product so-formed was filtered and re-crystallized from ethanol.

Method III (Us). Chloroacetonitrile (0.1 mol) was added to a solution of compounds **4a–i** (0.1 mol) in triethyl amine (20 mL), under Us irradiation at 40°C for 30 min. The reaction mixture was left to cool to room temperature, and then poured into ice-cold water. The solid product so-formed was filtered and re-crystallized from ethanol.

*2-(4-Amino-5-cyano-3-cyclohexylcarbamoyl-pyrazol-1-yl)-benzoic acid methyl ester (**13a**).* Brown crystals from ethanol; mp >300°C; IR ν_{max} cm^{-1}: 3438, 3395, 3277 (NH, NH_2), 3088 (CH aromatic), 2933 (CH aliphatic), 2261 (CN), and 1648 (C=O); ^{1}H NMR; ($CDCl_3$); δ = 1.18–3.77 (m, 11H, cyclohexyl H), 3.93 (s, 3H, ester CH_3), 6.67 (s, 2H, NH_2), 7.20 (t, 1H, Ar H, J = 7 Hz), 7.44 (t, 1H, Ar H, J = 7 Hz), 7.63 (d, 1H, Ar H, J = 8 Hz), 7.94 (d, 1H, Ar H, J = 8 Hz), and 9.75 (t, 1H, NH, J = 7 Hz) ppm; MS: 367 [M^+]. Analysis calculated for $C_{19}H_{21}N_5O_3$ (367.41): C, 62.11; H, 5.76; and N, 19.06. Found: C, 62.26; H, 5.80; and N, 19.17

*4-Amino-1-(4-chlorophenyl)-5-cyano-1H-pyrazole-3-cyclohexylic acid butyl amide (**13b**).* Brown crystals from ethanol; mp 117°C; IR ν_{max} cm^{-1}: 3472, 3378, 3329 (NH, NH_2), 3020 (CH aromatic), 2957 (CH aliphatic), 2212 (CN), and 1644 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 0.91 (t, 3H, CH_3, J = 7 Hz), 1.37 (m, 2H, CH_2, J = 7 Hz), 1.54 (m, 2H, CH_2, J = 7 Hz), 3.38 (q, 2H, CH_2, J = 7 Hz), 6.71 (s, 2H, NH_2), 7.43 (d, 2H, Ar H, J = 8 Hz), 7.59 (d, 2H, Ar H, J = 8 Hz), and 9.34 (t, 1H, NH, J = 5 Hz) ppm; ^{13}C NMR; (DMSO-d_6); δ = 13.78, 20.14, 31.80, 38.71 (butyl carbons), 116.93 (CN), 110.93, 123.07, 129.66, 132.87 (C_6H_4–Cl-*p*), 134.48, 137.01, 143.09 (pyrazole carbons), and 162.25 (C=O) ppm; MS: 317 [M^+]. Analysis calculated for $C_{15}H_{16}ClN_5O$ (317.78): C, 56.70; H, 5.08; and N, 22.04. Found: C, 56.62; H, 5.20; and N, 22.29.

*4-Amino-1-(4-chlorophenyl)-5-cyano-1H-pyrazole-3-cyclohexylic acid hexyl amide (**13c**).* Brown crystals from ethanol; mp 125°C; IR ν_{max} cm^{-1}: 3450, 3428, 3388 (NH, NH_2), 3109 (CH aromatic), 2926 (CH aliphatic), 2210 (CN), and 1645 (C=O); ^{1}H NMR; (DMSO-d_6); δ = 0.88 (t, 3H, CH_3, J = 6 Hz), 1.30 (m, 6H, 3CH_2), 1.57 (m, 2H, CH_2, J = 7 Hz), 3.38 (t, 2H, CH_2, J = 7 Hz), 6.49 (s, 2H, NH_2), 7.15 (d, 2H, Ar H, J = 8 Hz), 7.36 (d, 2H, Ar H, J = 8 Hz), and 8.96 (t, 1H, NH, J = 5 Hz) ppm; MS: 345 [M^+]. Analysis calculated for $C_{17}H_{20}ClN_5O$ (345.83): C, 59.04; H, 5.83; and N, 20.25. Found: C, 59.17; H, 5.42; and N, 20.54.

*4-Amino-1-(4-chlorophenyl)-5-cyano-1H-pyrazole-3-cyclohexylic acid benzyl amide (**13d**).* Brown crystals from ethanol; mp 130°C; IR ν_{max} cm^{-1}: 3371, 3326, 3299 (NH, NH_2), 3064 (CH aromatic), 2923 (CH aliphatic), 2225 (CN), and 1644 (C=O) cm^{-1}; ^{1}H NMR; (DMSO-d_6); δ = 4.28 (d, 2H, phCH_2, J = 5 Hz), 6.21 (s, 2H, NH_2), 7.25–8.10 (m, 9H, Ar–H), and 8.89 (t, 1H, NH, J = 5 Hz) ppm; MS: 351 [M^+]. Analysis calculated for $C_{18}H_{14}ClN_5O$ (351.80): C, 61.46; H, 4.01; and N, 19.91. Found: C, 61.54; H, 4.20; and N, 19.83.

*4-Amino-5-cyano-1-(4-nitrophenyl)-1H-pyrazole-3-cyclohexylic acid hexyl amide (**13e**).* Brown crystals from ethanol; mp 153°C; IR ν_{max} cm^{-1}: 3401, 3358, 3226 (NH, NH_2), 3090 (CH aromatic), 2927 (CH aliphatic), 2218 (CN), and 1660 (C=O); ^{1}H NMR; ($CDCl_3$); δ = 0.88 (t, 3H, CH_3, J = 6 Hz), 1.32 (m, 6H, 3CH_2), 1.58 (m, 2H, CH_2, J = 7 Hz), 3.40 (t, 2H, CH_2, J = 7 Hz), 6.59 (s, 2H, NH_2), 7.40 (d, 2H, Ar H, J = 8 Hz), 7.95 (d, 2H, Ar H, J = 8 Hz), and 9.62 (t, 1H, NH, J = 5 Hz) ppm; MS: 356 [M^+]. Analysis calculated for $C_{17}H_{20}N_6O_3$ (356.39): C, 57.29; H, 5.66; and N, 23.58. Found: C, 57.20; H, 5.72; and N, 23.68.

Table 2. Crystal data of compound **4c**.

Chemical formula	$C_{17}H_{20}N_4O_3$
M	328.372
System	Monoclinic
space group	$P2_1/c$
a	9.9877 (6) Å
b	18.0058 (8) Å
c	9.8843 (4) Å
α	90.00°
β	96.078 (2)°
V	1767.6 (2) $Å^3$
Z	4
Dc	1.234 mg m^{-3}
κ	2.910–24.713°
μ(Mo–Kα)	0.09 mm^{-1}
T	298 K
Measured reflections	4990
Independent reflections	3497
Observed reflections	1335
R_{int}	0.031
R(all)	0.140
wR(ref)	0.184
wR(all)	0.238
S(ref)	1.429
S(all)	1.364
D/s_{max}	0.027
Dr_{max}	0.38e $Å^3$
Dr_{min}	−0.41e $Å^3$

X-ray crystallography

A single crystal of compound **4c** 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) (*21*) Mo–Kα radiation (λ = 0.71073 Å) and a graphite monochromator were used for data collection. The chemical formula and ring labeling system is shown in Figure 1. Crystallographic data (Table 2, excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 686225. 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].

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(26) Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications nos. CCDC. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).
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