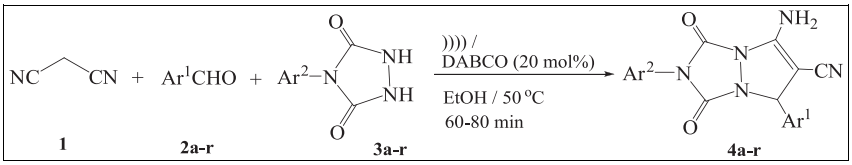
1,4-Diazabicyclo[2.2.2]octane-Catalyzed One-Pot Synthesis of Pyrazolo [1,2-*a*][1,2,4]triazole-1,3-diones under Ultrasound Acceleration

Davood Azarifar,* Razieh Nejat-Yami, and Mohammad Ali Zolfigol

Faculty of Chemistry, University of Bu-Ali Sina, 65178, Hamedan, Iran
*E-mail: azarifar@basu.ac.ir
Received August 27, 2011
DOI 10.1002/jhet.1706
Published online 00 Month 2013 in Wiley Online Library (wileyonlinelibrary.com).



1,4-Diazabicyclo[2.2.2]octane has been explored as an efficient catalyst to effect the three-component condensation reactions between malononitrile, 4-arylurazoles, and aromatic aldehydes in ethanol under ultrasound irradiation conditions. The reactions proceeded very rapidly under mild conditions to furnish the corresponding pyrazolo[1,2-*a*][1,2,4]triazole-1,3-dione derivatives in excellent yields.

J. Heterocyclic Chem., **00,** 00 (2013).

INTRODUCTION

A wide range of naturally occurring compounds belongs to nitrogen-containing heterocyclic compounds. Many of these heterocycles are of significant biological and synthetic importance, which act as pharmaceuticals, agrochemicals, and polyfunctionalized fragments [1–10]. Among these heterocyclic compounds, 1,2,4-triazolidine-3,5-dione containing heterocycles, so-called urazoles, have received considerable interest in synthetic and industrial chemistry. Also, these compounds have found immense technological applications in the manufacture of herbicides and antifungal compounds, and in the production of plastics such as automobile air bags and blowing agents [11,12]. Also, pyrazolourazoles as their fused derivatives with diverse structures have attracted much interest because of their wide range of biological properties such as analgesic, antibacterial, anti-inflammatory, antidiabetic, and psychoanaleptic activities [13–18]. Regarding the vital importance of these urazole derivatives, many novel methods have been reported for their synthesis in recent years [19–24], and development of new approaches for their synthesis seems to be interesting challenge.

On the other hand, application of ultrasound [25–30] in a so-called "sonochemistry" has received enormous interest as a versatile and challenging technique in organic synthesis [31]. It is a known fact that ultrasonic irradiation technique can not only enhance the reaction rates but also have profound effect on the yields of various organic reactions [25–30]. The phenomenon called "acoustic cavitations" is responsible for the beneficial effects of ultrasound on chemical reactions. Namely, the molecules of the liquid are separated during the rarefaction cycle of the wave, generating bubbles that undergo subsequent implosive collapse in a liquid, which produces unusual chemical and physical environments. These rapid and violent implosions of the bubbles generate localized "hot spots" with a transient temperature of roughly 5000°C, pressures of about 1000 atm, and heating and cooling rates above 10 billion °C per second [32]. Such localized hot spots can be considered as microreactors in which the energy of sound is transformed into a useful chemical form.

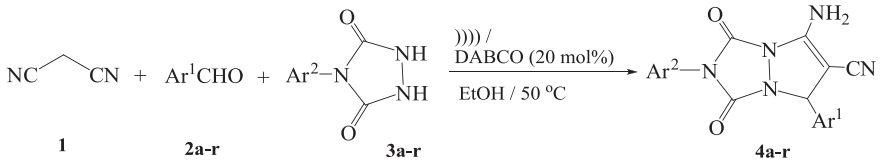
Moreover, one-pot multicomponent reactions have proven to be more advantageous over conventional linear-type synthesis [33], because the multistep reactions usually suffer from complex isolation procedures and produce significant amounts of waste products. In addition, one-pot processes provide rapid and efficient approach to organic transformations including diverse synthesis of polyfunctionalized heterocycles of synthetic importance [5].

As mentioned previously, among the important heterocyclic compounds, pyrazolo-fused heterocycles such as pyrazolo[1,2-*a*][1,2,4]triazole-1,3-dione derivatives are of synthetic and biological importance, and a number of methods have been previously reported for their synthesis [34–40]. Bazgir *et al*. [41] have recently reported the triethylamine-catalyzed synthesis of 1*H*-pyrazolo[1,2-*b*] phthalazine-5,10-diones.

RESULTS AND DISCUSSION

In connection with our continuing interest in the synthesis of pyrazoles [42–44] and also regarding the efficiency of one-pot processes joined with ultrasonic irradiation technique in organic reactions [45,46], we were encouraged to examine a one-pot three-component condensation among malononitrile, 4-arylurazoles, and aromatic and aliphatic aldehydes under the catalytic effect of 1,4-diazabicyclo [2.2.2]octane (DABCO) 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 (Scheme 1).

Scheme 1

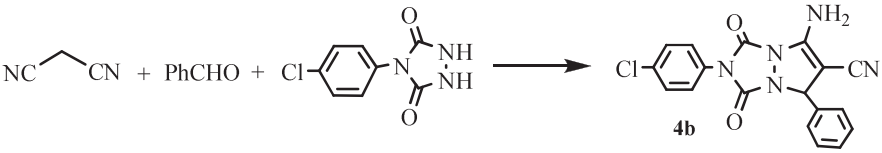


To establish the conditions for the titled reactions, we preliminary examined the model condensation reaction among malononitrile (1 mmol), benzaldehyde (1 mmol), and 4-(4-chlorophenyl)urazole (1 mmol) as test compounds.

The effects of solvent, catalyst, and other conditions on the reaction were studied using various solvents such as EtOH, MeCN, CH_2Cl_2, and H_2O with a variety of basic and acidic catalysts (Table 1). As seen in Table 1, it was observed that the reaction worked out best at 50°C under ultrasonication in terms of reaction time (35 min) and the yield (95%, entry 9) in the presence of 20 mol% DABCO catalyst. Ethanol was found to be the solvent of choice. Also, among the basic catalysts DABCO, Et_3N, and DBU employed in this reaction, DABCO was proved to be the most effective catalyst to provide the highest possible yield (95%) in shortest reaction time (35 min). To substantiate the catalytic effect of DABCO, the reaction was performed in the absence of the catalyst. As a result, no detectable amount of respective product was formed after a long (300 min) ultrasonication in EtOH (entry 1). Also, using lower or higher amounts of the catalyst did not have any significant effect on the yield of the product (entries 7

Table 1

Optimization of the reaction conditions.[a]



Entry	Condition	Method	Catalyst (mol%)	Time (min)	Yield (%)[b]
1	EtOH/50 °C	Ultrasound	None	120	–
2	EtOH /80 °C	Reflux	DABCO (20)	90	Trace
3	EtOH/rt	High speed stirring	DABCO (20)	90	Trace
4	EtOH/rt	Ultrasound	DABCO (20)	90	Trace
5	EtOH/30°C	Ultrasound	DABCO (20)	60	<30
6	EtOH/40°C	Ultrasound	DABCO (20)	45	82
7	EtOH/50°C	Ultrasound	DABCO (10)	40	90
8	EtOH/60°C	Ultrasound	DABCO (20)	35	93
9	EtOH/50°C	Ultrasound	DABCO (20)	35	95
10	EtOH/50°C	Ultrasound	DABCO (30)	35	93
11	EtOH/50°C	Ultrasound	Et_3N (20)	50	82
12	EtOH/50°C	Ultrasound	Et_3N (30)	50	83
13	EtOH/80°C	Reflux	Et_3N (30)	120	Trace
14	EtOH/50°C	Ultrasound	DBU (20)	60	<20
15	EtOH/80°C	Reflux	DBU (20)	120	Trace
16	EtOH/50°C	Ultrasound	HClO4.SiO2 (1)	120	–
17	EtOH/80°C	Reflux	HClO4.SiO2 (1)	120	–
18	EtOH/50°C	Ultrasound	SSA(1)	120	–
19	EtOH/80°C	Reflux	SSA (1)	120	–
20	EtOH/50°C	Ultrasound	LiBr (10)	120	–
21	EtOH/50°C	MW (100 W)	DABCO (20)	60	<20
22	EtOH/50°C	Solvent free (80°C)	DABCO (20)	300	<20
23	H_2O/50°C	Ultrasound	DABCO (20)	70	35
24	CH_3CN/50°C	Ultrasound	DABCO (20)	70	45
25	CH_3CN	Reflux	DABCO (20)	70	Trace
26	CH_3CN/50°C	High speed stirring	DABCO (20)	70	Trace
27	CH_2Cl_2/40°C	Ultrasound	DABCO (20)	70	<20

[a]Conditions: malononitrile (1 mmol), 4-(4-chlorophenyl)urazole (1 mmol), and benzaldehyde (1 mmol).
[b]Isolated yield.

and 10). Also, the role of ultrasound irradiation in the reaction was evaluated by conducting the reaction under conventional heating at room temperature and reflux point (~80°C), which resulted in the formation of only trace amounts of the product (entries 2 and 3). Application of microwave irradiation (100 W) was also examined in this reaction, which resulted in a very low yield (<20%) of the product (entry 21). It is interesting to note that when acid catalysts such as silica-supported $HClO_4$, silica sulfuric acid, and LiBr were employed in this reaction either under sonication or conventional reflux condition in EtOH, no respective product was detected (entries 16–20).

To develop the scope of these reactions, a series of aromatic aldehydes **2a–2o** as well as aliphatic ones **2p–2r** were subjected to condensation with various 4-arylurazoles **3a–3r** in the presence of malononitrile **1** under the optimized conditions (ultrasonication at 50°C in EtOH using 20 mol% DABCO catalyst). As evident from the experimental results (Table 2), almost all the aromatic aldehydes reacted in relatively short reaction times (30–55 min) to afford the corresponding pyrazolo[1,2-*a*][1,2,4]triazole-1, 3-diones **4a–4o** in excellent yields (85–98%). The structures of the products were fully characterized on the basis of their elemental and spectral (IR, ^{1}H NMR, ^{13}C NMR, and MS) analysis. It is interesting to note that essential improvements in the yields and also in the rates of the titled reactions occur with using DABCO in comparison with triethylamine, which was used as the catalyst to affect the same type of reactions in our previously reported work [45]. However, it appears that this method is unsuitable for the synthesis of pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones derived from aliphatic aldehydes (entries **p–r**).

Table 2

Ultrasonic-accelerated synthesis of pyrazolo[1,2-*a*][1,2,4]triazole-1, 3-diones **4a–4r** catalyzed by DABCO.[a]

Entry	Ar^1	Ar^2	Time (min)	Yield (%)[b]
a	C_6H_5	C_6H_5	30	98 [45]
b	C_6H_5	4-ClC_6H_4	35	95
c	4-MeC_6H_4	C_6H_5	40	95 [45]
d	4-ClC_6H_4	C_6H_5	20	95 [45]
e	4-ClC_6H_4	4-ClC_6H_4	40	98
f	4-FC_6H_4	C_6H_5	45	90 [45]
g	4-$NO_2C_6H_4$	4-ClC_6H_4	45	98
h	4-$NO_2C_6H_4$	2,4-$Cl_2C_6H_3$	45	96
i	4-$NO_2C_6H_4$	4-$NO_2C_6H_4$	55	85
j	C_6H_5	4-$MeOC_6H_4$	50	92
k	4-CNC_6H_4	C_6H_5	45	95 [45]
l	4-$NO_2C_6H_4$	4-$MeOC_6H_4$	45	94
m	C_6H_5	4-$Me_3CC_6H_4$	50	90
n	4-$NO_2C_6H_4$	4-$Me_3CC_6H_4$	50	92
o	Pyridin-4-yl	C_6H_5	30	94 [45]
p	C_2H_5	C_6H_5	120	–
q	β-PhC_2H_4	C_6H_5	120	–
r	n-C_6H_{13}	C_6H_5	120	–

[a]Conditions: aldehyde (1 mmol), malononitrile (1 mmol), 4-arylurazole (1 mmol), DABCO catalyst (20 mol%), ultrasonication at 50°C, in EtOH.
[b]Isolated yield.

A possible mechanism to explain the formation of pyrazolo [1,2-*a*][1,2,4]triazole-1,3-diones **4a–4o** is depicted in Scheme 2. As shown in this scheme, it seems likely that the reaction initiates with a Knoevenagel-type condensation reaction of malononitrile **1** with aromatic aldehyde **2** under the catalytic effect of DABCO to yield a dehydrated condensed malononitrile derivative (**A**). The subsequent Michael-type addition of intermediate (**A**) to 4-arylurazole **3** provides a second intermediate (**B**), which undergoes successive cyclization to (**C**) and DABCO-catalyzed tautomerization to afford the expected product.

In summary, we have developed a rapid and reliable synthetic procedure that provides easy access to hitherto unknown pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones in relatively excellent yields and short reaction times via a three-component cyclo-condensation reaction of aromatic aldehydes, malononitrile, and 4-arylurazoles catalyzed by DABCO as a cost-effective and readily available nontoxic compound under ultrasound irradiation conditions.

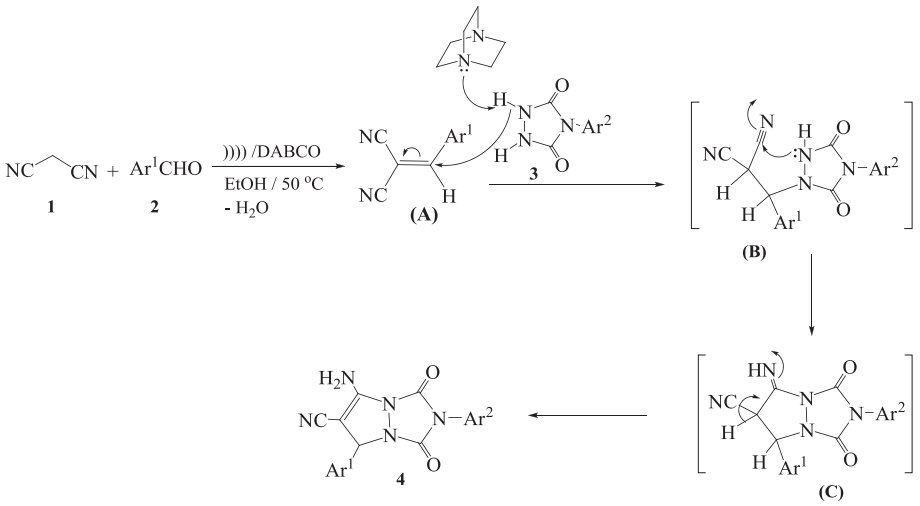
EXPERIMENTAL

Chemicals used in this work were purchased from Fluka (Muenchen, Germany) and Merck (Buchs, Switzerland) 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 the use of a Bruker DRX-300 AVANCE instrument at 300.13 and 75.47 MHz, respectively, using Me_4Si as internal standard. Mass spectra were recorded with a Finnigan-MAT 8430 spectrometer operating at an ionization potential of 70 ev. Melting points were measured on an SMPI apparatus. Elemental analysis for C, H, and N atoms were performed using a PerkinElmer 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. Urazoles were synthesized according to the reported procedures [47–51].

General procedure for the synthesis of pyrazolo[1,2-*a*][1,2,4]triazole-1,3-diones (4). A mixture of malononitrile **1** (0.07 g, 1 mmol), aldehyde **2** (1 mmol), 4-arylurazole **3** (1 mmol), and DABCO (0.023 g, 0.2 mmol) in EtOH (10 mL) was sonicated at 50°C for an appropriate time (Table 2). After completion of the reaction as monitored by TLC analysis, the reaction mixture was filtered, and the separated solid was washed with ethanol (2 × 3 mL) to afford almost pure products **4**. The structures of the products were fully established on the basis of their ^{1}H NMR, ^{13}C NMR, and IR spectra as well as the elemental and MS spectral analysis for the new compounds as given in the succeeding text.

7-Amino-2-(4-chlorophenyl)-1,2,3,5-tetrahydro-1,3-dioxo-5-phenylpyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (4b). White powder; mp > 300°C; FTIR (KBr): 3441 (NH_2), 3314

Scheme 2



(NH$_2$), 2193 (CN), 1769 (C=O), 1714 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 5.85 (s, 1H, CH), 7.20–7.72 (m, 11H, Ar–H and NH$_2$); ^{13}C NMR (75 MHz, DMSO-d_6): δ 61.9 (*C*-aliphatic), 64.5 (=*C*–CN) , 116.8 (CN), 127.5 (Ar), 128.9 (Ar), 129.2 (Ar), 129.5 (Ar), 130.1 (Ar), 134.6 (Ar), 137.9 (Ar), 145.7 (Ar), 150.4 (C=O), 150.6 (C=O), 153.8 (=*C*–NH$_2$); MS (EI, 70 ev): *m/z* (%) = 365 (M$^+$); *Anal*. Calcd for $C_{18}H_{12}ClN_5O_2$: C, 59.11; H, 3.31; N, 19.15%. Found: C, 59.02; H, 3.14; N, 19.06%.

7-Amino-2,5-bis(4-chlorophenyl)-1,2,3,5-tetrahydro-1,3-dioxo-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (4e). White powder; mp > 300°C; FTIR (KBr): 3401 (NH$_2$), 3317 (NH$_2$), 2198 (CN), 1774 (C=O), 1715 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 5.86 (s, 1H, CH), 7.49–7.68 (m, 10H, Ar–H and NH$_2$); ^{13}C NMR (75 MHz, DMSO-d_6): δ 61.5 (*C*-aliphatic), 63.9 (=*C*–CN), 116.9 (CN), 129.0 (Ar), 129.3 (Ar), 129.5 (Ar), 129.6 (Ar), 130.0 (Ar), 130.3 (Ar), 133.7 (Ar), 138.5 (Ar), 150.4 (C=O), 150.7 (C=O), 153.9 (=*C*–NH$_2$); MS (EI, 70 ev): *m/z* (%) = 399 (M$^+$); *Anal*. Calcd for $C_{18}H_{11}Cl_2N_5O_2$: C, 54.02; H, 2.77; N, 17.50%. Found: C, 53.92; H, 2.68; N, 17.43%.

7-Amino-2-(4-chlorophenyl)-1,2,3,5-tetrahydro-5-(4-nitrophenyl)-1,3-dioxo-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (4g). White powder; mp > 300°C; FTIR (KBr): 3405 (NH$_2$), 3311 (NH$_2$), 2192 (CN), 1763 (C=O), 1713 (C=O), 1608 (NO$_2$), 1348 (NO$_2$), 852 (C–NO$_2$) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.01 (s, 1H, CH), 7.71–8.33 (m, 10H, Ar–H and NH$_2$); ^{13}C NMR (75 MHz, DMSO-d_6): δ 61.2 (*C*-aliphatic), 63.5 (=*C*–CN), 116.8 (CN), 124.6 (Ar), 128.8 (Ar), 129.0 (Ar), 129.6 (Ar), 130.2 (Ar), 133.7 (Ar), 146.6 (Ar), 148.0 (Ar), 150.6 (C=O), 150.8 (C=O), 153.9 (=*C*–NH$_2$); MS (EI, 70 ev): *m/z* (%) = 410 (M$^+$); *Anal*. Calcd for $C_{18}H_{11}ClN_6O_4$: C, 52.64; H, 2.70; N, 20.46%. Found: C, 52.56; H, 2.64; N, 20.42%.

7-Amino-2-(2,4-dichlorophenyl)-1,2,3,5-tetrahydro-5-(4-nitrophenyl)-1,3-dioxo-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (4h). White powder; mp > 300 °C; FTIR (KBr): 3473 (NH$_2$), 3332 (NH$_2$), 2205 (CN), 1782 (C=O), 1743 (C=O), 1653 (NO$_2$), 1348 (NO$_2$), 845 (C–NO$_2$) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.01 (s, 1H, CH), 7.50–8.33 (m, 9H, Ar–H and NH$_2$); ^{13}C NMR (75 MHz, DMSO-d_6): δ 61.2 (*C*-aliphatic), 63.5 (=*C*–CN), 116.7 (CN), 124.6 (Ar), 127.5 (Ar), 128.7 (Ar), 129.0 (Ar), 130.5 (Ar), 131.6 (Ar), 131.7 (Ar), 146.5 (Ar), 150.4 (C=O), 150.6 (C=O), 153.5 (=*C*–NH$_2$); MS (EI, 70 ev): *m/z* (%) = 444 (M$^+$); *Anal*. Calcd for $C_{18}H_{10}Cl_2N_6O_4$: C, 48.56; H, 2.26; N, 18.88%. Found: C, 48.42; H, 2.18; N, 18.76%.

7-Amino-1,2,3,5-tetrahydro-2,5-bis(4-nitrophenyl)-1,3-dioxo-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (4i). White powder; mp > 300°C; FTIR (KBr): 3442 (NH$_2$), 3327 (NH$_2$), 2201 (CN), 1775 (C=O), 1725 (C=O), 1682 (NO$_2$), 1664 (NO$_2$), 1372 (NO$_2$), 1351 (NO$_2$), 847 (C–NO$_2$) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.13 (s, 1H, CH); 7.61–8.43 (m, 10H, Ar–H and NH$_2$); ^{13}C NMR (75 MHz, DMSO-d_6): δ 61.8 (*C*-aliphatic), 63.9 (=*C*–CN), 116.9 (CN), 124.6 (Ar), 128.7 (Ar), 129.0 (Ar), 129.6 (Ar), 131.0 (Ar), 133.6 (Ar), 146.8 (Ar), 148.9 (Ar), 150.6 (C=O), 150.9 (C=O), 153.9 (=*C*–NH$_2$); MS (EI, 70 ev): *m/z* (%) = 421 (M$^+$); *Anal*. Calcd for $C_{18}H_{11}N_7O_6$: C, 51.32; H, 2.63; N, 23.27%. Found: C, 51.23; H, 2.54; N, 23.22%.

7-Amino-1,2,3,5-tetrahydro-2-(4-methoxyphenyl)-1,3-dioxo-5-phenylpyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (4j). Yellow powder; mp > 300°C; FTIR (KBr): 3422 (NH$_2$), 3307 (NH$_2$), 2191 (CN), 1763 (C=O), 1724 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.83 (s, 3H, OCH$_3$), 5.86 (s, 1H, CH), 7.05–7.62 (m, 11H, Ar–H and NH$_2$); ^{13}C NMR (75 MHz, DMSO-d_6): δ 55.9 (OCH$_3$), 61.9 (*C*-aliphatic), 64.5 (=*C*–CN), 114.7 (Ar), 117.1(CN), 123.9 (Ar), 127.5 (Ar), 128.8 (Ar), 129.0 (Ar), 129.2 (Ar), 139.6 (Ar), 150.5 (Ar), 151.4 (C=O), 154.4 (C=O), 159.7 (=*C*–NH$_2$); MS (EI, 70 ev): *m/z* (%) = 361 (M$^+$); *Anal*. Calcd for $C_{19}H_{15}N_5O_3$: C, 63.16; H, 4.18; N, 19.38%. Found: C, 63.04; H, 4.12; N, 19.34%.

7-Amino-1,2,3,5-tetrahydro-2-(4-methoxyphenyl)-5-(4-nitrophenyl)-1,3-dioxo-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (4l). White powder; mp > 300°C; FTIR (KBr): 3383 (NH_2), 3322 (NH_2), 2206 (CN), 1776 (C═O), 1732 (C═O), 1583 (NO_2), 1346 (NO_2), 848 (C–NO_2) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 3.82 (s, 3H, OCH_3), 5.89 (s, 1H, CH), 7.05–7.63 (m, 10H, Ar–H and NH_2); ^{13}C NMR (75 MHz, DMSO-d_6): δ 55.8 (OCH_3), 61.9 (*C*-aliphatic), 64.6 (═*C*–CN), 114.7 (Ar), 117.3 (CN), 123.9 (Ar), 127.5 (Ar), 128.9 (Ar), 129.1(Ar), 139.6 (Ar), 146.3 (Ar), 150.5 (Ar), 151.4 (C═O), 154.5 (C═O), 159.7 (═*C*–NH_2); MS (EI, 70 ev): *m/z* (%) = 406 (M^+); *Anal*. Calcd for $C_{19}H_{14}N_6O_5$: C, 56.17; H, 3.47; N, 20.68%. Found: C, 56.07; H, 3.38; N, 20.58%.

7-Amino-1,2,3,5-tetrahydro-1,3-dioxo-5-phenyl-2-(4-t*-butylphenyl) pyrazolo[1,2-*a*][*1,2,4*]triazole-6-carbonitrile *(4m). Yellow powder; mp > 300°C; FTIR (KBr): 3358 (NH_2), 3316 (NH_2), 2183 (CN), 1764 (C═O), 1725 (C═O) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.34 (s, 9H, $C(CH_3)_3$), 6.21 (s, 1H, CH), 7.31–8.03 (m, 11H, Ar–H and NH_2); ^{13}C NMR (75 MHz, DMSO-d_6): δ 31.2 (CH_3), 34.3 (C $(CH_3)_3$), 61.1 (*C*-aliphatic), 63.4 (═*C*–CN), 116.3 (CN), 124.3 (Ar), 126.6 (Ar), 127.8 (Ar), 128.6 (Ar), 133.4 (Ar), 146.6 (Ar), 148.1 (Ar), 150.6 (Ar), 151.3 (C═O), 151.7 (C═O), 153.3 (═*C*–NH_2); MS (EI, 70 ev): *m/z* (%) = 387 (M^+); *Anal*. Calcd for $C_{22}H_{21}N_5O_2$: C, 68.21; H, 5.46; N, 18.08%. Found: C, 68.17; H, 5.38; N, 18.03%.

7-Amino-1,2,3,5-tetrahydro-5-(4-nitrophenyl)-1,3-dioxo-2-(4-t*-butylphenyl)pyrazolo[*1,2-a*][*1,2,4*]triazole-6-carbonitrile *(4n). White powder; mp > 300°C; FTIR (KBr): 3368 (NH_2), 3318 (NH_2), 2187 (CN), 1766 (C═O), 1711 (C═O), 1597 (NO_2), 1363 (NO_2), 854 (C–N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.30 (s, 9H, $C(CH_3)_3$), 6.02 (s, 1H, CH), 7.38–8.33 (m, 10H, Ar–H and NH_2); ^{13}C NMR (75 MHz, DMSO-d_6): δ 31.4 (CH_3), 34.9 ($C(CH_3)_3$), 61.3 (*C*-aliphatic), 63.6 (═*C*–CN), 116.8 (CN), 124.6 (Ar), 124.8 (Ar), 126.3 (Ar), 126.9 (Ar), 128.7 (Ar), 133.1 (Ar), 148.0 (Ar), 150.7 (Ar), 151.2 (C═O), 151.8 (C═O), 154.4 (═*C*–NH_2); MS (EI, 70 ev): *m/z* (%) = 432 (M^+); *Anal*. Calcd for $C_{22}H_{20}N_6O_4$: C, 61.11; H, 4.66, N, 19.43%. Found: C, 61.02; H, 4.57; N, 19.38%.

REFERENCES AND NOTES

[1] Franklin, E. C. Heterocyclic Chem Rev 1935, 16, 305.
[2] Bergstrom, F. W. Chem Rev 1944, 35, 77.
[3] Lichtenthaler, F. W. Acc Chem Res 2002, 35, 728.
[4] Dömling, A.; Ugi, I. Angew Chem Int Ed 2000, 39, 3168.
[5] Dömling, A. Chem Rev 2006, 106, 17.
[6] Sheibani, H.; Babaie, M. Synth Commun 2010, 40, 257.
[7] Sheibani, H.; Seifi, M.; Bazgir, A. Synth Commun 2009, 39, 1055.
[8] Guo, S.; Wang, S.; Li, J. Synth Commun 2007, 37, 2111.
[9] Azarifar, D.; Maleki, B. Synth Commun 2005, 35, 2581.
[10] Wang, S.; Ren, Z.; Cao, W.; Tong, W. Synth Commun 2001, 31, 673.
[11] Mallakpour, S.; Rafiee, Z. J Appl Polym Sci 2007, 103, 947.
[12] Mallakpour, S.; Rafiee, Z. Polym Bull 2006, 56, 293.
[13] Bebernitz, G. R.; Argentieri, G.; Battle, B.; Brennan, C.; Balkan, B.; Burkey, B. F.; Eckhardt, M.; Gao, J.; Kapa, P.; Strohschein, R. J.; Schuster, H. F.; Wilson, M.; Xu, D. D. J Med Chem 2001, 44, 2601.
[14] Bekhit, A. A.; Fahmy, H. T. Y.; Rostom, S. A. F.; Baraka, A. M. Eur J Med Chem 2003, 38, 27.
[15] Eid, A. I.; Kira, M. A.; Fahmy, H. H. J Pharm Belg 1978, 33, 303.
[16] Park, H.-A.; Lee, K.; Park, S.-J.; Ahn, B.; Lee, J.-C.; Cho, H. Y.; Lee, K. I. Bioorg Med Chem Lett 2005, 15, 3307.
[17] Parmar, S. S.; Pandey, B. R.; Dwivedic, C.; Harbison, R. D. J Pharm Sci 1974, 63, 1152.
[18] Takabatake, E.; Kodama, R.; Tanaka, Y.; Dohmori, R.; Tachizawa, H.; Naito, T. Chem Pharm Bull 1970, 18, 1900.
[19] Boldi, A. M.; Johnson, C. R.; Eissa, H. O. Tetrahedron Lett 1999, 40, 619.
[20] Arroya, Y.; Rodriguez, J. F.; Santos, M.; Sanz Tejedor, M. A.; Vaco, I.; GarciaRuano, J. L. Tetrahedron: Asymmetry 2004, 15, 1059.
[21] Tanaka, S.; Seguchi, K.; Itoh, K.; Sera, A. J Chem Soc, Perkin Trans 1994, 1, 2335.
[22] Deghati, P. Y. F.; Wanner, M. J.; Koomen, G. J. Tetrahedron Lett 1998, 39, 4561.
[23] Meehan, S.; Little, R. D. A. J Org Chem 1997, 62, 3779.
[24] Menard, C.; Doris, E.; Mioskowski, C. Tetrahedron Lett 2003, 44, 6591.
[25] Suslick, K. S. Sonochemistry and Sonoluminiscence in Encyclopedia of Physical Science and Technology; Academic Press: San Diego, 2001.
[26] Mason, T. J.; Peters, D. Practical Sonochemistry; Ellis Horwood Limited: New York, 1991.
[27] Luche, J. L. Synthetic Organic Sonochemistry; Plenum: New York, 1998.
[28] Mason, T. J. Ultrason Sonochem 2007, 14, 476.
[29] Suslick, K. S. Sonochemistry in Comprehensive Coordination Chemistry; Elsevier Science: New York, 2003, Vol. 2, p.731.
[30] Putterman, S. J.; Weninger, K. R. Ann Rev Fluid Mech 2000, 32, 445.
[31] Lim, H. J.; Keum, G.; Kang, S. B.; Chung, B. Y.; Kim, Y. Tetrahedron Lett 1998, 39, 4367.
[32] Martins, M. A. P.; Pereira, C. M. P.; Cunico, W.; Moura, S.; Rosa, F.; Peres, R. L.; Machado, P.; Zanatta, N.; Bonacorso, H. G. Ultrason Sonochem 2006, 13, 364.
[33] Ugi, I.; Dömling, A. Endeavor 1994, 18, 115.
[34] Adib, M.; Sayahi, M. H.; Mahmoodi, N.; Bijanzadeh, H. R. Helv Chim Acta 2006, 89, 1176.
[35] Ghahremanzadeh, R.; Imani Shakibaei, G.; Bazgir, A. Synlett 2008, 1129.
[36] Teimouri, M. B. Tetrahedron 2006, 62, 10849.
[37] Shaterian, H. R.; Hosseinian, A.; Ghashang, M. Arkivoc 2009, 2, 59.
[38] Aziz Elassar, A. Z. A.; Elkholy, Y. M.; Elnagdi, M. H. Pharmazie 1996, 51, 714.
[39] Shaterian, H. R.; Ghashang, M.; Feyzi, M. Appl Catal A Gen 2008, 345, 128.
[40] Al-Assar, F.; Zelenin, K. N.; Lesiovskaya, E. E.; Bezhan, I. P.; Chakchir, B. A. Pharm Chem J 2002, 36, 598.
[41] Nabid, M. R.; Tabatabaei Rezaei S.J.; Ghahremanzadeh, R.; Bazgir, A. Ultrason Sonochem 2010, 17, 159.
[42] Azarifar, D.; Zolfigol, M. A.; Maleki, B. Synthesis 2004, 1744.
[43] Azarifar, D.; Maleki, B.; Mohammadi, K. Heterocycles 2007, 71, 683.
[44] Azarifar, D.; Khosravi, K. J Chin Chem Soc 2009, 56, 43.
[45] Azarifar, D.; Nejat-Yami, R. Heterocycles 2010, 81, 2063.
[46] Azarifar, D.; Sheikh, D. Heteroatom Chem 2011, 22, 106.
[47] Mallakpour, S.; Rafiee, Z. Synth Commun 2007, 37, 1927.
[48] Mallakpour, S.; Rafiee, Z. Synlett 2007, 8, 1255.
[49] Mallakpour, S. J Chem Educ 1992, 69, 238.
[50] Mallakpour, S.; Rezazadeh, S. Iranian Polym J 2004, 13, 29.
[51] Zolfigol, M. A.; Chehardoli, G.; Ghaemi, E.; Madrakian, E.; Zare, R.; Azadbakht, T.; Niknam, K.; Mallakpour, S. Monatsh Chem 2008, 139, 261.