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ULTRASONIC-ASSISTED ONE-POT SYNTHESIS OF PYRAZOLO[1,2-*a*][1,2,4]TRIAZOLE-1,3-DIONES

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Abstract – A facile and efficient one-pot three-component synthesis of pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones via condensation reaction between malononitrile, 4-phenylurazole and aromatic aldehydes in ethanol under the catalytic effect of triethylamine and ultrasonic-irradiation conditions has been explored. The advantages of this protocol include a simple workup, high rates, use of inexpensive non-toxic catalyst, improved yields, and use of ethanol as a relatively environmentally benign solvent.

INTRODUCTION

With respect to a wide number of books,[1] and articles[2] published in recent years, applications of ultrasounds in a so called "sonochemistry" have attracted much attention since it offers a versatile and challenging technique in organic synthesis.[3] Ultrasonic irradiation has been demonstrated to be quite useful in a large variety of organic synthesis, providing high yields, short reaction times and mild conditions.[1,2] On the other hand, one-pot multi-component reactions have proven to be more advantageous over conventional linear-type synthesis,[4,5] since the multi-step reactions are usually subjected to complex isolation procedures and produce significant amounts of waste materials. In addition, multi-component processes provide rapid and efficient approach to organic transformations including diverse synthesis of polyfunctionalized heterocycles.[6] These compounds are of significant biological and pharmaceutical importance that play vital roles in the drug discovery process.[4,6] Polyfunctionalized heterocyclic fragments form important moieties of a large number of a variety of natural products and medicinal agents.[4,6] As a result, the multi-component synthesis of polyfunctionalized heterocyclic compounds is progressively becoming more challenging in organic and medicinal chemistry.[7]

Nitrogen-containing heterocyclic compounds are widespread in nature and have received considerable attention due to their biological activities as pharmaceuticals, agrochemicals and functional materials.[7-9]

Among these, heterocycles possessing the urazole (1,2,4-triazolidine-3,5-diones) moieties have attracted considerable attention as useful synthetic reagents in the laboratory as well as in industry. Urazoles have found immense technological applications in the manufacture of herbicides and antifungal compounds.[10] They have been also employed in the production of automobile air bags and in plastics as blowing agent as well as in other polymeric materials.[11,12] In addition, 1,2,4-triazolidine-3,5-dione moiety has a documented prominence in a number of biological and medicinal agents such as antitumor drugs,[13] and hypolipidemically active compounds,[14] pesticides[15] and insecticides.[16] Novel methods for preparing heterocycles containing an urazole moiety have attracted much interest in recent years.[17] On the other hand, pyrazoles are another important class of *N*-heterocyclic compounds of diverse structures with a wide range of interesting biological properties, such as analgesic, anti-pyretic, anti-bacterial, anti-inflammatory, anti-diabetic and psychoanaleptic activities.[18]

Considering the important biological properties of the fused pyrazolourazoles, a number of methods have been previously reported for the synthesis of these heterocycles.[19] In 2010, Nikpassand *et al.*,[20] have reported a convenient ultrasound-promoted regioselective synthesis of fused polycyclic 4-aryl-3-methyl-4,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridines. Recently, Pizzuti and his co-workers have efficiently utilized ultrasound in the synthesis of novel 4,5-dihydro-1*H*-pyrazole derivatives.[21] Also, a convenient protocol for the hydrochloric acid-catalyzed synthesis of 5-aryl-1,3-diphenylpyrazoles under ultrasound irradiation has been reported.[22] A one-pot easy conversion of Baylis-Hillman adducts into arylpyrazoles under ultrasound irradiation have been recently reported.[23]

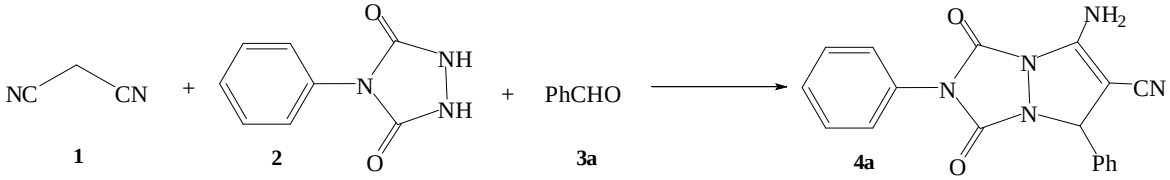
As part of our ongoing efforts on the synthesis of pyrazole derivatives,[24] we report herein a one-pot three-component condensation reaction between malononitrile, 4-phenylurazole and aromatic aldehydes under catalytic effect of triethylamine and ultrasonic-irradiation conditions as a new approach for the synthesis of new derivatives of pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones.

RESULTS AND DISCUSSION

With regard to the previous reports on three-component reactions for the synthesis of fused-ring heterocycles including pyrazole-fused heterocycles,[25-30] we were encouraged to preliminary examine polycondensation reaction of a mixture of malononitrile **1**, 4-phenylurazole **2**, and benzaldehyde **3a** in ethanol using a catalytic amount of triethylamine as an inexpensive and readily available catalyst under ultrasonic irradiation conditions. In this reaction, pyrazolo[1,2-*a*][1,2,4]triazole-1,3-dione **4a** was afforded in 93% yield after 45 min irradiation at 50 °C. To achieve suitable reaction conditions, i.e., lower reaction times and temperature for the synthesis of pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones **4**, various solvents and reaction conditions were investigated in the reaction of malononitrile **1**, 4-phenylurazole **2**, and benzaldehyde **3a** as a model reaction (Table **1**). As shown in Table **1**, the reaction worked out best at

50 °C under ultrasonic irradiation with a 20 mol% Et_3N as the catalyst. Effects of solvents on the yield of the product **4a** were tested at ultrasonic-irradiation conditions. Ethanol (93%) was a much better solvent in terms of yields than H_2O (60%), acetonitrile (20%) and dichloroethane (< 10%). It is to mention that the starting materials in the case of the solvents acetonitrile and dichloroethane were remained intact and no by-products were detected. It was observed that, using lower or higher amounts of catalyst under the same reaction time and temperature resulted in lower yields (Table **1**). To study the effect of temperature, the reaction was also performed at various temperatures (rt, 30, 40, 50 and 60 °C) under sonication. Apparently, higher reaction temperature did not affect the reaction yield (Table **1**). When the reaction was carried out in the absence of the catalyst, no detectable amount of respective product was formed and the starting materials remained almost intact. To show the role of ultrasound, the reaction was investigated without ultrasonic irradiation at the same temperature (50 °C) in various solvents. In all cases it was observed that the use of ultrasound leads to the faster reaction and higher yields.

Table 1. Effect of reaction conditions.[a]

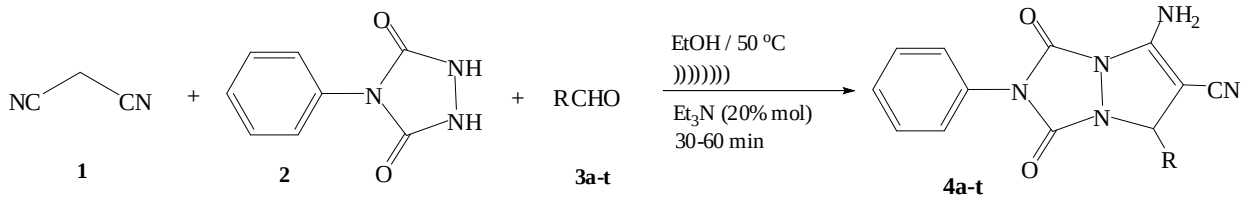


Entry	Conditions	Method	Catalyst (mol%)	Time (min)	Yield (%)
1	EtOH / 50 °C	ultrasound	None	240	trace
2	EtOH / 50 °C	ultrasound	Et_3N (10)	60	55
3	EtOH/ 50 °C	ultrasound	Et_3N (20)	45	93
4	EtOH / 50 °C	ultrasound	Et_3N (30)	45	94
5	EtOH / 60 °C	ultrasound	Et_3N (20)	60	94
6	EtOH / 40 °C	ultrasound	Et_3N (20)	60	86
7	EtOH / 30 °C	ultrasound	Et_3N (20)	60	<20
8	EtOH / rt	ultrasound	Et_3N (20)	60	trace
9	EtOH / 50 °C	high speed stirring	Et_3N (30)	240	trace
10	H_2O / 50 °C	ultrasound	Et_3N (20)	60	60
11	H_2O / 50 °C	high speed stirring	Et_3N (20)	240	trace
12	MeCN / 50 °C	ultrasound	Et_3N (20)	60	20
13	MeCN / 50 °C	high speed stirring	Et_3N (20)	240	trace
14	$ClCH_2CH_2Cl$ / 50 °C	ultrasound	Et_3N (20)	60	<10
15	1,2-$Cl_2C_2H_4$ / 50 °C	high speed stirring	Et_3N (20)	240	trace

[a] Malononitrile (1 mmol), 4-phenylurazole (1 mmol), benzaldehyde (1 mmol).

This achievement encouraged us to extend this reaction to a variety of aromatic aldehydes **3b-p** under similar conditions (EtOH/Et_3N/ultrasound), furnishing the respective pyrazolo[1,2-*a*][1,2,4]triazole-1,3-

diones **4b-p** in good to excellent yields in 30-60 min (Scheme **1**). The results are summarized in Table **2**. The structures of the products **4a-p** were fully established by their spectral (^{1}H and ^{13}C NMR, IR, MS) and elemental analysis.



Scheme 1

It is interesting to note that, the attempt to react the aliphatic aldehydes such as propanal **3q**, 3-phenylpropanal **3r**, *n*-heptanal **3s,** and *n*-octanal **3t** for the synthesis of their respective pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones **4q-t** under the same reaction conditions was failed (Table **2**). ^{1}H NMR and IR spectral analysis of the reaction mixtures indicated no sign of the formation of respective products and all three components of the reaction mixtures were found intact. This implies that the present protocol cannot be suitable for the synthesis of pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones derived from aqliphatic aldehydes. The lack of reactivity between the aliphatic aldehydes and malononitrile has already been reported by X. Lu *et al*. in the one-pot synthesis of cyclopentenes.[31]

We were also interested in using similar reaction conditions (EtOH/Et_3N/ultrasound), for the one-pot reaction of ethyl cyanoacetate with benzaldehyde **3** and 4-phenylurazole **2**, but unfortunately the reactions were found sluggish and no pyrazolotriazole compound was detected.

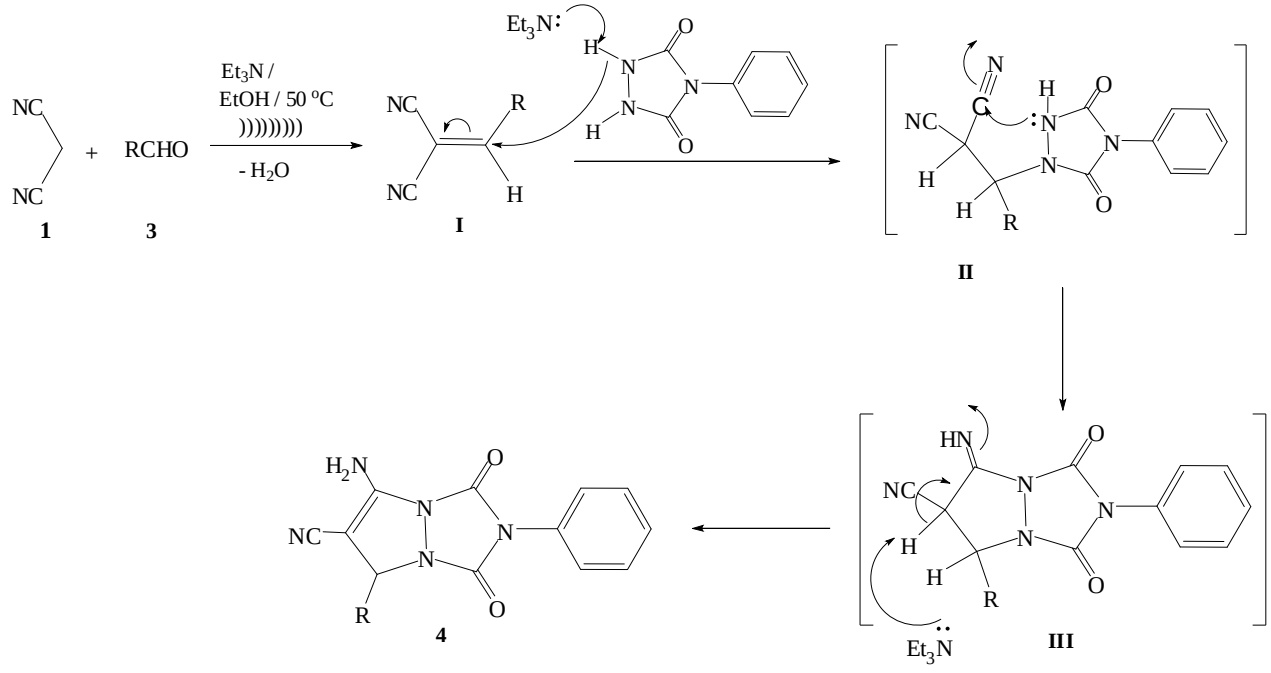
Table 2. Ultrasonic-assisted synthesis of 1*H*-pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones.[a]

Product 4	R	Time (min)	Yield (%)[b]
a	Ph	45	93
b	2-ClC_6H_4	30	92
c	3-ClC_6H_4	30	90
d	4-ClC_6H_4	30	91
e	2,4-$Cl_2C_6H_3$	60	86
f	2-$NO_2C_6H_4$	30	91
g	3-$NO_2C_6H_4$	30	90
h	4-$NO_2C_6H_4$	30	93
i	4-FC_6H_4	60	85
j	4-MeC_6H_4	60	83
k	2-BrC_6H_4	30	90
l	3-BrC_6H_4	30	94
m	4-BrC_6H_4	30	92

n	pyridin-4-yl	45	87
o	pyridin-3-yl	30	91
p	4-NCC_6H_4	60	90
q	Et	120	-
r	3-PhC_2H_4	120	-
s	*n*-C_6H_{13}	120	-
t	*n*-C_7H_{15}	120	-

[a] Malononitrile (1 mmol), 4-phenylurazole (1 mmol), aldehyde (1 mmol), triethylamine (0.02 g, 20 mol%), ultrasound, reaction temperature 50 °C.
[b] Isolated yields.

A possible mechanism for the formation of **4a-t** is proposed in Scheme 2. In this process the aldehyde **3** initially condenses with malononitrile **1** under the catalytic effect of Et_3N to afford the dehydrated condensed malononitrile derivative **I**. This step can be regarded as Knoevenagel addition. Then the subsequent Michael type addition of the 4-phenylurazole **2** to **I** occurs to give the intermediate **II** followed by successive cyclization to **III** and Et_3N-catalyzed isomerization to afford the corresponding product **4a-t**.



Scheme 2

In summary, we have developed a rapid and reliable synthetic procedure that provides access to hitherto unknown pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones **4a-p** in high yields and short reaction times by a three-component cyclo-condensation reaction of aromatic aldehydes, malononitrile and 4-phenylurazole using Et_3N as an inexpensive and readily available catalyst under ultrasonic irradiation.

EXPERIMENTAL

Chemicals used in this work were purchased from Fluka and Merk chemical companies and used without purification. IR spectra were recorded on a Shimadzu 435-U-04 FT spectrophotometer from KBr pellets. ^{1}H and ^{13}C NMR spectra were measured for samples in DMSO-d_6 with a 500 MHz Bruker instrument at 500.13 and 125.77 MHz respectively, using Me_4Si as internal standard. Mass spectra were recorded with a spectrometer FINNIGAN-MAT 8430 operating at an ionization potential of 70 ev. Melting points were measured on a SMPI apparatus. Elemental analysis for C, H and N atoms were performed using a Perkin–Elmer 2400 series analyzer. Ultrasonication was performed in a TRANSSONI 660/H ultrasound cleaner with a frequency of 35 KHz and an output power of 70 W. The reactions were performed in open vessels.

Typical procedure for the synthesis of pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones (4):

A mixture of malononitrile (0.07 g, 1 mmol), benzaldehyde (0.12 g, 1 mmol), 4-phenylurazole (0.18 g, 1 mmol), and Et_3N (0.02 g, 20% mol) in EtOH (10 mL) was sonicated at 50 °C for 45 min. After the completion of the reaction as monitored by TLC analysis, the reaction mixture was filtered and the precipitate was washed with ethanol (2 × 3 ml) to afford almost a pure product **4a**. The structures of the products **4a-p** were fully established by their spectral (^{1}H and ^{13}C NMR, IR, MS) and elemental analysis as given below.

7-1,3-dioxo-2,5-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4a)

White powder; mp >210 °C; IR (KBr) (ν_{max}/cm^{-1}): 3431, 3317, 2191, 1774, 1712. MS, m/z (%): 331 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 5.95 (1H, s, CH), 7.08–8.12 (12H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 61.2, 63.3, 116.2, 126.1, 126.9, 127.7, 128.3, 128.5, 128.7, 129.5, 129.8, 130.2, 130.5, 133.4, 145.1, 150.1, 150.5, 153.3. *Anal*. Calcd for $C_{18}H_{13}N_5O_2$: C, 65.25; H, 3.93; N, 21.15%. Found: C, 65.21; H, 3.86; N, 21.08%.

7-Amino-5-(2-chlorophenyl)-1,3-dioxo-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4b)

White powder; mp >218 °C; IR (KBr) (ν_{max}/cm^{-1}): 3394, 3315, 2202, 1778, 1718. MS, m/z (%): 365 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 6.27 (1H, s, CH), 7.39–7.66 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 61.1, 61.6, 116.0, 125.9, 126.8, 128.0, 128.7, 128.8, 129.0, 129.5, 129.8, 130.3, 130.9, 131.7, 135.9, 150.1, 150.5, 153.5. *Anal*. Calcd for $C_{18}H_{12}ClN_5O_2$: C, 59.18; H, 3.28; N, 19.18%. Found: C, 59.14; H, 3.25; N, 19.14%.

7-Amino-5-(3-chlorophenyl)-1,3-dioxo-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-

carbonitrile (4c)

White powder; mp >216 °C; IR (KBr) (ν_{max}/cm^{-1}): 3445, 3330, 2197, 1772, 1715. MS, m/z (%): 365 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 6.17 (1H, s, CH), 7.23–7.80 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 61.2, 63.2, 116.3, 121.1, 126.8, 127.2, 128.1, 128.3, 128.8, 129.2, 129.8, 130.7, 135.2, 135.9, 145.6, 150.3, 150.6, 153.6. *Anal*. Calcd for $C_{18}H_{12}ClN_5O_2$: C, 59.18; H, 3.28; N, 19.18%. Found: C, 59.12; H, 3.23; N, 19.08%.

7-Amino-5-(4-chlorophenyl)-1,3-dioxo-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4d)

White powder; mp >221 °C; IR (KBr) (ν_{max}/cm^{-1}): 3455, 3325, 2200, 1783, 1719. MS, m/z (%): 365 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 5.89 (1H, s, CH), 7.42–7.67 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 61.2, 63.3, 116.3, 126.7, 126.8, 128.6, 128.8, 128.9, 129.0, 129.4, 129.5, 130.9, 133.2, 138.0, 145.4, 150.4, 150.5, 153.5. *Anal*. Calcd for $C_{18}H_{12}ClN_5O_2$: C, 59.18; H, 3.28; N, 19.18%. Found: C, 59.13; H, 3.25; N, 19.12%.

7-Amino-5-(2,4-dichlorophenyl)-1,3-dioxo-2-phenyl-1,2,3-dihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4e)

White powder; mp >200 °C; IR (KBr) (ν_{max}/cm^{-1}): 3475, 3336, 2200, 1783, 1750. MS, m/z (%): 399 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 6.22 (1H, s, CH), 7.43–7.70 (10H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 60.5, 61.1, 116.0, 126.7, 128.3, 128.7, 129.0, 129.2, 129.4, 129.9, 130.9, 131.0, 132.7, 134.0, 135.1, 150.2, 150.5, 153.5. *Anal.* Calcd for $C_{18}H_{11}Cl_2N_5O_2$: C, 54.02; H, 2.77; N, 17.50%. Found: C, 54.12; H, 2.71; N, 17.48%.

7-Amino-1,3-dioxo-5-(2-nitrophenyl)-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4f)

Yellow powder; mp >215 °C; IR (KBr) (ν_{max}/cm^{-1}): 3429, 3325, 2208, 1776, 1748. MS, m/z (%): 376 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 6.50 (1H, s, CH), 7.42–8.11 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 60.0, 61.0, 116.0, 124.7, 126.7, 126.8, 128.7, 129.0, 129.4, 130.0, 130.9, 133.9, 134.7, 145.4, 147.5, 150.4, 150.6, 153.8. *Anal*. Calcd for $C_{18}H_{12}N_6O_4$: C, 57.44; H, 3.19; N, 22.34%. Found: C, 57.38; H, 3.15; N, 22.26%.

7-Amino-1,3-dioxo-5-(3-nitrophenyl)-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4g)

White powder; mp >214 °C; IR (KBr) (ν_{max}/cm^{-1}): 3437, 3317, 2196, 1770, 1728. MS, m/z (%): 376 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 6.08 (1H, s, CH), 7.43–8.35 (11H, m, H–Ar and NH_2). ^{13}C NMR

(125 MHz, DMSO-d_6): δ_C 60.8, 63.0, 116.3, 121.5, 123.6, 126.8, 128.7, 129.0, 130.6, 130.9, 133.6, 141.5, 148.1, 150.3, 150.5, 153.7. *Anal*. Calcd for $C_{18}H_{12}N_6O_4$: C, 57.44; H, 3.19; N, 22.34%. Found: C, 57.41; H, 3.08; N, 22.30%.

7-Amino-1,3-dioxo-5-(4-nitrophenyl)-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4h)

Yellow powder; mp >218 °C; IR (KBr) (ν_{max}/cm^{-1}): 3399, 3332, 2211, 1786, 1745. MS, m/z (%): 376 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 5.97 (1H, s, CH), 7.44–8.32 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 61.0, 63.2, 116.37, 124.2, 126.9, 128.4, 128.9, 129.1, 129.6, 131.0, 46.28, 47.8, 150.37, 150.6, 153.7. *Anal*. Calcd for $C_{18}H_{12}N_6O_4$: C, 57.44; H, 3.19; N, 22.34%. Found: C, 57.38; H, 3.13; N, 22.32%.

7-Amino-1,3-dioxo-5-(4-fluorophenyl)-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4i)

White powder; mp >222 °C; IR (KBr) (ν_{max}/cm^{-1}): 3367, 3311, 2198, 1784, 1724. MS, m/z (%): 349 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 5.88 (1H, s, CH), 7.25–7.60 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 61.3, 63.4, 116.4, 126.7, 126.8, 128.6, 128.9, 129.2, 129.3, 129.4, 129.5, 129.9, 131.0, 135.3, 145.4, 150.0, 150.4, 153.5. *Anal*. Calcd for $C_{18}H_{12}FN_5O_2$: C, 61.89; H, 3.44, N, 20.05%. Found: C, 61.86; H, 3.45; N, 19.97%.

7-Amino-1,3-dioxo-2-phenyl-5-p-tolyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4j)

Yellow powder; mp >217 °C; IR (KBr) (ν_{max}/cm^{-1}): 3368, 3318, 2190, 1772, 1711. MS, m/z (%): 345 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 2.48 (3H, s, CH_3), 5.81 (1H, s, CH), 7.28–7.55 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 25.1, 61.3, 63.2, 116.4, 126.3, 126.5, 128.3, 128.8, 129.0, 129.5, 129.7, 129.9, 133.1 137.7, 144.2, 150.1, 150.6, 153.4. *Anal*. Calcd for $C_{19}H_{15}N_5O_2$: C, 66.08; H, 4.35; N, 20.29%. Found: C, 66.04; H, 4.32; N, 20.23%.

7-Amino-5-(2-bromophenyl)-1,3-dioxo-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4k)

White powder; mp >223 °C; IR (KBr) (ν_{max}/cm^{-1}): 3490, 3325, 2185, 1782, 1748. MS, m/z (%): 410 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 6.28 (1H, s, CH), 7.30–7.68 (11H, m, H–Ar and NH2). ^{13}C NMR (125 MHz, DM SO-d_6): δ_C 61.3, 63.7, 116.1, 121.7, 126.7, 126.8, 128.6, 128.7, 129.0, 129.4, 129.7, 130.5, 131.0, 133.0, 137.5, 150.1, 150.5, 153.5. *Anal*. Calcd acetonitrile (20%) and dichloroethane for for $C_{18}H_{12}BrN_5O_2$: C, 52.68; H, 2.92; N, 17.07%. Found: C, 52.63; H, 2.87; N, 17.02%.

7-Amino-5-(3-bromophenyl)-1,3-dioxo-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4l)

White powder; mp >221 °C; IR (KBr) (ν_{max}/cm^{-1}): 3428, 3335, 2208, 1783, 1722. MS, m/z (%): 410 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 5.88 (1H, s, CH), 7.40–7.68 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 61.1, 63.1, 116.4, 121.9, 126.0, 126.8, 128.6, 128.9, 129.4, 129.6, 130.9, 131.0, 131.4, 141.8, 145.4, 150.1, 150.4, 153.5. *Anal*. Calcd for $C_{18}H_{12}BrN_5O_2$: C, 52.68; H, 2.92; N, 17.07%. Found: C, 52.65; H, 2.89; N, 16.98%.

7-Amino-5-(4-bromophenyl)-1,3-dioxo-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4m)

White powder; mp >224 °C; IR (KBr) (ν_{max}/cm^{-1}): 3449, 3323, 2200, 1782, 1718. MS, m/z (%): 410 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 5.77 (1H, s, CH), 7.00–7.60 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 60.8, 61.3, 116.4, 126.5, 126.9, 127.8, 128.7, 129.0, 129.5, 129.9, 130.2, 131.1, 133.3, 137.7, 144.5, 150.1, 150.5, 153.3. *Anal.* Calcd for $C_{18}H_{12}BrN_5O_2$: C, 52.68; H, 2.92; N, 17.07%. Found: C, 52.62; H, 2.90; N, 17.02%.

7-Amino-1,3-dioxo-2-phenyl-5-(pyridin-4-yl)-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4n)

White powder; mp >198 °C; IR (KBr) (ν_{max}/cm^{-1}): 3392, 3319, 2200, 1786, 1725. MS, m/z (%): 332 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 6.17 (1H, s, CH), 7.23–7.98 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 61.2, 63.3, 116.3, 126.1, 126.5, 127.2, 128.5, 128.8, 129.2, 129.5, 129.8, 130.7, 135.2, 146.2, 150.1, 150.3, 153.6. *Anal*. Calcd for $C_{17}H_{12}N_6O_2$: C, 61.44; H, 3.61; N, 25.30%. Found: C, 61.40; H, 3.56; N, 25.23%.

7-Amino-1,3-dioxo-2-phenyl-5-(pyridin-3-yl)-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4o)

White powder; mp >195 °C; IR (KBr) (ν_{max}/cm^{-1}): 3415, 3317, 2194, 1789, 1725. MS, m/z (%): 332 (M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 5.96 (1H, s, CH), 7.42–8.61 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 60.6, 61.9, 116.3, 123.9, 126.7, 128.6, 128.9, 129.4, 130.9, 134.5, 134.8, 148.4, 149.9, 150.1, 150.4, 153.6. *Anal*. Calcd for for $C_{17}H_{12}N_6O_2$: C, 61.44; H, 3.61; N, 25.30%. Found: C, 61.37; H, 3.58; N, 25.25%.

7-Amino-5-(4-cyanophenyl)-1,3-dioxo-2-phenyl-1,2,3-trihydropyrazolo[1,2-*a*][1,2,4]triazole-6-carbonitrile (4p)

White powder; mp >225 °C; IR (KBr) (ν_{max}/cm^{-1}): 3373, 3311, 2233, 2192, 1778, 1724. MS, m/z (%): 356

(M^+). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 5.96 (1H, s, CH), 7.42–7.93 (11H, m, H–Ar and NH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 60.8, 63.3, 111.4, 116.3, 118.5, 126.8, 127.9, 128.6, 128.9, 130.9, 132.8, 144.3, 150.2, 150.5, 153.6. *Anal*. Calcd for for $C_{19}H_{12}N_6O_2$: C, 64.04; H, 3.77; N, 23.59%. Found: C, 64.02; H, 3.74; N, 23.55%.

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REFERENCES

1. (a) K. S. Suslick, 'Sonochemistry and Sonoluminiscence in Encyclopedia of Physical Science and Technology,' Vol. 17, 3rd ed., Academic Press, San Diego, 2001; (b) T. J. Mason and D. Peters, 'Practical Sonochemistry,' 2nd ed., Ellis Hoewood, London, 2002; (c) J. L. Luche, 'Synthetic Organic Sonochemistry,' Plenum, New York, 1998, and the references cited therein.
2. (a) T. J. Mason, *Ultrason. Sonochem.*, 2007, **14**, 476; (b) K. S. Suslick, 'Sonochemistry in Comprehensive Coordination Chemistry,' Vol. 2, Elsevier Science, New York, 2003, p. 731; (c) S. J. Putterman and K. R. Weninger, *Ann. Rev. Fluid Mech.*, 2000, **32**, 445.
3. H. J. Lim, G. Keum, S. B. Kang, B. Y. Chung, and Y. Kim, *Tetrahedron Lett.*, 1998, **39**, 4367.
4. I. Ugi and A. Dömling, *Angew. Chem. Int. Ed.*, 2000, **39**, 3168.
5. I. Ugi and A. Dömling, *Endeavor,* 1994, **18**, 115.
6. A. Dömling, *Chem. Rev.*, 2006, **106**, 17.
7. E. C. Franklin, *Chem. Rev.*, 1935, **16**, 305.
8. F. W. Bergstrom, *Chem. Rev.*, 1944, **35**, 77.
9. F. W. Lichtenthaler, *Acc. Chem. Res.*, 2002, **35**, 728.
10. T. Jikihara, K. Matsuya, H. Ohta, S. Suzuki, and O. Wakabayashi, US Patent 4,249,934; 1981 (*Chem. Abstr*., 1981, **95**, 62219 y).
11. S. Mallakpour and Z. Rafiee, *Polym. Bull.*, 2006, **56**, 293.
12. S. Mallakpour and Z. Rafiee, *J. Appl. Polym. Sci.*, 2007, **103**, 947.
13. I. H. Hall, O. T. Wong, R. Simlot, M. C. Miller, and R. A. Izydore, *Anticancer Res*., 1992, **12**, 1355.
14. R. A. Izydore and I. H. Hall, US Patent 4,866,058; 1990 (*Chem. Abstr.*, 1990, **112**, 151876 x).
15. D. Ovadia, N. Peleg, and P. Bracha, US Patent 4,087,534; 1978.
16. B. Von Bredow and H. Brechbuehler, *Ger. Offen*., 2,343,347; 1974.
17. (a) A. M. Boldi, C. R. Johnson, and H. O. Eissa, *Tetrahedron Lett.*, 1999, **40**, 619; (b) S. Tanaka, K. Seguchi, K. Itoh, and A. Sera, *J. Chem. Soc., Perkin Trans. 1*, 1994, 2335; (c) Y. Arroya, J. F.

Rodriguez, M. Santos, M. A. Sanz Tejedor, I. Vaco, and J. L. GarciaRuano, *Tetrahedron: Asymmetry*, 2004, **15**, 1059; (d) P. Y. F. Deghati, M. J. Wanner, and G. J. Koomen, *Tetrahedron Lett*., 1998, **39**, 4561; (e) S. Meehan and R. D. Little, *J. Org. Chem*., 1997, **62**, 3779; (f) C. Menard, E. Doris, and C. Mioskowski, *Tetrahedron Lett*., 2003, **44**, 6591.

18. (a) G. R. Bebernitz, G. Argentieri, B. Battle, C. Brennan, B. Balkan, B. F. Burkey, M. Eckhardt, J. Gao, P. Kapa, R. J. Strohschein, H. F. Schuster, M. Wilson, and D. D. Xu, *J. Med. Chem*., 2001, **44**, 2601; (b) A. A. Bekhit, H. T. Y. Fahmy, S. A. F. Rostom, and A. M. Baraka, *Eur. J. Med. Chem*., 2003, **38**, 27; (c) A. I. Eid, M. A. Kira, and H. H. Fahmy, *J. Pharm. Belg*., 1978, **33,** 303; (d) H.-A. Park, K. Lee, S.-J. Park, B. Ahn, J.-C. Lee, H. Y. Cho, and K.-I. Lee, *Bioorg. Med. Chem. Lett*., 2005, **15**, 3307; (e) S. S. Parmar, B. R. Pandey, C. Dwivedic, and R. D. Harbison, *J. Pharm. Sci*., 1974, **63**, 1152; (f) E. Takabatake, R. Kodama, Y. Tanaka, R. Dohmori, H. Tachizawa, and T. Naito, *Chem. Pharm. Bull*., 1970, **18**, 1900.
19. M. Adib, M. H. Sayahi, N. Mahmoodi, and H. R. Bijanzadeh, *Helv. Chim. Acta,* 2006, **89**, 1176.
20. M. Nikpassand, M. Mamaghani, F. Shirini, and K. Tabatabaeian, *Ultrason. Sonochem*., 2010, **17**, 301.
21. (a) L. Pizzuti, P. L. G. Martins, B. A. Ribeiro, F. H. Quina, E. Pinto, A. F. C. Flores, D. Venzke, and C. M. P. Pereira, *Ultrason. Sonochem*., 2010, **17**, 34; (b) L. Pizzuti, L. A. Piovesan, A. F. C. Flores, F. H. Quina, and C. M. Pereira, *Ultrason. Sonochem*., 2009, **16**, 728.
22. J.-T. Li, Y. Yin, L. Li, and M.-X. Sun, *Ultrason. Sonochem*., 2010, **17**, 11.
23. M. Mamaghani and S. Dastmard, *ARKIVOC*, 2009, **2**, 168.
24. (a) D. Azarifar, B. Maleki, and K. Mohammadi, *Heterocycles*, 2007, **71**, 683; and references cited therein; (b) D. Azarifar and K. Khosravi, *J. Chin. Chem. Soc*., 2009, **56**, 43.
25. (a) R. Ghahremanzadeh, G. Imani Shakibaei, and A. Bazgir, *Synlett*, 2008, 1129; (b) M. R. Nabid, S. J. Tabatabaei Rezaei, R. Ghahremanzadeh, and A. Bazgir, *Ultrason. Sonochem*., 2010, **17**, 159.
26. M. B. Teimouri, *Tetrahedron*, 2006, **62**, 10849.
27. H. R. Shaterian, A. Hosseinian, and M. Ghashang, *ARKIVOC*, 2009, **2**, 59.
28. A. Z. A. Aziz Elassar, Y. M. Elkholy, and M. H. Elnagdi, *Pharmazie*, 1996, **51**, 714.
29. H. R. Shaterian, M. Ghashang, and M. Feyzi, *Appl. Catal. A Gen*., 2008, **345**, 128.
30. F. Al-Assar, K. N. Zelenin, E. E. Lesiovskaya, I. P. Bezhan, and B. A. Chakchir, *Pharm. Chem. J.,* 2002, **36**, 598.
31. X. Lu, Z. Lu, and X. Zhang, *Tetrahedron*, 2006, **62**, 457.