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ROYAL SOCIETY OF CHEMISTRY

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View Article Online
DOI: 10.1039/C5RA13805A

Journal Name

ARTICLE

Glycerol: more benign and biodegradable promoting medium for catalyst-free one-pot multi-component synthesis of triazolo[1,2-*a*]indazole-triones

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

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The one-pot three component synthesis of triazolo[1,2-*a*]indazole-triones was conducted successfuly under catalyst-free condition in glycerol as a benign, nontoxic and biodegradable promoting medium. A broad range of substrates including aromatic aldehydes are condensed with carbonyl compounds possessing a reactive α-methylene group and urazole derivatives. All reactions are completed in short times and the products are obtained in good to excellent yields. Moreover, presented method was applied successfuly in large scale synthesis of titled compounds.

Introduction

The growing awareness of the pressing need for more benign and sustainable technologies has focused attention on the use of atom efficient catalytic methodologies as well as the use of alternative reaction media that circumvent the problems associated with many of the traditional volatile organic solvents. Based on the Green Chemistry protocols[1a] there are several issues that influence the choice of a solvent as a benign and applicable reaction medium. It should be relatively nontoxic and relatively nonhazardous and it must be not flammable or corrosive. The solvent should also be recoverable and should not be released to the environment. Moreover, these green solvents have to be cheap and easy to handle and recycle.[1] During the past decade, various alternatives have been reported to apply as a more benign reaction medium for organic transformations.[2-6] Various fascinating results of these media are undeniable but, application of these alternatives is combination with strict limitations such as need to very expensive equipments[7] or high prices and lack of data about the toxicity and bio-compatibility[8] of them or product separation for aqueous-based processes.[9] In fact, a global benign solvent doesn't exist and the scientific community is continuously searching for new sustainable media in order to widen their use in organic processes.

Glycerol is a non-volatile, inflammable, very cheap and biodegradable material that is produced as a by-product during the biodiesel synthesis. This compound introduces a unique solubility profile. Most of inorganic salts, acids, bases, enzymes and many transition metal complexes are soluble in glycerol. Furthermore, it also dissolves organic compounds that are poorly miscible in water. Moreover, many hydrophobic solvents such as ethers and hydrocarbons are immiscible in glycerol. This solubility profile makes the reaction products able to be separated from the reaction medium with a simple extraction step. Moreover, the high boiling point of glycerol (290 ^{o}C) is an important advantage and provides higher temperature that making possible reaction that does not proceed in low boiling point solvents. The non-toxicity of glycerol (LD_{50}= 12600 mg/Kg (oral rat)), its biodegradability and non-flammability for which no special handling precautions or storage is required makes it a worthy candidate for application in the synthesis of pharmaceutically active ingredients in which the toxicity and residue of solvents have to be carefully controlled. Because of these unique properties, there is a large number of reports on the application of glycerol as an efficient and convenient solvent in organic transformations.[10] More recently Hei *et al.* demonstrated that glycerol is an effective promoting medium for electrophilic activation of aldehydes and they showed that some reactions which have been conventionally carried out using acid catalysts, can be performed under catalyst-free conditions in the presence of glycerol as a reaction medium.[11]

Heterocyclic compounds are an important branch of chemicals because they are the main building blocks of a large variety of products, such as molecular materials, natural and biologically active compounds and also in regularly marketed drugs. For that reason, sustainable synthetic strategies have turned into a crucial current research. From this viewpoint, one-pot procedures involving multi-step transformations represent powerful methodological means, which prevent the isolation (and purification) of intermediates leading to selective and advantageous processes.[12a-c] Two important classes of heterocyclic compounds are triazoles and indazoles. The main reason of interest on indazoles is its distribution in the structure of natural products. Various alkaloids such as Nigellicine, Nigeglanine, and Nigellidine

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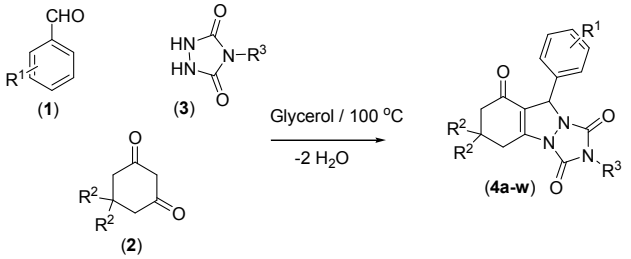
DOI: 10.1039/C5RA13805A

are indazoles.[12d] Moreover there are various kinds of tetrazole-contained chemicals that are used as antifungal drugs such as fluconazole[13a], isavuconazole[13b], itraconazole[13c], voriconazole[13d], pramiconazole[13e], ravuconazole[13f], and posaconazole[13f]. In addition, epoxiconazole[13g], triadimenol[13h], propiconazole[13i], metconazole[13j], cyproconazole[13g], tebuconazole[13k], flusilazole[13l] and paclobutrazol[13m] are the other triazole-contained chemicals that are used as plant protection fungicides. Triazolo[1,2-*a*]indazole-triones and their derivatives are a class of very useful compounds that their chemical structures consist of indazole and triazole backbones at the same time. They have been widely used as medicine intermediates because of their biological and pharmacological properties.[13n] However there are only a few reported methods for the synthesis of these compounds such as application of *p*-toluenesulfunic acid (PTSA)[14], sulfonated polyrythene glycol (PEG-OSO_3H)[15], melamine trisulfonic acid (MTSA)[16], tungstosilicic acid[17], silica nanoparticles prepared from rice husk[18], quinuclidine stabilized on $FeNi_3$ nanoparticles[19], camphor-10-sulfonic acid[20], $ZrOCl_2.8H_2O$[21] and sulfamic acid.[22] Despite the available methodologies, there still exists a demand for devising a more efficient and environmentally benign procedure which allows the ready synthesis of these polycyclic systems.

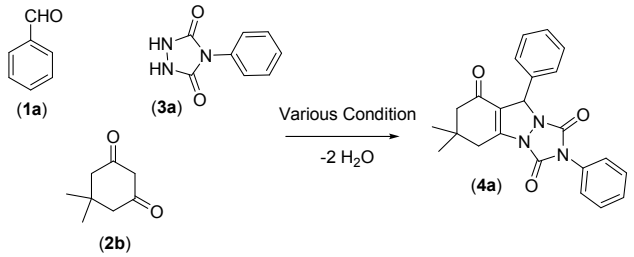
Based on the above facts we herein report a catalyst-free one-pot three component synthesis of triazolo[1,2-*a*]indazole-triones in glycerol as a biodegradable and benign solvent (Scheme 1). To the best of our knowledge this is the first report of catalyst-free synthesis of triazolo[1,2-*a*]indazole-triones.



Scheme 1. The catalyst-free one-pot three component synthesis of triazolo[1,2-*a*]indazole-triones in glycerol as a biodegradable and benign solvent.

Results and discussion

Initially, the reaction between benzaldehyde (**1a**), dimedone (**2b**) and *N*-phenyl urazole (**3a**) was investigated in different solvents under catalyst-free conditions at various temperatures (Scheme 2), and the results are listed in Table 1.



Scheme 2. The one-pot three component condensation reaction of benzaldehyde (**1a**), dimedone (**2a**) and *N*-phenyl urazole (**3a**) under various conditions.

Only a trace amount of products were detected in toluene, DMF, DMSO, ethyl acetate and in neat conditions (Table 1, entries 1,2,5,6,13). While the reaction proceeded sluggishly in ethanol, a huge improvement was observed in polyethylene glycol and ethylene glycol (Table 1, entries 3,4,7). Although water was proved to be capable of promoting the reaction, in this case, a gummy solid was obtained which makes the separation of products very hard (Table 1, entry 14). Inspired by the observed determinant effect of alcoholic solvents on the reaction, we then investigated the efficiency of glycerol as a solvent for this reaction. As we expected, the reaction proceeded very well, and 94% yield was obtained under identical conditions (Table 1, entry 12). As shown in Table 1, the best results were obtained at 100 °C in the presence of glycerol (1 mL). Interestingly, all starting materials are soluble in glycerol, so at the start of the reaction, a solution, which seemed to be nearly transparent, was observed. All obtained products were found to be insoluble in glycerol, so with progress of the reaction, wrought products sediment slowly from the reaction mixture.

Table 1. The catalyst-free condensation reaction between benzaldehyde (**1a**, 1 mmol), dimedone (**2b**, 1 mmol) and *N*-phenyl urazole (**3a**, 1 mmol) under various conditions

Entry	Solvent (1 mL)	Temp (^oC)	Time (h)	Yield (%)[a]
1	DMF	100	12	Trace
2	DMSO	100	12	Trace
3	Ethanol	Reflux	12	51
4	Poly ethylene glycol 400	100	4	80
5	Toluene	100	12	Trace
6	Ethyl acetate	Reflux	12	Trace
7	Ethylene glycol	100	4	82
8	Glycerol	r.t.	8	33
9	Glycerol	50	8	71
10	Glycerol	60	6	78
11	Glycerol	80	4	86
12	Glycerol	100	4	94
13	-	100	8	Trace
14	Water	100	8	69
14	Choline chloride/Glycerol 1:1	100	8	91
16	Choline chloride/Glycerol 1:2	100	8	93
17	Choline chloride/Glycerol 1:3	100	8	93
18	$Et_2(EtOH)NCl$[b]/Glycerol 1:2	100	8	83
19	$Et_2(EtOH)NCl$/Glycerol 1:3	100	8	86

[a] Isolated yields. [b] *N,N*-diethylenethanol ammonium chloride.

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Table 2. The catalyst-free one-pot three-component synthesis of triazolo[1,2-*a*]indazole-triones in glycerol at 100 °C.

Entry	R^1	R^2	R^3	Product	(m.p. °C)	1 mmol Scale			25 mmol Scale		
						Time (h)	Yield (%)[a]	A. E. (%)[b]	Time (h)	Yield (%)[a]	A. E. (%)[b]
1	C_6H_5	CH_3	C_6H_5	**4a**	191-192 (190-192)[15]	4	94	86	7	90	82
2	*p*-Br-C_6H_4	CH_3	C_6H_5	**4b**	183-184 (185-187)[15]	4	94	87	7	91	84
3	*m*-Br-C_6H_4	CH_3	C_6H_5	**4c**	170-172 (172-174)[15]	6	92	85	10	89	82
4	*p*-Cl-C_6H_4	CH_3	C_6H_5	**4d**	170-171 (173-175)[15]	4	92	84	7	90	83
5	*o*-Cl-C_6H_4	CH_3	C_6H_5	**4e**	179-180, (177-178)[15]	6	91	83	8	88	81
6	*p*-F-C_6H_4	CH_3	C_6H_5	**4f**	104-106, (105-108[15]	3	92	84	6	90	82
7	*p*-CH_3-C_6H_4	CH_3	C_6H_5	**4g**	166-167 (163-164)[15]	6	90	82	10	90	82
8	*p*-$CH(CH_3)_2$-C_6H_4	CH_3	C_6H_5	**4h**	162-164 (164-166)[15]	6	90	83	10	88	81
9	*p*-NO_2-C_6H_4	CH_3	C_6H_5	**4i**	173-174 (175-177)[15]	3	94	86	6	91	84
10	*m*-NO_2-C_6H_4	CH_3	C_6H_5	**4j**	132-135 (131-133)[15]	3	93	85	7	92	84
11	*p*-CN-C_6H_4	CH_3	C_6H_5	**4k**	240-241 (240-242)[15]	3	91	83	7	90	82
12	*p*-CF_3-C_6H_4	CH_3	C_6H_5	**4l**	186-188 (184-186)[15]	3	93	86	6	89	82
13	*m*-OCH_3-C_6H_4	CH_3	C_6H_5	**4m**	104-106 (106-107)[15]	6	90	82	10	83	76
14	2-Naphthyl	CH_3	C_6H_5	**4n**	140-141 (139-142)[15]	6	91	84	10	85	78

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15[b]	4-OH-C_6H_3	CH_3	C_6H_5	**4o**	226-228 (225-228)[15]	7	90	82	12	83	76
16	C_6H_5	CH_3	C_6H_{11}	**4p**	114-116 (112-114)[15]	6	90	82	9	88	80
17	*m*-OC_6H_4-C_6H_4	CH_3	C_6H_{11}	**4q**	170-172 (167-169)[15]	8	91	83	9	90	82
18	C_6H_5	H	C_6H_5	**4r**	198-199	6	89	80	8	84	76
19	*p*-Cl-C_6H_4	H	C_6H_5	**4s**	205-207	6	92	84	19	88	80
20	*p*-CH_3-C_6H_4	H	C_6H_5	**4t**	202-204	6	90	78	10	87	75
21	*p*-NO_2-C_6H_4	H	C_6H_5	**4u**	206-208	5	90	82	7	85	78
22	*p*-CN-C_6H_4	H	C_6H_5	**4v**	251-253	5	91	83	7	89	81
23	*m*-NO_2-C_6H_4	H	C_6H_5	**4w**	183-185	5	92	84	7	89	81

[a] Isolated yields. [b] Atom economy.

The model reaction was also examined in the presence of various glycerol-based eutectic solvents as another green reaction media[23] at 100 °C (Table 1, entries 14-19) and in all cases high yields of products were obtained. However, glycerol was selected as the best promoting medium for this reaction because it is a readily available material and there is no need to a pre-treatment step as this is necessary for the production of eutectic systems.

It should be noted that the synthesis of triazolo[1,2-*a*]indazole-triones *via* a one-pot three component condensation reaction between aldehydes, carbonyl compounds possessing a reactive α-methylene group and urazoles are generally carried out in the presence of various acids or metal-containing catalysts with the aid of organic solvents. Obviously, these reported methods not only generate a lot of organic or inorganic wastes during the work-up procedure, but also suffer from the difficulty of removing trace amounts of residue metal species from the product when it is applied in pharmaceutical synthesis. Particularly, in the case of solid acids, a large amount of organic solvent has to be used for the separation and recovery of the catalyst owing to the fact that both the catalyst and the product are solid. Performing the model reaction in glycerol not only offers a high reaction yield, but also avoids the generation of toxic wastes, the use of large amount of organic solvents or catalysts and tedious post-treatment. Therefore, our system is an attractive strategy for the synthesis of the target compound from the viewpoint of green synthesis. With these results in hand, we then investigated the substrate scopes and limitations of the synthesis of triazolo[1,2-*a*]indazole-triones in glycerol as a promoting medium, and the results are listed in Table 2. As it is shown in Table 2, all reactions proceeded efficiently and the desired products were produced in good to excellent yields in relatively short reaction times without formation of any by-products. Aromatic aldehydes having electron withdrawing groups (Table 2, entries 6, 9, 10, 11, 12, 21, 22, 23) reacted at faster rates compared with those that substituted with electron releasing groups (Table 2, entries 8, 13, 17, 20). The reactivity of aliphatic aldehydes was also investigated with the condensation of butyraldehyde with dimedone and *N*-phenylurazole and unfortunately only a mixture of starting materials and unknown products was obtained even after a long time (24h).

Due to the high hydrophilicity of glycerol, separation of the products from the reaction mixture could be realized by adding water at 100 °C. This simple procedure allows easy scale up of our methodology. In another study, to recognize the applicability of our method at large scales, we examined reactions in scales of 25 mmol and the obtained results are summarized in Table 2. As shown in Table 2, the reactions were successfully performed at large scales without significant loss of yield.

In another study phthalhydrazide (**5**, 1 mmol) was applied instead of *N*-phenyl urazole in one-pot condensation with benzaldehyde (**1a**, 1 mmol) and dimedone (**2b**, 1 mmol) under optimized reaction condition (Scheme 3) and desired product (**6**) was obtained as a white powder after 4h in 90% yield. Moreover, this reaction was applied in 25 mmol scale and desired product was obtained after 8 h in 85% yield. These results demonstrate the efficiency of glycerol

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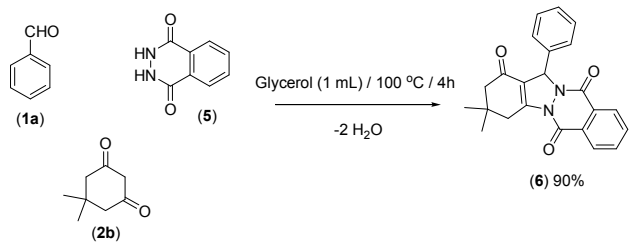
as a promoting medium for the synthesis of indazolo[2,1-*b*]phthalazine-triones as the other important derivatives of indazoles. Besides, these results approve the efficiency of glycerol as a promoting medium in such multi component reactions that are conducted through an intramolecular cyclocondensation reaction.



Scheme 3. The one-pot three component condensation reaction of benzaldehyde (**1a**, 1mmol), dimedone (**2a**, 1 mmol) and phthalhydrazide (**5**, 1 mmol) in the presence of glycerol (1 mL) at 100 °C.

It is well known that presented method for the synthesis of titled compounds is a multi-component approach that is established based on electrophilic alkylation of aldehydes with a nucleophile with the aid of an intramolecular condensation that is fully studied in the literature.[24] Moreover, the mechanism of condensation of aldehydes, reactive carbonyl compounds possessing a α-methylene group and urazoles in the presence of various catalytic systems is fully described.[14, 15] However, in this work, any kind of catalyst was not applied and the reaction was just preceded in the presence of glycerol as a benign reaction medium. As it has been mentioned by Safaei *et al.*[25], it may be speculated that the polar amphoteric hydroxyl groups of the glycerol facilitate the interaction of weak acidic and basic components due to the stabilization of the corresponding transition states and intermediates by hydrogen bonding. Moreover, we think that hydrogen bonding between polar parts of electrophiles and nucleophiles may lead to the increase in their nucleophilicity as well as electrophilicity. So, in addition to its unique properties a benign and non-hazardous reaction medium, glycerol can act as an activator in this reaction.

Conclusion

In summary, a highly efficient, catalyst-free and more benign procedure was reported for one-pot three component synthesis of triazolo[1,2-*a*]indazole-triones using glycerol as an inexpensive, biodegradable and commercially available promoting medium. This method avoids the use of hazardous catalysts or solvents. The promising points for the presented methodology are large-scale availability, high efficiency, high yields of products, short reaction times, facile work up and product isolation and finally, agreement with green chemistry protocols, that making it a useful and attractive process for the synthesis of triazolo[1,2-*a*]indazole-trione derivatives. Compared with previously reported systems composed of acid or base catalysts and organic solvents, application of glycerol as a solvent not only makes the product separation much easier, but also shows higher environmental compatibility and sustainability due to the avoidance of a quenching step, reduced reliance on toxic organic solvents, and minimization of waste.

Experimental

All chemicals were purchased from Merck or Fluka Chemical Companies. The ^{1}H NMR (250 MHz) and ^{13}C NMR (62.5 MHz) were run on a Bruker Avance DPX-250, FT-NMR spectrometer (δ in ppm). Microanalysis was performed on a PerkineElmer 240-B microanalyzer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes. The progress of the reaction and the purity of compounds were monitored by TLC analytical silica gel plates (Merck 60 F250).

General procedure for the synthesis of triazolo[1,2-*a*]indazole-trione derivatives

To a mixture of aldehyde (1 mmol), carbonyl compound possessing a reactive α-methylene group (1 mmol) and urazole (1 mmol) in a 10 mL round-bottomed flask connected to a reflux condenser, was added glycerol (1 mL), and the resulting mixture was stirred in an oil-bath (100 °C). The progress nof the reaction was monitored by TLC using EtOAc/*n*-hexane (1:5) as an eluent. After completion of the reaction, warm water (5 mL) was added. Glycerol dissolved in the water and the insoluble crude products were isolated by simple filtration. The crude products were dissolved in warm EtOH (6 mL) and were allowed to stand at room temperature for 5-6 h. The crystalline solids were collected and dried.

General procedure for the large scale synthesis of triazolo[1,2-*a*]indazole-trione derivatives

To a mixture of aldehyde (25 mmol), carbonyl compound possessing a reactive α-methylene group (25 mmol) and urazole (25 mmol) in a 100 mL round-bottomed, two necked flask fitted with an efficient mechanical stirrer and a reflux condenser, was added glycerol (25 mL), and the resulting mixture was stirred in an oil-bath (100 °C). The progress of the reaction was monitored by TLC using EtOAc/*n*-hexane (1 : 5) as an eluent. After completion of the reaction, warm water (25 mL) was added. Glycerol dissolved in the water and the insoluble crude products were isolated by simple filtration. The crude products were dissolved in warm EtOH or (30 mL) and were allowed to stand at room temperature for 24 h.

Selected Spectral Data:

6,7-dihydro-2,9-diphenyl-[1,2,4]triazolo[1,2-*a*]indazole-1,3,8(2*H*,5*H*,9*H*)-trione (4r)

White powder, υ_{max} (KBr) 3050, 2965, 1720, 1655, 1610, 1375 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) 1.65-1.82 (m, 2H), 1.89-1.98 (m, 2H), 2.01-2.81 (m, 2H), 6.22 (s, 1H,), 7.40-7.50 (m, 10H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 21.4, 21.9, 34.3, 64.4, 120.0, 123.4, 126.4, 127.5, 127.9, 128.52, 128.59, 132.9, 135.0, 137.0, 150.8, 152.0, 192.0. Anal. Calcd for $C_{21}H_{17}N_3O_3$: C, 70.18; H, 4.77; N, 11.69 %. Found: C, 71.21; H, 4.72; N, 11.73 %.

9-(4-chlorophenyl)-6,7-dihydro-2-phenyl-[1,2,4]triazolo[1,2-*a*]indazole-1,3,8(2*H*,5*H*,9*H*)-trione (4s)

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White powder, υ_{max} (KBr) 3050, 2950, 1665, 1615, 1200 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) 2.15-2.25 (m, 2H), 2.42-2.47 (m, 2H), 2.99-3.06 (m, 2H), 6.16 (s, 1H), 7.32-7.48 (m, 9H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 21.9, 22.6, 34.6, 64.8, 119.1, 122.6, 126.6, 127.8, 128.8, 129.4, 132.1, 132.2, 133.9, 136.5, 150.6, 152.5, 192.0. Anal. Calcd for $C_{21}H_{16}ClN_3O_3$: C, 64.05; H, 4.09; N, 10.67%. Found: C, 64.10; H, 4.16; N, 10.55 %.

6,7-dihydro-2-phenyl-9-*p*-tolyl-[1,2,4]triazolo[1,2-*a*]indazole-1,3,8(2*H*,5*H*,9*H*)-trione (4t)

White powder, υ_{max} (KBr) 3060, 2940, 1670, 1620, 1210 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) 1.28 (s, 3H), 1.70 (m, 2H), 1.89 (m, 2H), 2.53 (m, 2H), 6.20 (s, 1H), 7.20 (d, *J*= 8.0 Hz, 2H), 7.35 (d, *J*= 8.0 Hz, 2H), 7.40-7.48 (m, 1H), 7.55-7.59 (m, 4H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 20.9, 21.8, 22.7, 66.9, 121.9, 126.5, 127.8, 129.1, 130.2, 130.3, 132.5, 133.7, 136.5, 136.7, 153.8, 154.5, 190.5. Anal. Calcd for $C_{22}H_{19}N_3O_3$: C, 70.76; H, 5.13; N, 11.25%. Found: C, 70.64; H, 5.19; N, 11.12 %.

6,7-dihydro-9-(4-nitrophenyl)-2-phenyl-[1,2,4]triazolo[1,2-*a*]indazole-1,3,8(2*H*,5*H*,9*H*)-trione (4u)

White powder, υ_{max} (KBr) 3050, 2960, 1650, 1610, 1200 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) 2.06-2.29 (m, 2H), 2.31-2.37 (m, 2H), 2.88-2.95 (m, 2H), 6.18 (s, 1H), 7.33-7.42 (m, 5H), 7.66 (dd, *J*= 8.75, 3.75 Hz, 2H), 8.13 (dd, *J*= 8.75, 3.75 Hz, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 21.3, 22.0, 34.8, 63.5, 119.5, 122.5, 124.4, 126.4, 127.9, 128.6, 132.8, 135.6, 135.9, 143.7, 150.9, 151.5, 192.0. Anal. Calcd for $C_{21}H_{16}N_4O_5$: C, 62.37; H, 3.99; N, 13.86%. Found: C, 62.42; H, 3.85; N, 13.93 %.

4-(1,2,3,5,6,7,8,9-octahydro-1,3,8-trioxo-2-phenyl-[1,2,4]triazolo[1,2-*a*]indazol-9-yl)benzonitrile (4v)

White powder, υ_{max} (KBr) 3040, 2950, 2250, 1650, 1620, 1200 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) 1.70 (m, 2H), 1.81 (m, 2H), 2.52 (m, 2H), 6.31 (s, 1H), 7.43-7.52 (br, 5H), 7.70 (d, *J*= 7.5 Hz, 2H), 8.01 (d, *J*= 7.5 Hz, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 21.5, 22.9, 36.8, 67.3, 112.0, 119.5, 121.7, 125.8, 128.5, 129.0, 130.6, 131.7, 132.5, 137.8, 140.9, 151.6, 153.0, 192.0. Anal. Calcd for $C_{22}H_{16}N_4O_3$: C, 68.74; H, 4.20; N, 14.58%. Found: C, 68.68; H, 4.29; N, 14.66%.

6,7-dihydro-9-(3-nitrophenyl)-2-phenyl-[1,2,4]triazolo[1,2-*a*]indazole-1,3,8(2*H*,5*H*,9*H*)-trione (4w)

White powder, υ_{max} (KBr) 3050, 2970, 1670, 1610, 1220 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) 1.76 (m, 2H), 1.88 (m, 2H), 2.59 (m, 2H), 6.30 (s, 1H), 7.44-7.58 (m, 5H), 7.63 (t, *J*= 7.5 Hz, 1H), 7.95 (d, *J*= 7.0 Hz, 1H), 8.20 (d, *J*= 7.0 Hz, 1H), 8.34 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 21.7, 22.9, 36.7, 67.0, 121.9, 122.6, 125.5, 128.5, 129.1, 129.8, 130.5, 132.7, 134.1, 137.6, 146.5, 152.7, 152.9, 191.7. Anal. Calcd for $C_{21}H_{16}N_4O_5$: C, 62.37; H, 3.99; N, 13.86%. Found: C, 62.44; H, 4.11; N, 13.74%.

3,4-dihydro-3,3-dimethyl-13-phenyl-2H-indazolo[1,2-b]phthalazine-1,6,11(13H)-trione (6)

White powder, υ_{max} (KBr) 3045, 2985, 1665, 1620, 1210 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.23 (s, 6H), 2.36 (Distorted AB System, 2H), 3.26 (AB System, *J*= 19.0 Hz, 1H), 3.44 (AB System, *J*= 19.0 Hz, 1H), 6.47 (s, 1H), 7.30 (d, *J*= 6.0 Hz, 1H), 7.36 (t, *J*= 7.5 Hz, 2H), 7.44 (d, *J*= 7.0 Hz, 2H), 7.86 (dd, *J*= 6.0, 3.5 Hz, 2H), 8.29 (t, *J*= 7.5 Hz, 1H), 8.37 (dd, *J*= 6.0, 3.5 Hz, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 28.9, 29.1, 35.0, 38.4, 65.3, 119.0, 127.5, 128.1, 128.4, 129.11, 129.14, 129.4, 129.5, 133.9, 134.9, 136.8, 151.2, 154.7, 156.4, 192.5. Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52%. Found: C, 74.29; H, 5.38; N, 7.63%.

Acknowledgements

The authors gratefully appreciate the Shiraz University Research Councils for the financial support of this work.

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DOI: 10.1039/C5RA13805A

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