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Highly efficient synthesis of triazolo[1,2-*a*]indazole-triones and novel spiro triazolo[1,2-*a*]indazole-tetraones under solvent-free conditions

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ABSTRACT

A new, convenient, and high yielding procedure for the synthesis of triazolo[1,2-*a*]indazole-triones by the condensation reaction between dimedone, aryl aldehydes, and ueazoles in the presence of a catalytic amount of sulfonated polyethylene glycol (PEG-SO_3H) as a highly stable and reusable eco-friendly degradable polymeric catalyst is described under solvent-free conditions. This procedure has also been applied successfully for the synthesis of novel spiro triazolo[1,2-*a*]indazole-tetraones.

1. Introduction

Heterocyclic compounds occur very widely in nature and are essential to life. Nitrogen-containing heterocyclic molecules constitute the largest portion of chemical entities, which are part of many natural products, fine chemicals, and biologically active pharmaceuticals vital for enhancing the quality of life.[1] Amongst them, urazole derivatives are very interesting compounds, found to have some biological as well as pharmaceutical activity, such as anti-cancer and hypolipidemic.[2] These compounds are also used in the preparation of herbicides,[3] pesticides,[4] insecticides,[5] and polymeric materials with unique properties, such as heat-resistant coatings,[6] tyre rubbers with high gripability,[7] and melamine resins.[8] One of the most important biologically active compound containing a urazole moiety in its structure is compound **a**, that has been shown to have HSP inhibitory[9] (Fig. 1). Beside this several indolines, spiro-annulated with heterocycles at the 3-position, have shown good biological activities.[10,11] These compounds are the core structure of many pharmacological agents and natural alkaloids.[12–14] For example, spirotryprostatins (**b**), natural alkaloids isolated from the fermentation broth of *Aspergillus fumigatus*, have been identified as novel inhibitors of microtubule assembly.[14] Moreover, Compound (**c**) has shown antimicrobial activity[10] (Fig. 1).

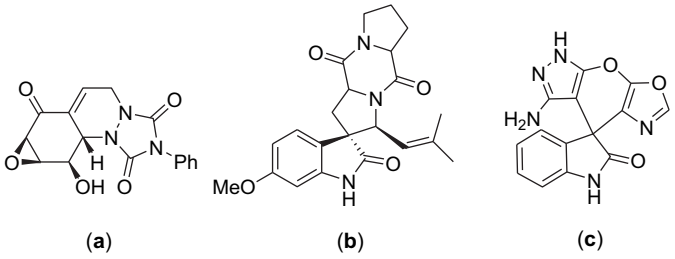

Fig. 1. Biological active compounds base on urazole and/or spirooxindole derivatives.

Multi-component reactions (MCRs), have many advantages over conventional synthetic methodologies, such as higher productivity, simple procedures, and facile execution, and play an important role in combinatorial chemistry.[15] Despite the spectacular investment in, and organic growth of, combinatorial chemistry as a platform technology within the pharmaceutical industry during two past decades, few new MCRs were discovered or developed. Typical examples are Biginelli,[16] Passerini,[17] Ugi,[15b,18] and Mannich[19] reactions that used successfully in many organic syntheses. Upon these facts, great efforts have been and still are being made to find and develop new MCRs.

The utility of polymer catalysts is now well-recognized because of their ease of workup and of separation of products and catalysts, from the economical point of view, and in application to industrial processes, etc.[20] In general, catalysts are immobilized on polymers

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via coordinate or covalent bonds. High reactivity, lack of diffusion phenomena, and analytical simplicity (advantageous features of homogeneous solution chemistry) beside the ready isolation and purification of products (advantageous features of solid phase methods)[21] introduce PEGs as an important group of polymeric supports for the preparation of polymer supported catalysts. Sulfonated polyethylene glycol (PEG-SO_3H) is an interesting example of PEG-supported catalysts that functionalized by acidic groups, and has been used for the synthesis of 3,4-dihydropyrimidones[22] and thiocyanohydrines.[23]

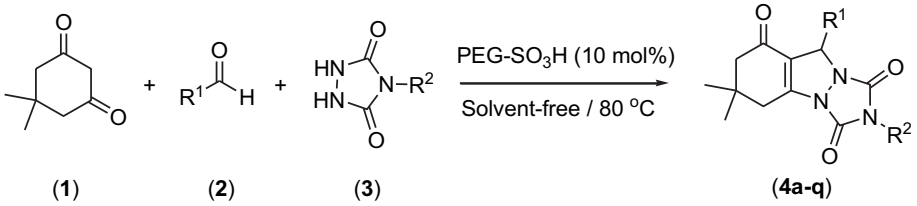
The resultant pharmacological interest in compounds, which belong to the urazole, indoline, and spirooxindole family, has led us to develop the synthesis of some novel spiro triazolo[1,2-*a*]indazole-tetraones. In continuation of our interest in using the solid acid catalysts in organic transformations,[24] herein we report the catalytic activity of sulfonated polyethylene glycol as an eco-friendly degradable polymeric catalyst for the synthesis of triazolo[1,2-*a*]indazole-triones and novel spiro triazolo[1,2-*a*]indazole-tetraone derivatives via the one-pot three-component reaction of dimedone, carbonyl compounds and 4-substituted urazoles under solvent-free conditions (Schemes 1 and 3).

40 min. Increasing the amount of PEG-SO_3H to more than 20 mol % showed no substantial improvement in the yield, whereas the yield decreased by decreasing the amount of the catalyst to 5 mol %. Moreover, it was observed that the reaction did not proceed efficiently in the absence of PEG-SO_3H after a long time (3 h).

In the next step, the scope and efficiency of the catalyst were explored under the optimized reaction conditions for the condensation of different 4-substituted urazoles with a broad range of structurally diverse aldehydes and dimedone to furnish the corresponding products (Scheme 1). The results are displayed in Table 2. As it can be seen the triazolo[1,2-*a*]indazole-trione derivatives were obtained in high yields and short reaction times.

The influence of electron-withdrawing and electron-donating substituents on the aromatic ring of aldehydes upon the reaction yields was investigated. The results showed that both electron-withdrawing and electron-donating substituents had no significant effect on the reaction yields (Table 2, entries 2, and 8–13). Moreover, the presence of halogen on the aromatic ring of aldehydes had negligible effect on the reaction results (Table 2, entries 3–7).

Interestingly, the catalyst was effectively used for the synthesis of a complex structure, bis-triazolo[1,2-*a*]indazole-trione with the



Scheme 1. One-pot three-component synthesis of triazolo[1,2-*a*]indazole-triones in the presence of PEG-SO_3H (10 mol %) at 80 °C under solvent-free conditions.

2. Results and discussions

Our initial efforts focused on the search for a catalyst for the condensation reaction between dimedone, aryl aldehydes, and urazoles. For this purpose, the condensation reaction between dimedone (1 mmol), benzaldehyde (1 mmol), and 4-phenylurazole (1 mmol) for the synthesis of compound **4a** was selected as a model reaction in the presence of different catalytic systems and the results are summarized in Table 1.

After extensive screening, we found that the optimized best yields and time profiles were obtained with 10 mol % of PEG-SO_3H under solvent-free conditions at 80 °C, which furnished the corresponding triazolo[1,2-*a*]indazole-trione **4a** in 91% yield within

condensation reaction between dimedone, terphthaldehyde, and 4-phenylurazole for the first time (Table 3, entry 15). The reaction of 2 equiv of dimedone and 4-phenylurazole with terephthalaldehyde proceeded rapidly to give compound **4o** in 89% yield. Compound **4o** has two carbon chiral centers and could exist in two diastereomeric forms. We proposed a mechanism for the formation of these diastereomeric compounds in Scheme 2. First, in the presence of PEG-SO_3H two molecules of dimedone are added to a molecule of therphetalaldehyde by aldol condensation to form intermediate **a**. Then, an urazole molecule is added to this intermediate by Michael addition reaction and intra molecular cyclization to form intermediate **b**. After that, there are two path ways for the addition of second urazole molecule to this intermediate (path 1 and 2) that

Table 1
One-pot three-component synthesis of compound **4a** from dimedone (1 mmol), benzaldehyde (1 mmol), and 4-phenylurazole (1 mmol) in the presence of various catalytic systems (10 mol %)

Entry	Catalyst	Reaction conditions	Time (min)	Yield[a] (%)
1	SiO_2-OSO_3H[b] (0.5 g)	Solvent-free, 80 °C	240	81
2	P_2O_5/SiO_2 (5% w/w)	Solvent-free, 80 °C	240	57
3	$NaHSO_4 \cdot SiO_2$	Solvent-free, 80 °C	360	46
4	$InCl_3 \cdot 3H_2O$	Solvent-free, 80 °C	180	50
5	$(NH_4)_6Mo_7O_{24} \cdot 4H_2O$	Solvent-free, 80 °C	180	26
6	[Bmim]HSO_4	Solvent-free, 80 °C	240	50
7	[Bmim]OH	Solvent-free, 80 °C	360	34
8	ZnO	Solvent-free, 80 °C	480	Trace
9	$Ni(OAc)_2$	Solvent-free, 80 °C	240	20
10	PEG-SO_3H	Solvent-free, 80 °C	40	91
11	PEG-SO_3H	H_2O, 80 °C	240	Trace
12	PEG-SO_3H	EtOH, reflux	240	65
13	PEG-SO_3H	CH_3CN, reflux	240	76
14	PEG-SO_3H	$CHCl_3$, reflux	240	52
15	PEG-SO_3H	EtOAc, reflux	240	43
16	—	Solvent-free, 80 °C	240	Trace

[a] Isolated yields.
[b] Silica sulfuric acid (for the preparation of this catalyst see Ref. 26).

Table 2
One-pot three-component synthesis of triazolo[1,2-*a*]indazole-triones in the presence of PEG-SO_3H as a catalyst under solvent-free conditions at 80 °C

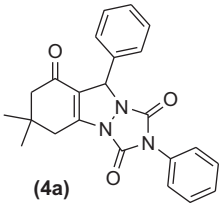
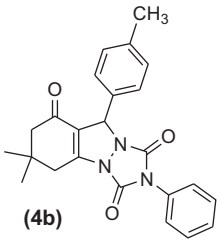
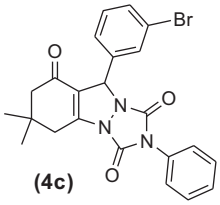
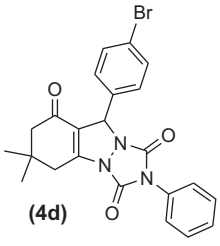
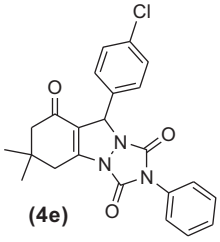
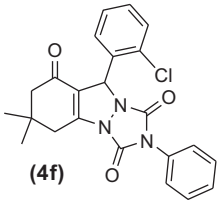
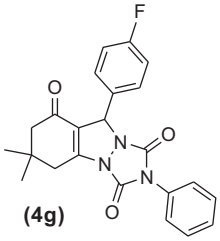
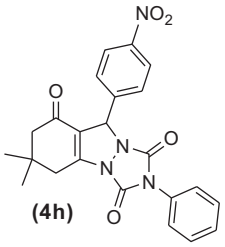
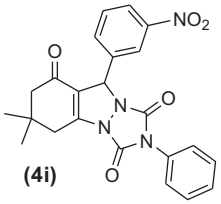
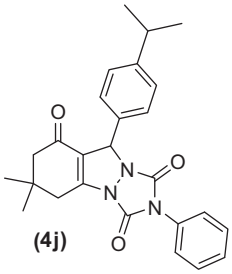
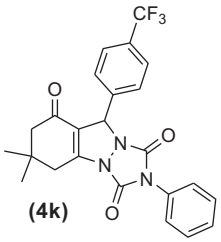
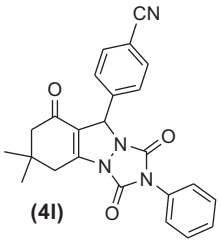
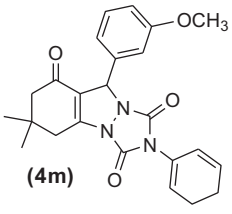
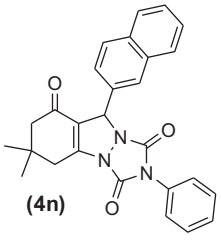
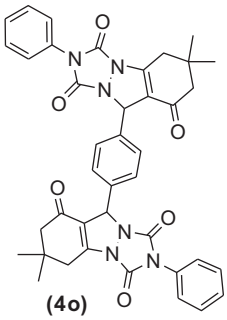
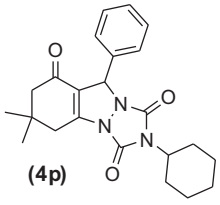
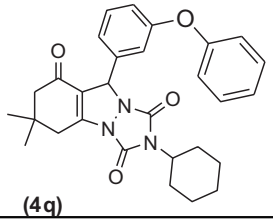
Entry	R^1	R^2	Product	Time (min)	Yield[a] (%)
1	C_6H_5	C_6H_5	 (4a)	40	91
2	*p*-CH_3–C_6H_4	C_6H_5	 (4b)	45	89
3	*m*-Br–C_6H_4	C_6H_5	 (4c)	35	83
4	*p*-Br–C_6H_4	C_6H_5	 (4d)	35	91
5	*p*-Cl–C_6H_4	C_6H_5	 (4e)	35	90
6	*o*-Cl–C_6H_4	C_6H_5	 (4f)	65	84
7	*p*-F–C_6H_4	C_6H_5	 (4g)	40	90

Table 2 (*continued*)

Entry	R^1	R^2	Product	Time (min)	Yield[a] (%)
8	*p*-NO_2–C_6H_4	C_6H_5	 **(4h)**	30	92
9	*m*-NO_2–C_6H_4	C_6H_5	 **(4i)**	30	91
10	*p*-$CH(CH_3)_2$–C_6H_4	C_6H_5	 **(4j)**	55	89
11	*p*-CF_3–C_6H_4	C_6H_5	 **(4k)**	35	90
12	*p*-CN–C_6H_4	C_6H_5	 **(4l)**	40	89
13	*m*-OCH_3–C_6H_4	C_6H_5	 **(4m)**	65	88
14	2-Naphthyl	C_6H_5	 **(4n)**	60	90

(*continued on next page*)

Table 2 (*continued*)

Entry	R^1	R^2	Product	Time (min)	Yield[a] (%)
15[b]	4-OHC–C_6H_3	C_6H_5	 **(4o)**	180	89
16	C_6H_5	C_6H_{11}	 **(4p)**	360	82
17	*m*-OC_6H_4–C_6H_4	C_6H_{11}	 **(4q)**	300	88

[a] Isolated yields.
[b] Reaction conditions: dimedone (2 equiv), 4-phenylurazole (2 equiv) and terephthaldehyde (1 equiv).

Table 3
One-pot three-component synthesis of spiro triazolo[1,2-*a*]indazole-tetraones in the presence of PEG-SO_3H as a catalyst under solvent-free conditions at 80 °C

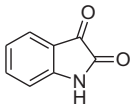
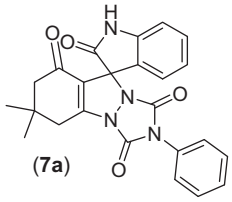
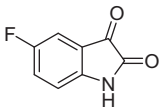
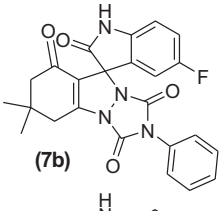
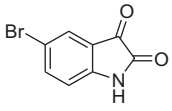
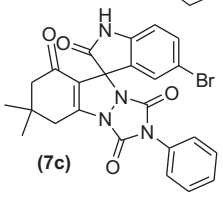
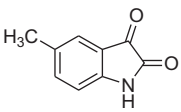
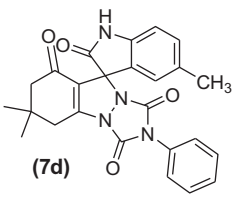
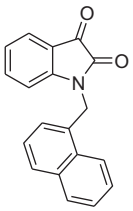
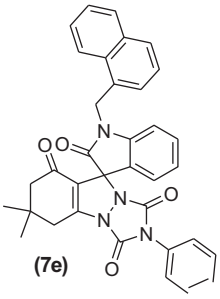
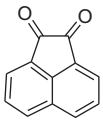
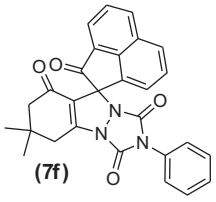
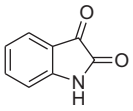
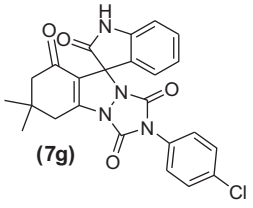
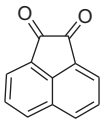
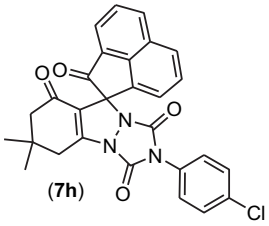
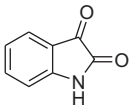
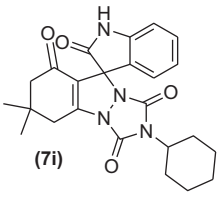
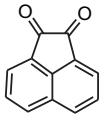
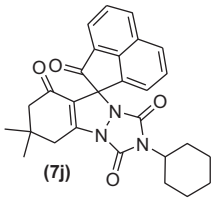
Entry	Substrate	R^3	Product	Time (h)	Yield[a] (%)
1		C_6H_5	 **(7a)**	6	89
2		C_6H_5	 **(7b)**	8	90
3		C_6H_5	 **(7c)**	5	92
4		C_6H_5	 **(7d)**	5	86

Table 3 (*continued*)

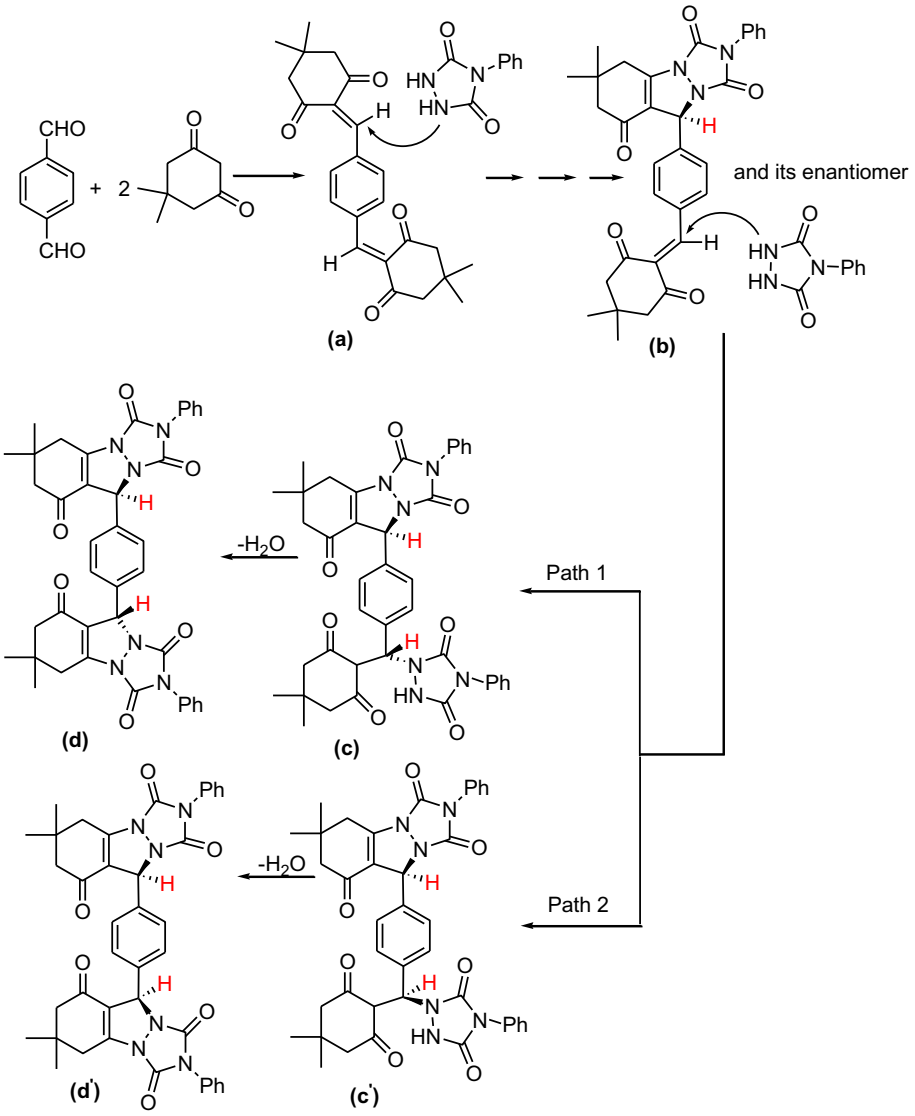
Entry	Substrate	R^3	Product	Time (h)	Yield[a] (%)
5		C_6H_5	 **(7e)**	7	89
6		C_6H_5	 **(7f)**	3	92
7		*p*-Cl–C_6H_4	 **(7g)**	7	90
8		*p*-Cl–C_6H_4	 **(7h)**	4	91
9		C_6H_{11}	 **(7i)**	8	87
10		C_6H_{11}	 **(7j)**	4	89

[a] Isolated yield.

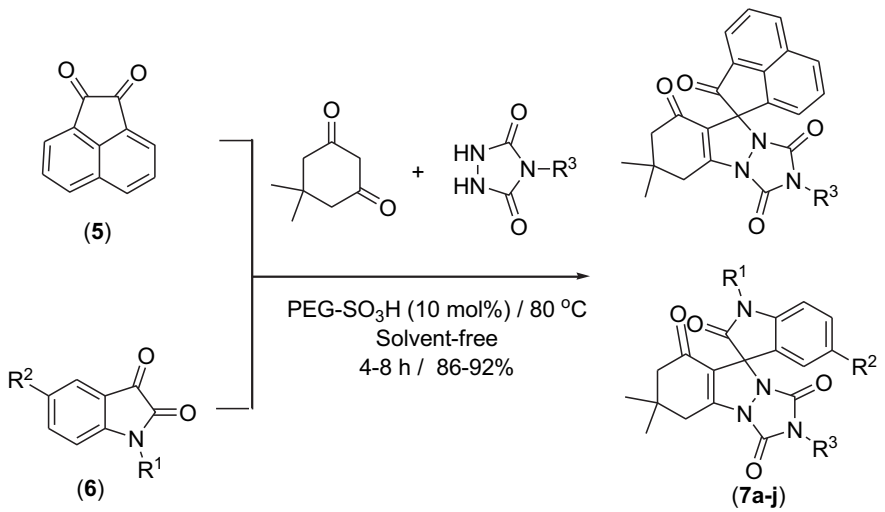
lead to form of two diastereomeric intermediates **c** and **c′**. Finally, the intra molecular cyclization and elimination reaction lead to form of two diastereomeric form for compound **4o** (**d** and **d′**).

NMR data show that we only obtained a single diastereomeric form for compound **4o** in this reaction condition. We tried to get its crystallographic structure but unfortunately, we could not get single crystal and X-ray structure for compound **4o**. So, according to these observations, we think that this diastereomeric selectivity referred to this fact that the addition of second urazole molecule can be done from the less hindered side of intermediate **b** and according to the bulky structure of molecules and catalyst, intermediate **c** has the less activation energy in comparison with intermediate **c′** and compound **4o** has the stereo structure of **d** shown in Scheme 2.

After the successful synthesis of triazolo[1,2-*a*]indazole-triones, this catalytic system was used for the synthesis of new spiro triazolo [1,2-*a*]indazole-tetraone derivatives for the first time. For this purpose, dimedone and 4-substituted urazoles were condensed with acenaphthenequinone (**5**) and or isatin derivatives (**6**) under optimized reaction conditions to afford the corresponding products (**7a**–**j**) (Scheme 3). The results of the reactions are summarized in Table 3.



Scheme 2. Two diastereomeric forms of compound **4o**.



Scheme 3. One-pot three-component synthesis of triazolo[1,2-*a*]indazole-tetraones in the presence of PEG-SO_3H as a catalyst under solvent-free conditions at 80 °C.

Various structurally diverse of spiro triazolo[1,2-*a*]indazole-tetraones were synthesized by the condensation reaction of dimedone, 4-substituted urazoles, and acenaphthenequinone as well as isatin derivatives in the presence of PEG-SO_3H as an efficient catalyst.

The experimental procedure is remarkably simple because after the completion of the reaction, water was added to the reaction mixture and the insoluble crude products were isolated by simple filtration and recrystallized to obtain pure products. In order to resumption of catalyst, water was evaporated in reduced pressure and recovered catalyst was washed by diethyl ether two times and reused for another reaction. Any loose of rates or yields was observed by use of recovered PEG-SO_3H for five cycle of reactions.

3. Conclusions

In conclusion, an extremely efficient method has been developed for the synthesis of triazolo[1,2-*a*]indazole-triones and novel spiro triazolo[1,2-*a*]indazole-tetraones via a one-pot three-component condensation reaction using sulfonated polyethylene glycol as an eco-friendly degradable polymeric catalyst. This method is bestowed with several unique merits, such as high conversions, simplicity in operation, cost efficiency, use of solvent-free and mild conditions, simple workup, high yields and usage in synthesis of complex molecules.

4. Experimental

4.1. General

All chemicals were purchased from Merck or Fluka Chemical Companies. The ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) were run on a Bruker Avance DPX-250, FT-NMR spectrometer (δ in ppm). Microanalysis was performed on a Perkin–Elmer 240-B micro-analyzer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

4.2. Preparation of PEG-SO_3H

At 0 °C, chlorosulfonic acid (1.16 g, 10 mmol) was added to a solution of PEG-6000 (6.0 g, 1 mmol) in CH_2Cl_2 (10 mL). Then the resulting solution was stirred at room temperature overnight, and the solution was concentrated under vacuum. Appropriate ether (50 mL) was added, and the precipitate filtered and washed with ether (30 mL) three times to afford the PEG-SO_3H.[23]

4.3. Typical procedure for the synthesis of triazolo[1,2-*a*] indazole-trione (4a)

Dimedone (0.14 g, 1 mmol), benzaldehyde (0.1 g, 1 mmol), and 4-phenylurazole (0.177 g, 1 mmol) were mixed with PEG-SO_3H (0.6 g, 0.1 mmol) and the obtained mixture was stirred magnetically at 80 °C for 40 min. After the completion of the reaction warm water (20 mL) was added and the mixture stirred for about 5 min. The insoluble crude product was filtered and recrystallized from EtOH/H_2O 4:1 and the pure product was obtained (0.352 g, 91%). In order to recover the catalyst, the filtrate was dried under reduced pressure and recovered catalyst was washed with diethyl ether and reused after drying under reduced pressure. The equivalent procedure was used for the synthesis of triazolo[1,2-*a*]indazole-tetraones.

4.4. Selected spectral data

4.4.1. 6,6-Dimethyl-2,9-diphenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a] indazole-1,3,8(2H,5H,9H)-trione, ***4a****, (0.352 g, 91%).* White powder, mp=190–192 °C (188–190 °C),[25] ν_{max} (KBr) 3040, 2960, 1720, 1650, 1610, 1370 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.23 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 2.37 (Distorted AB system, 2H, CH_2), 2.94–2.95 (Distorted AB System, 2H, CH_2), 6.24 (s, 1H, C*H*–Ph), 7.42–7.52 (10H, m, Ph). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.1, 28.6, 34.8, 35.4, 51.6, 64.7, 120.4, 125.6, 127.3, 128.7, 128.9, 129.1, 130.6, 131.5, 136.8, 149.0, 150.6, 151.1, 192.0. Anal. Calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85%. Found: C, 71.28; H, 5.33; N, 10.91%.

4.4.2. 6,6-Dimethyl-2-phenyl-9-p-tolyl-6,7-dihydro-[1,2,4]triazolo [1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4b****, (0.357 g, 89%).* White powder, mp=163–164 °C (160–162 °C),[25] ν_{max} (KBr) 3030, 2940, 1720, 1670, 1620, 1380 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.23 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 2.36–2.49 (m, 5H, Ph-C*H*$_3$, and CH_2), 2.88 (AB System, ^2J=16.0 Hz, 1H, CH_2), 2.96 (AB System, ^2J=16.0 Hz, 1H, CH_2), 6.20 (s, 1H, C*H*–Ar), 7.22 (d, J=8.0 Hz, 2H, Ar), 7.34 (d, J=8.0 Hz, 2H, Ar), 7.42–7.45 (m, 1H, Ar), 7.55 (d, J=4.0 Hz, 4H, Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 21.6, 28.7, 29.1, 35.1, 35.9, 51.7, 64.4, 120.6, 126.0, 127.4, 129.1, 129.7, 130.0, 131.2, 134.2, 139.1, 139.3, 150.8, 151.2, 192.3. Anal. Calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47%. Found: C, 71.72; H, 5.86; N, 10.59%.

4.4.3. 9-(3-Bromophenyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4] triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4c****, (0.387 g, 83%).* White powder, mp=172–174 °C (174–176 °C),[25] ν_{max} (KBr) 3060, 2960, 1720, 1660, 1620, 1380 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.22 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 2.36–2.37 (Distorted AB System, 2H, CH_2), 2.93–2.95 (Distorted AB System, 2H, CH_2), 6.20 (s, 1H, C*H*–Ar), 7.34–7.52 (m, 9H, Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.8, 29.0, 35.2, 35.9, 51.7, 63.8, 120.0, 125.9, 126.0, 127.5, 129.2, 129.4, 129.7, 130.5, 131.0, 135.2, 139.3, 149.5, 151.5, 151.7, 192.3. Anal. Calcd for $C_{23}H_{20}BrN_3O_3$: C, 59.24; H, 4.32; N, 9.01%. Found: C, 59.33; H, 4.29; N, 8.89%.

4.4.4. 9-(4-Bromophenyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4] triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4d****, (0.424 g, 91%).* White powder, mp=185–187 °C (184–186 °C),[25] ν_{max} (KBr) 3050, 2960, 1660, 1610, 140, 1380 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.21 (s, 6H, CH_3), 2.34 (Distorted AB System, 2H, CH_2), 2.84–2.96 (Distorted AB System, 2H, CH_2), 6.17 (s, 1H, C*H*–Ar), 7.35–7.55 (m, 9H, Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.6, 29.1, 35.1, 35.9, 51.7, 63.9, 120.1, 123.3, 125.9, 129.2, 129.7, 131.1, 132.4, 136.4, 149.5, 149.9, 151.3, 151.6, 192.3. Anal. Calcd for $C_{23}H_{20}BrN_3O_3$: C, 59.24; H, 4.32; N, 9.01%. Found: C, 59.25; H, 4.33; N, 8.99%.

4.4.5. 9-(4-Chlorophenyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4] triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4e****, (0.379 g, 90%).* White powder, mp=173–175 °C (166–168 °C),[25] ν_{max} (KBr) 3050, 2950, 1660, 1610, 1200 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.22 (s, 6H, CH_3), 2.34 (AB System, ^2J=19.0 Hz, 1H, CH_2), 2.39 (AB System, ^2J=19.0 Hz, 1H, CH_2), 2.90 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.96 (AB System, ^2J=18.5 Hz, 1H, CH_2), 6.21 (s, 1H, C*H*–Ar), 7.38–7.51 (m, 9H, Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.1, 28.8, 34.5, 35.3, 51.1, 63.6, 119.4, 125.5, 128.3, 128.7, 129.0, 129.3, 130.6, 134.3, 135.5, 149.2, 151.1, 151.4, 191.9. Anal. Calcd for $C_{23}H_{20}ClN_3O_3$: C, 65.48; H, 4.78; N, 9.96%. Found: C, 65.59; H, 4.88; N, 9.81%.

4.4.6. 9-(2-Chlorophenyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4] triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4f****, (0.354 g, 84%).* White powder, mp=177–178 °C (173–175 °C),[25] ν_{max} (KBr) 3050, 2950, 1720, 1650, 1610, 1380 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.23 (s, 6H, CH_3), 2.31 (AB System, ^2J=16.5 Hz, 1H, CH_2), 2.35 (AB System, ^2J=16.5 Hz, 1H, CH_2), 2.90 (AB System, ^2J=17.0 Hz, 1H, CH_2), 2.99 (AB System, ^2J=17.0 Hz, 1H, CH_2), 6.37 (s, 1H, C*H*–Ar), 7.32–7.50 (m, 9H, Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.6, 29.3, 35.0, 35.8, 51.6,

63.9, 118.9, 126.1, 127.9, 129.1, 129.6, 130.9, 131.1, 131.2, 131.7, 132.4, 133.2, 148.7, 150.4, 151.1, 192.0. Anal. Calcd for $C_{23}H_{20}ClN_3O_3$: C, 65.48; H, 4.78; N, 9.96%. Found: C, 65.38; H, 4.75; N, 9.88%.

4.4.7. 9-(4-Fluorophenyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4g****, (0.364 g, 90%).* White powder, mp=105–108 °C (102–103 °C),[25] ν_{max} (KBr) 3060, 2960, 1730, 1680, 1620, 1500, 1380 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.25 (s, 6H, CH_3), 2.36 (AB System, ^2J=16.5 Hz, 1H, CH_2), 2.43 (AB System, ^2J=16.5 Hz, 1H, CH_2), 2.95–2.96 (m, 2H, CH_2), 6.24 (s, 1H, C*H*–Ar), 7.11 (t, *J*=8.2 Hz, 2H, Ar), 7.45–7.48 (m, 3H, Ar), 7.52–7.53 (m, 4H, Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.5, 29.1, 35.1, 35.9, 51.6, 63.9, 120.7, 126.9, 129.2, 129.7, 131.5, 132.9, 137.4, 149.5, 149.9, 151.6, 151.7, 161.3 (d, $^1J_{C-F}$=273.5 Hz), 193.4. ^{19}F NMR (470.5 MHz, $CDCl_3$): δ (ppm) −113.2 (s, 1F). Anal. Calcd for $C_{23}H_{20}FN_3O_3$: C, 68.14; H, 4.97; N, 10.36%. Found: C, 68.19; H, 5.02; N, 10.18%.

4.4.8. 6,6-Dimethyl-9-(4-nitrophenyl)-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4h****, (0.397 g, 92%).* White powder, mp=179–181 °C (175–177 °C),[25] ν_{max} (KBr) 3040, 2960, 1730, 1660, 1610, 1520, 1410, 1390, 1350 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.21 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 2.35 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.42 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.91 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.98 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.89–3.00 (m, 2H, CH_2), 6.32 (s, 1H, C*H*–Ar), 7.47 (s, 1H, H–Ar), 7.53 (s, 4H, H–Ar), 7.75 (d, *J*=7.6 Hz, 2H, H–Ar), 8.27 (d, *J*=7.6 Hz, 2H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.6, 29.0, 35.2, 36.0, 51.6, 63.7, 119.6, 124.5, 125.9, 128.5, 129.4, 129.8, 130.9, 144.2, 148.5, 149.6, 152.0, 152.2, 192.3. Anal. Calcd for $C_{23}H_{20}N_4O_5$: C, 63.88; H, 4.66; N, 12.96%. Found: C, 63.95; H, 4.56; N, 12.93%.

4.4.9. 6,6-Dimethyl-9-(3-nitrophenyl)-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4i****, (0.393 g, 91%).* White powder, mp=131–133 °C (126–128 °C),[25] ν_{max} (KBr) 3060, 2960, 1720, 1650, 1620, 1520, 1400, 1380 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.20 (s, 6H, CH_3), 2.35 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.41 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.92 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.98 (AB System, ^2J=18.5 Hz, 1H, CH_2), 6.34 (s, 1H, C*H*–Ar), 7.46–7.52 (m, 5H, H–Ar), 7.61 (t, *J*=7.5 Hz, 1H, H–Ar), 7.91 (d, *J*=7.0 Hz, 1H, H–Ar), 8.22 (d, *J*=7.0 Hz, 1H, H–Ar), 8.32 (s, 1H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.7, 28.9, 35.2, 33.9, 51.6, 63.6, 119.5, 122.3, 124.1, 126.0, 129.3, 129.8, 130.3, 130.9, 134.2, 139.7, 148.9, 149.6, 11.3, 152.1, 192.4. Anal. Calcd for $C_{23}H_{20}N_4O_5$: C, 63.88; H, 4.66; N, 12.96%. Found: C, 63.81; H, 4.69; N, 12.92%.

4.4.10. 9-(4-Isopropylphenyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4j****, (0.382 g, 89%).* White powder, mp=164–166 °C, ν_{max} (KBr) 3040, 2950, 1710, 1640, 1600, 1390 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.23 (s, 3H, CH_3), 1.26 (s, 6H, $CH(CH_3)_2$), 1.27 (s, 3H, CH_3), 2.37–2.38 (m, 2H, CH_2), 2.90–2.95 (m, 3H, CH_2, and $CH(CH_3)_2$), 6.23 (s, 1H, C*H*–Ar), 7.28 (t, *J*=8.0 Hz, 2H, H–Ar), 7.38 (d, *J*=8.5 Hz, 2H, H–Ar), 7.42–7.45 (m, 1H, H–Ar), 7.50–7.51 (m, 4H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 24.3, 28.8, 29.1, 34.2, 35.1, 35.9, 51.7, 64.3, 120.5, 126.0, 127.44, 127.48, 129.1, 129.7, 131.2, 134.5, 149.4, 149.9, 151.0, 151.3, 191.3. Anal. Calcd for $C_{26}H_{27}N_3O_3$: C, 72.71; H, 6.34; N, 9.78%. Found: C, 72.75; H, 6.32; N, 9.83%.

4.4.11. 6,6-Dimethyl-2-phenyl-9-(4-(trifluoromethyl)phenyl)-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4k****, (0.409 g, 90%).* White powder, mp=184–185 °C, ν_{max} (KBr) 3020, 2970, 1850, 1720, 1670, 1610, 1405, 1380, 1305, 1250, 1110 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.23 (s, 6H, CH_3), 2.34 (AB System, ^2J=18.6 Hz, 1H, CH_2), 2.40 (AB System, ^2J=18.6 Hz, 1H, CH_2), 2.91 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.97 (AB System, ^2J=18.5 Hz, 1H, CH_2), 6.28 (s, 1H, C*H*–Ar), 7.43–7.45 (m, 1H, H–Ar), 7.51–7.54 (m, 4H, H–Ar), 7.63 (d, *J*=8.2 Hz, 2H, H–Ar), 7.69 (d, *J*=8.2 Hz, 2H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.6, 29.1, 35.2, 35.9, 51.9, 63.9, 120.0, 124.2 (q, $^1J_{C-F}$=278.7 Hz), 126.0, 126.32, 126.35, 127.9, 129.3, 129.8, 131.0, 131.5, 141.2, 149.6, 151.6, 192.3. ^{19}F NMR (470.5 MHz, $CDCl_3$): δ (ppm) -63.0 (s, 3F), Anal. Calcd for $C_{24}H_{20}F_3N_3O_3$: C, 63.29; H, 4.43; N, 9.23%. Found: C, 63.32; H, 4.46; N, 9.28%.

4.4.12. 4-(6,6-Dimethyl-1,3,8-trioxo-2-phenyl-1,2,3,5,6,7,8,9-octahydro-[1,2,4]triazolo[1,2-a]indazol-9-yl)benzonitrile, ***4l****, (0.367 g, 89%).* White powder, mp=240–242 °C, ν_{max} (KBr) 3040, 2960, 2210, 1730, 1710, 1670, 1610, 1370 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.20 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 2.35 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.41 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.87–2.98 (m, 2H, CH_2), 6.25 (s, 1H, C*H*–Ar), 7.43–7.54 (m, 4H, H–Ar), 7.62 (d, *J*=8.0 Hz, 2H, H–Ar), 7.69 (d, *J*=8.0 Hz, 2H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.7, 29.0, 35.2, 35.9, 51.6, 63.9, 113.0, 118.8, 119.6, 125.9, 128.3, 129.3, 129.8, 130.9, 133.1, 142.4, 149.6, 151.9, 152.0, 192.3. Anal. Calcd for $C_{24}H_{20}N_4O_3$: C, 69.89; H, 4.89; N, 13.58%. Found: C, 69.92; H, 4.85; N, 13.62%.

4.4.13. 9-(3-Methoxyphenyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4m****, (0.367 g, 88%).* White powder, mp=106–107 °C, ν_{max} (KBr) 3050, 2960, 1720, 1660, 1490, 1280 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.24 (s, 6H, CH_3), 2.35 (AB System, ^2J=16.5 Hz, 1H, CH_2), 2.39 (AB System, ^2J=16.5 Hz, 1H, CH_2), 2.92 (AB System, ^2J=18.5 Hz, 1H, CH_2), 2.96 (AB System, ^2J=18.5 Hz, 1H, CH_2), 3.84 (s, 3H, Ar–OCH_3), 6.20 (s, 1H, C*H*–Ar), 6.90–6.91 (m, 1H, H–Ar), 7.02 (s, 1H, H–Ar), 7.04 (d, *J*=7.5 Hz, 1H, H–Ar), 7.33 (t, *J*=7.75 Hz, 1H, H–Ar), 7.2–7.46 (m, 1H, H–Ar), 7.51 (d, *J*=4.0 Hz, 2H, Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.4, 29.2, 34.9, 35.8, 51.6, 53.4, 63.9, 111.8, 115.7, 116.8, 119.3, 120.4, 123.6, 124.1, 130.7, 130.8, 147.5, 157.2, 157.3, 159.4, 163.5, 196.5. Anal. Calcd for $C_{24}H_{23}N_3O_4$: C, 69.05; H, 5.55; N, 10.07%. Found: C, 69.09; H, 5.61; N, 10.11%.

4.4.14. 6,6-Dimethyl-9-(naphthalen-2-yl)-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4n****, (0.393 g, 90%).* White powder, mp=139–142 °C, ν_{max} (KBr) 3050, 2950, 1700, 1615, 1600, 1390 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.24 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 2.37 (Distorted AB System, 2H, CH_2), 2.97 (AB System, ^2J=15.0 Hz, 1H, CH_2), 3.01 (AB System, ^2J=15.0 Hz, 1H, CH_2), 6.41 (s, 1H, C*H*–Ar), 7.42–7.56 (m, 8H, H–Ar), 7.85–7.86 (m, 1H, H–Ar), 7.88–7.91 (m, 2H, H–Ar), 7.96 (s, 1H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.7, 29.1, 35.2, 36.0, 51.7, 64.8, 120.6, 124.5, 126.0, 126.8, 126.9, 127.2, 128.1, 128.7, 131.1, 133.6, 133.8, 134.5, 149.5, 151.1, 151.5, 192.3. Anal. Calcd for $C_{27}H_{23}N_3O_3$: C, 74.12; H, 5.30; N, 9.60%. Found: C, 74.18; H, 5.36; N, 6.99%.

4.4.15. 9,9′-(1,4-Phenylene)bis(6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione), ***4o****, (0.620 g, 89%).* White powder, mp=225–228 °C dec, ν_{max} (KBr) 3080, 2950, 1710, 1650, 1390 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.22 (s, 6H, CH_3), 1.24 (s, 6H, CH_3), 2.34 (AB System, ^2J=18.0 Hz, 2H, CH_2), 2.39 (AB System, ^2J=18.0 Hz, 2H, CH_2), 2.89 (AB System, ^2J=19.0 Hz, 2H, CH_2), 2.96 (AB System, ^2J=19.0 Hz, 2H, CH_2), 6.26 (s, 2H, C*H*–Ar), 7.42–7.52 (m, 14H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.9, 29.07, 35.1, 35.9, 51.7, 63.9, 120.2, 126.0, 128.05, 128.08, 129.2, 129.7, 131.1, 137.9, 149.6, 151.3, 151.4, 192.3. Anal. Calcd for $C_{40}H_{36}N_6O_6$: C, 68.95; H, 5.21; N, 12.06%. Found: C, 68.98; H, 5.29; N, 12.13%.

4.4.16. 2-Cyclohexyl-6,6-dimethyl-9-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4p****, (0.322 g, 82%).* Yellow powder, mp=112–114 °C, ν_{max} (KBr) 3050, 2950, 1705, 1670, 1620, 1380 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 1.21 (s, 6H, CH_3), 1.33–1.39 (m, 2H, CH_2), 1.69–1.72 (m, 2H, CH_2), 1.79–1.81 (m, 2H, CH_2), 1.87–1.89 (m, 2H, CH_2), 2.08–2.17 (m, 2H, CH_2), 2.33 (s, 2H, CH_2), 2.83–2.91 (m, 2H, CH_2), 3.88–3.94 (m, 1H, N–C*H*C_5H_{10}), 6.11 (s, 1H,

C*H*–Ar), 7.33–7.34 (m, 1H, H–Ph), 7.38–7.42 (m, 4H, H–Ph). ^{13}C NMR ($CDCl_3$, 125 MHz): δ (ppm) 25.2, 26.0, 28.6, 29.1, 29.7, 29.7, 35.1, 35.9, 51.6, 53.2, 64.2, 120.2, 127.4, 129.1, 120.2, 137.6, 150.7, 151.4, 152.9, 192.4. Anal. Calcd for $C_{23}H_{27}N_3O_3$: C, 70.21; H, 6.92; N, 10.68%. Found: C, 70.25; H, 6.98; N, 10.77%.

4.4.17. 2-Cyclohexyl-6,6-dimethyl-9-(3-phenoxyphenyl)-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione, ***4q****, (0.427 g, 88%).* White powder, mp=167–169 °C, ν_{max} (KBr) 3050, 2960, 1720, 1660, 1490 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 1.21 (s, 6H, CH_3), 1.25–1.36 (m, 2H, CH_2), 1.69–1.89 (m, 6H, CH_2), 2.11–2.16 (m, 2H, CH_2), 2.33 (m, 2H, CH_2), 2.86 (m, 2H, CH_2), 3.89–3.92 (m, 1H, N–C*H*C_5H_{10}), 6.09 (s, 1H, C*H*–Ar), 6.75 (s, 1H), 6.80 (d, *J*=8.0 Hz, 1H, H–Ar), 6.91 (d, *J*=8.0 Hz, 1H, H–Ar), 6.97–7.01 (m, 5H, H–Ar), 7.13 (t, *J*=7.2 Hz, 1H, H–Ar), 7.29 (t, *J*=7.7 Hz, 1H, H–Ar), 7.37 (t, *J*=8.0 Hz, 2H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 25.9, 26.0, 26.1, 28.6, 29.7, 33.1, 35.3, 51.6, 53.2, 64.2, 113.2, 117.4, 118.0, 119.4, 120.4, 123.0, 124.3, 130.8, 130.8, 147.8, 157.2, 157.5, 159.3, 163.5, 196.4. Anal. Calcd for $C_{29}H_{31}N_3O_4$: C, 71.73; H, 6.43; N, 8.65%. Found: C, 71.71; H, 6.48; N, 8.74%.

4.4.18. 6,6-Dimethyl-2-phenyl-6,7-dihydro-1H-spiro[[1,2,4]triazolo [1,2-a]indazole-9,3′-indoline]-1,2′,3,8(2H,5H)-tetraone, ***7a****, (0.381 g, 89%).* White powder, mp=298–300 °C dec, ν_{max} (KBr) 3310, 3050, 2950, 1790, 1740, 1650, 1600, 1360 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.22 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 2.20–2.40 (m, 2H, CH_2), 2.93 (AB System, ^2J=16.0 Hz, 1H, CH_2), 3.09 (AB System, ^2J=16.0 Hz, 1H, CH_2), 6.96 (d, *J*=7.0 Hz, 1H, H–Ar), 7.26–7.51 (m, 8H, H–Ar), 8.40 (s, 1H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.3, 29.1, 35.3, 35.5, 51.3, 71.3, 111.4, 119.0, 125.1, 125.8, 126.2, 129.1, 129.5, 131.1, 131.5, 132.5, 140.3, 140.3, 148.0, 152.1, 171.1, 191.2. Anal. Calcd for $C_{24}H_{20}N_4O_4$: C, 67.28; H, 4.71; N, 13.08%. Found: C, 67.22; H, 473; N, 13.11%.

4.4.19. 5′-Fluoro-6,6-dimethyl-2-phenyl-6,7-dihydro-1H-spiro [[1,2,4]triazolo[1,2-a]indazole-9,3′-indoline]-1,2′,3,8(2H,5H)-tetraone, ***7b****, (0.401 g, 90%).* White powder, mp=311–313 °C dec, ν_{max} (KBr) 3390, 3060, 2950, 1730, 1710, 1690, 1630 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.05 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 2.03–2.20 (m, 2H, CH_2), 2.75–2.91 (m, 2H, CH_2), 6.78–7.32 (m, 8H, H–Ar), 10.41 (s, 1H, NH). ^{13}C NMR (125 MHz, $CDCl_3$/DMSO-d_6): δ (ppm) 28.2, 29.00, 35.3, 35.8, 51.3, 71.3, 112.2, 117.6, 118.1, 118.9, 119.9, 126.2, 129.2, 129.5, 130.9, 139.0, 178.8, 150.0, 152.1, 159.8 (d, $^1J_{C-F}$=275.0 Hz), 171.9, 191.1. ^{19}F NMR (470.5 MHz, DMSO-d_6): δ (ppm) -121.3 (s, 1F). Anal. Calcd for $C_{24}H_{19}FN_4O_4$: C, 64.57; H, 4.29; N, 12.55%. Found: C, 64.49; H, 4.33; N, 12.59%.

4.4.20. 5′-Bromo-6,6-dimethyl-2-phenyl-6,7-dihydro-1H-spiro [[1,2,4]triazolo[1,2-a]indazole-9,3′-indoline]-1,2′,3,8(2H,5H)-tetraone, ***7c****, (0.466 g, 92%).* White powder, mp=292–293 °C, ν_{max} (KBr) 3350, 2950, 1790, 1705, 1680, 1610, 1490, 1380 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.22 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 2.30 (AB System, ^2J=16.0 Hz, 1H, CH_2), 2.38 (AB System, ^2J=16.0 Hz, 1H, CH_2), 2.93 (AB System, ^2J=18.5 Hz, 1H, CH_2), 3.09 (AB System, ^2J=18.5 Hz, 1H, CH_2), 6.64 (d, *J*=8.5 Hz, 1H, H–Ar), 7.34–7.36 (dd, *J*=2.0, 8.5 Hz, 1H, H–Ar), 7.39 (d, *J*=1.5 Hz, 1H, H–Ar), 7.43–7.53 (m, 5H, H–Ar), 8.40 (s 1H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.2, 29.2, 35.6, 36.0, 51.4, 71.2, 113.2, 116.1, 118.9, 126.3, 127.3, 127.7, 129.5, 129.8, 130.7, 134.2, 141.0, 148.5, 150.7, 153.0, 170.6, 191.7. Anal. Calcd for $C_{24}H_{19}BrN_4O_4$: C, 56.82; H, 3.77; N, 11.04%. Found: C, 56.88; H, 3.70; N, 11.12%.

4.4.21. 5′,6,6-Trimethyl-2-phenyl-6,7-dihydro-1H-spiro[[1,2,4]triazolo [1,2-a]indazole-9,3′-indoline]-1,2′,3,8(2H,5H)-tetraone, ***7d****, (0.380 g, 86%).* White powder, mp=308–310 °C, ν_{max} (KBr) 3410, 3045, 2950, 1790, 1750, 1730, 1650, 1605, 1500, 1370 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.13 (s, 6H, CH_3), 2.22 (s, 3H, Ar–C*H*$_3$), 2.64 (m, 2H, CH_2), 2.85–2.95 (m, 2H, CH_2), 6.76 (br, 1H, H–Ar), 6.98–7.00 (br, 2H, H–Ar), 7.93 (br, 5H, H–Ar), 9.94 (br, 1H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 21.4, 28.3, 29.0, 35.3, 35.9, 51.4, 71.1, 111.4, 119.5, 125.0, 125.5, 126.2, 129.1, 129.5, 131.0, 131.6, 132.7, 140.3, 148.4, 150.0, 152.0, 171.5, 191.2. Anal. Calcd for $C_{25}H_{22}N_4O_4$: C, 67.86; H, 5.01; N, 12.66%. Found: C, 67.88; H, 5.11; N, 12.71%.

4.4.22. 6,6-Dimethyl-1′-(naphthalen-1-ylmethyl)-2-phenyl-6,7-dihydro-1H-spiro[[1,2,4]triazolo[1,2-a]indazole-9,3′-indoline]-1,2′,3,8 (2H,5H)-tetraone, ***7e****, (0.506 g, 89%).* White powder, mp=294–296 °C dec, ν_{max} (KBr) 3040, 2950, 1780, 1710, 1700, 1650, 1600, 1390 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.11 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 2.37–2.41 (Distorted AB System, 2H, CH_2), 2.98 (AB System, ^2J=18.5 Hz, 1H, CH_2), 3.12 (AB System, ^2J=18.5 Hz, 1H, CH_2), 5.49 (AB System, ^2J=17.0 Hz, 1H, C*H*$_2$–Naphtyl), 5.61 (AB System, ^2J=17.0 Hz, 1H, C*H*$_2$-Naphtyl), 6.66 (d, *J*=8.0 Hz, 1H, H–Ar), 7.12 (t, *J*=7.5 Hz, 1H, H–Ar), 7.24 (t, *J*=7.7 Hz, 1H, H–Ar), 7.37 (d, *J*=7.0 Hz, 1H, H–Ar), 7.44–7.64 (m, 8H, H–Ar), 7.70 (d, *J*=7.0 Hz, 1H, H–Ar), 7.81 (d, *J*=8.0 Hz, 1H, H–Ar), 7.94 (d, *J*=7.5 Hz, 1H, H–Ar), 8.08 (d, *J*=8.5 Hz, 1H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.6, 28.9, 35.5, 36.1, 42.9, 51.5, 63.4, 111.12, 127.122.12, 122.84, 124.0, 124.2, 124.9, 126.2, 126.3, 126.8, 127.1, 127.8, 127.9, 128.3, 129.3, 129.6, 129.7, 131.3, 133.6, 133.8, 134.5, 144.9, 148.7, 152.5, 152.9, 171.7, 191.7. Anal. Calcd for $C_{36}H_{30}N_4O_4$: C, 74.21; H, 5.19; N, 9.62%. Found: C, 74.28; H, 5.10; N, 9.64%.

4.4.23. 6,6-Dimethyl-2-phenyl-6,7-dihydro-1H,2′H-spiro[[1,2,4]triazolo[1,2-a]indazole-9,1′-acenaphthylene]-1,2′,3,8(2H,5H)-tetraone, ***7f****, (0.426 g, 92%).* Yellow powder, mp=278–279 °C, ν_{max} (KBr) 3050, 2960, 1720, 1660, 1620, 1410, 1380 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.24 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 2.22 (AB System, ^2J=16.0 Hz, 1H, CH_2), 2.31 (AB System, ^2J=16.0 Hz, 1H, CH_2), 2.99 (AB System, ^2J=18.5 Hz, 1H, CH_2), 3.14 (AB System, ^2J=18.5 Hz, 1H, CH_2), 7.41 (t, *J*=6.7 Hz, 1H, H–Ar), 7.46–7.52 (m, 4H, H–Ar), 7.62 (d, *J*=7.0 Hz, 1H, H–Ar), 7.71 (t, *J*=7.5 Hz, 1H, H–Ar), 7.83 (d, *J*=7.5 Hz, 1H, H–Ar), 7.99 (d, *J*=8.0 Hz, 1H, H–Ar), 8.22 (d, *J*=8.0 Hz, 1H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.3, 29.2, 35.5, 36.0, 51.4, 71.2, 120.5, 121.1, 123.5, 126.2, 127.2, 128.9, 129.0, 129.2, 130.9, 131.0, 131.1, 133.2, 134.7, 142.8, 148.6, 150.5, 152.1, 191.3, 197.4. Anal. Calcd for $C_{28}H_{21}N_3O_4$: C, 72.56; H, 4.57; N, 9.07%. Found: C, 72.51; H, 4.63; N, 9.14%.

4.4.24. 2-(4-Chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H-spiro [[1,2,4]triazolo[1,2-a]indazole-9,3′-indoline]-1,2′,3,8(2H,5H)-tetraone, ***7g****, (0.416 g, 90%).* White powder, mp=303–304 °C dec, ν_{max} (KBr) 3350, 3060, 2950, 1770, 1710, 1650, 1600 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.19 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 2.31 (AB System, ^2J=16.0 Hz, 1H, CH_2), 2.35 (AB System, ^2J=16.0 Hz, 1H, CH_2), 2.93 (AB System, ^2J=18.5 Hz, 1H, CH_2), 3.06 (AB System, ^2J=18.5 Hz, 1H, CH_2), 6.90 (d, *J*=8.0 Hz, 1H, H–Ar), 7.10 (t, *J*=7.5 Hz, 1H, H–Ar), 7.26–7.34 (m, 2H, H–Ar), 7.43–7.47 (m, 4H, H–Ar), 7.88 (s, 1H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.4, 29.0, 35.5, 36.0, 51.4, 71.1, 111.6, 119.4, 121.1, 123.9, 124.6, 125.9, 126.5, 127.3, 129.9, 131.4, 135.1, 141.6, 152.3, 161.1, 171.1, 191.2. Anal. Calcd for $C_{24}H_{19}ClN_4O_4$: C, 62.27; H, 4.14; N, 12.10%. Found: C, 62.34; H, 4.16; N, 12.15%.

4.4.25. 2-(4-Chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H,2′H-spiro [[1,2,4]triazolo[1,2-a]indazole-9,1′-acenaphthylene]-1,2′,3,8(2H,5H)-tetraone, ***7h****, (0.453 g, 91%).* Yellow powder, mp=269–271 °C, ν_{max} (KBr) 3080, 2960, 1760, 1700, 1640, 1610, 1500, 1370 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.23 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 2.22 (AB System, ^2J=16.2 Hz, 1H, CH_2), 2.30 (AB System, ^2J=16.2 Hz, 1H, CH_2), 2.98 (AB System, ^2J=18.5 Hz, 1H, CH_2), 3.13 (AB System, ^2J=18.5 Hz, 1H, CH_2), 7.44–7.49 (m, 4H, H–Ar), 7.46–7.52 (m, 4H, H–Ar), 7.61 (d, *J*=7.0 Hz, 1H, H–Ar), 7.70 (d, *J*=8.5 Hz, 1H, H–Ar),

7.83 (t, J=7.5 Hz, 1H, H–Ar), 8.00 (d, J=8.5 Hz, 1H, H–Ar), 8.09 (d, J=7.0 Hz, 1H, H–Ar), 8.23 (d, J=8.0 Hz, 1H, Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.3, 29.2, 35.7, 36.0, 51.4, 71.0, 120.6, 121.1, 123.6, 127.2, 12.3, 128.9, 129.1, 129.6, 129.8, 130.8, 131.2, 133.3, 134.5, 135.0, 142.8, 148.2, 150.1, 151.9, 191.3, 197.3. Anal. Calcd for $C_{28}H_{20}ClN_3O_4$: C, 67.54; H, 4.05; N, 8.44%. Found: C, 67.61; H, 4.08; N, 8.51%.

4.4.26. 2-Cyclohexyl-6,6-dimethyl-6,7-dihydro-1H-spiro[[1,2,4]triazolo[1,2-a]indazole-9,3′-indoline]-1,2′,3,8(2H,5H)-tetraone, ***7i****, (0.378 g, 87%).* Yellow powder, mp=297–299 °C, ν_{max} (KBr) 3380, 2980, 1780, 1710, 1620, 1600, 1360 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.19 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.33–2.37 (m, 12H, CH_2), 2.90 (AB System, ^2J=14.2 Hz, 1H, CH_2), 3.08 (AB System, ^2J=14.2 Hz, 1H, CH_2), 3.63–3.87 (m, 1H, N–C*H*C$_5$H$_{10}$), 6.75 (m, 1H, H–Ar), 6.98 (m, 1H, H–Ar), 7.11–7.38 (m, 2H, H–Ar) 8.56 (br, 1H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 25.7, 26.0, 28.3, 29.0, 29.4, 29.7, 31.3, 35.5, 36.1, 51.9, 53.5, 71.1, 114.1, 115.1, 123.0, 127.0, 129.0, 129.1, 136.5, 143.7, 150.0, 152.0, 171.4, 197.8. Anal. Calcd for $C_{24}H_{26}N_4O_4$: C, 66.34; H, 6.03; N, 12.89%. Found: C, 66.39; H, 6.08; N, 12.83%.

4.4.27. 2-Cyclohexyl-6,6-dimethyl-6,7-dihydro-1H,2′H-spiro[[1,2,4]triazolo[1,2-a]indazole-9,1′-acenaphthylene]-1,2′,3,8(2H,5H)-tetraone, ***7j****, (0.417 g, 89%).* Yellow powder, mp=246–248 °C, ν_{max} (KBr) 3050, 2950, 1790, 1710, 1670, 1610 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.19 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.66 (m, 1H, CH_2), 1.85–1.87 (m, 4H, CH_2), 2.17–2.27 (m, 7H, CH_2), 2.91 (AB System, ^2J=18.5 Hz, 1H, CH_2), 3.08 (AB System, ^2J=18.5 Hz, 1H, CH_2), 3.84–3.91 (m, 1H, N–C*H*C$_5$H$_{10}$), 7.55 (d, J=6.5 Hz, 1H, H–Ar), 7.68 (t, J=7.5 Hz, 1H, H–Ar), 7.81 (t, J=7.7 Hz, 1H, H–Ar), 7.97 (d, J=8.5 Hz, 1H, H–Ar), 8.07 (d, J=7.0 Hz, 1H, H–Ar), 8.21 (d, J=8.5 Hz, 1H, H–Ar). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 25.2, 26.0, 28.4, 29.0, 29.6, 29.7, 31.3, 35.4, 36.0, 51.3, 53.5, 71.0, 120.1, 121.0, 123.3, 127.0, 128.9, 129.0, 130.9, 131.1, 133.0, 135.0, 142.7, 150.0, 152.0, 152.4, 191.4, 197.8. Anal. Calcd for $C_{28}H_{27}N_3O_4$: C, 71.62; H, 5.80; N, 8.95%. Found: C, 71.66; H, 5.87; N, 8.96%.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.11.029. These data include MOL files and InChiKeys of the most important compounds described in this article.

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