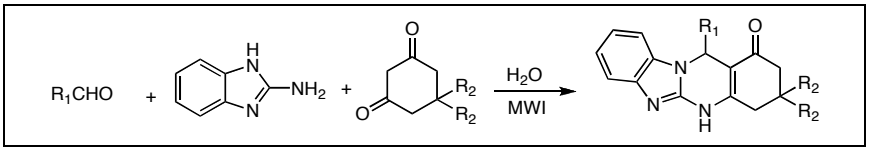
Green and High Efficient Synthesis of Triaza-benzo[*b*]fluoren-6-one Derivatives in Water under Microwave Irradiation

Qingqing Shao[a], Shujiang Tu*[a], Chunmei Li[a], Longji Cao[a], Dianxiang Zhou[a], Qian Wang[b], Bo Jiang[a], Yan Zhang[a], Wenjuan Hao[a]

[a]School of Chemistry and Chemical Engineering, Xuzhou Normal University, Key Laboratory of Biotechnology on Medical Plant, Xuzhou, Jiangsu 221116, PR China
[b]Xuzhou Medical College, Jiangsu 221004, PR China

Received June 28, 2007



Triaza-benzo[*b*]fluoren-6-one derivatives were synthesized *via* the three-component reaction of aldehyde, cyclohexane-1,3-dione compound and 2-aminobenzimidazole in water under microwave irradiation. The new protocol has the advantages of excellent yield, low cost, reduced environment impact, wide scope and convenient procedure.

J. Heterocyclic Chem., **45**, 411 (2008).

INTRODUCTION

The concept of "green chemistry" has been widely adopted to meet the fundamental scientific challenges of protecting human health and the environment while simultaneously achieving commercial viability [1]. The emerging area of green chemistry envisages minimum hazard as the performance criteria while designing new chemical processes. One of the thrust areas for achieving this target is to explore alternative reaction conditions and reaction media to accomplish the desired chemical transformations with minimum byproducts and waste generation, as well as eliminating the use of volatile and toxic organic solvents [2].

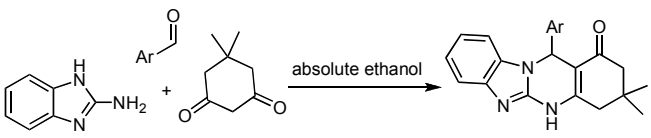
Organic reactions accelerated under the influence of microwave (MW) irradiation have attracted considerable attention in the past decade for the efficient and relatively friendlier synthesis of a variety of organic compounds [3]. The use of MW irradiation for the formation of several carbon-heteroatom and carbon-carbon bonds has been successfully demonstrated [4].

Nitrogen-containing heterocycles are known subunits in many natural products and biologically active pharmaceuticals [5]. Varied biological activities have been attributed to triaza-benzo[*b*]fluoren-6-one compounds, including analgesic, antiinflamatory, antipyretic [6-8], antimicrobial [9], anticonvulsant [10], fungicidal [11], antidepressant or other central nervous system affecting activities [12], and recently two original triaza-benzo[*b*]-fluoren-6-one compounds were described as a new class of potent antitumour compounds [13].

Developing efficient, selective and eco-friendly synthetic methods for applications in complex organic preparations is the ultimate goal of several research groups, including ours [14]. Among alternative, friendlier solvents, water is very benign [15] and has been utilized in combination with microwave irradiation [16] wherein activation of reactions can be achieved.

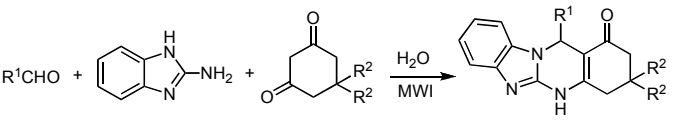
Braulio Insuasty [17] and co-workers have reported the reaction of aromatic aldehyde, 2-aminobenzimidazole and 5,5-dimethylcyclohexane-1,3-dione in absolute ethanol (Scheme 1). Their protocol gave moderate yields (60%-86%) except for the limitation: (i) narrow scope of only aromatic aldehyde, and only 5,5-dimethylcyclohexane-1,3-dione as the cyclic active methylene compound, (ii) organic solvent, (iii) long reaction time. Therefore, it is urgent to develop a more efficient and greener protocol to prepare triaza-benzo[*b*]fluoren-6-one compounds.

Scheme 1



We wish to report here the synthesis of triaza-benzo[*b*]fluoren-6-one derivatives occurring in aqueous media upon microwave irradiation in a simple and straight-forward manner (Scheme 2).

Scheme 2

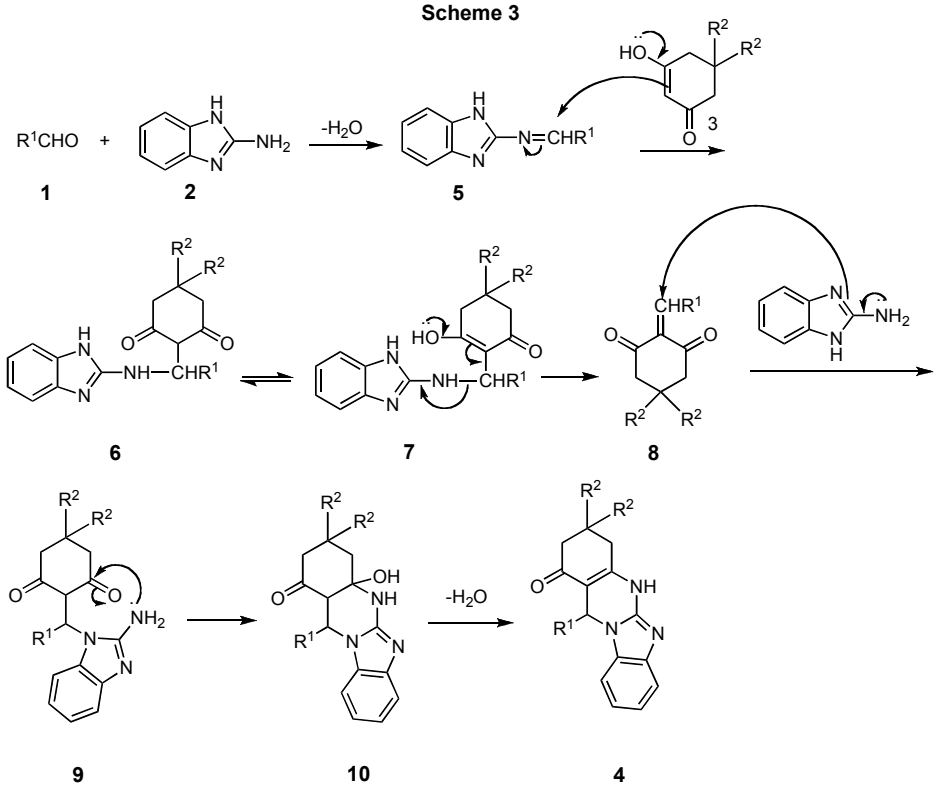


1 **2** **3** **4**

RESULTS AND DISCUSSION

To optimize the reaction temperature, the synthesis of **4a** was performed using water as the

Scheme 3



solvent at temperatures ranging from 70 °C to 95 °C, with an increment of 5 °C each time. The yield of product **4a** was increased and the reaction time was shortened when the temperature was increased from 70 °C to 85 °C. The yield leveled off when the temperature was further increased to 90 °C and 95 °C. Therefore, the most suitable temperature should be 85 °C.

In collection with Braulio's work, as well as to test the effect of water as solvent under microwave irradiation, we also examined the same reaction of synthesis of **4a** under microwave irradiation using ethyleneglycol, ethanol, glacial acetic acid and DMF as solvent, respectively. The results were summarized in Table 1.

Table 1

The comparison of water and organic solvents.

No	Solvent	temp (°C)	Time (min)	Yield(%)
1	Water	85	3	94
2	Glycol	85	5	94
3	DMF	85	4	93
4	EtOH	85	10	76
5	HOAc	85	20	50

It is shown in Table 1 that the reaction in water and in organic solvents of glycol and DMF afforded satisfying results, similarly. Water could be chosen as efficient and green solvent.

Microwave irradiation power was also optimized for the synthesis of **4a**. The most suitable initial irradiation power was 250 W.

Based on these optimized reaction conditions, a series of triaza-benzo[*b*]fluoren-6-one derivatives was synthesized by the reaction of equimolecular amounts of aldehyde, cyclohexane-1,3-dione compound and 2-aminobenzimidazole in water under microwave irradiation. The protocol could be applied not only to the aromatic aldehydes with either electron-withdrawing groups or electron-donating groups, but also to aliphatic aldehydes, which highlighted the wide scope of this three-component condensation. Furthermore, the procedure is easy to operate and the workup procedure is just simple filtration. A series of triaza-benzo[*b*]fluoren-6-one derivatives was synthesized. The results are summerized in Table 2.

The reaction of 4-chlorobenzaldehyde, 2-aminobenzimidazole, and cyclohexane-1,3-dione in water under conventional and MW heating conditions was investigated to demonstrate the specific microwave effect. We found that the reaction under conventional heating condition gave rise to a moderate yield (59%) within 40 min of reaction time. However, the same reaction under

Table 2

Synthesis of 4 in water under Microwave Irradiation Conditions at 85 °C

No	4	R^1	R^2	Time(min)	Yield(%)	Mp(°C)
1	**4a**	4-ClC_6H_4	H	3	94[a]	>300[a]
2	**4b**	4-BrC_6H_4	H	3	93[a]	>300[a]
3	**4c**	3,4-$OCH_2OC_6H_3$	H	4	93[a]	>300[a]
4	**4d**	$CH_3CH_2CH_2CH_2$	H	4	92[a]	>300[a]
5	**4e**	2-ClC_6H_4	H	2	97[a]	>300[a]
6	**4f**	C_6H_5	H	3	93[a]	>300[a]
7	**4g**	4-FC_6H_4	H	2	94[a]	>300[a]
8	**4h**	4-$N(CH_3)_2C_6H_4$	H	3	92[a]	>300[a]
9	**4i**	3-BrC_6H_4	H	2	94[a]	>300[a]
10	**4j**	4-$NO_2C_6H_4$	H	2	93[a]	>300[a]
11	**4k**	4-$CH_3C_6H_4$	H	3	91[a]	>300[a]
12	**4l**	3-$NO_2C_6H_4$	H	3	93[a]	>300[a]
13	**4m**	4-$CH_3OC_6H_4$	H	4	92[a]	>300[a]
14	**4n**	3,4-$(CH_3O)_2C_6H_3$	H	4	93[a]	>300[a]
15	**4o**	4-ClC_6H_4	CH_3	4	94[a](60)[b]	>300[a](393)[b]
16	**4p**	C_6H_5	CH_3	4	93[a](64)[b]	>300[a](368)[b]
17	**4q**	4-BrC_6H_4	CH_3	4	94[a](68)[b]	>300[a](369)[b]
18	**4r**	2-ClC_6H_4	CH_3	3	92[a]	>300[a]
19	**4s**	4-$CH_3OC_6H_4$	CH_3	4	94[a](70)[b]	>300[a](389)[b]
20	**4t**	3,4-$OCH_2OC_6H_3$	CH_3	4	94[a]	>300[a]
21	**4u**	3,4-$(CH_3O)_2C_6H_3$	CH_3	4	95[a]	>300[a]
22	**4v**	2,4-$Cl_2C_6H_3$	CH_3	3	95[a]	>300[a]
23	**4w**	3-BrC_6H_4	CH_3	3	94[a]	>300[a]
24	**4x**	4-FC_6H_4	CH_3	3	95[a]	>300[a]
25	**4y**	4-$CH_3C_6H_4$	CH_3	4	92[a]	>300[a]

[a] Isolated yield and melting point; [b] literature yield and melting point

microwave irradiation for only 3 min afforded excellent product yield (94%). Microwave-assisted reaction exhibited several advantages over the conventional heating by not only significantly reducing the reaction time but also by improving the reaction yield dramatically.

The formation of triaza-benzo[*b*]fluoren-6-one derivatives **4** could be explained by the reaction sequence presented in Scheme 3. It is easier for aldehydes to react with 2-aminobenzimidazole than with cyclic β-dicarbonyl compounds. Therefore, we proposed that the reaction proceeded *via* a sequence of condensation, addition, elimination, addition, cyclization and dehydration. First, the condensation of aldehyde and 2-aminobenzimidazole gave Schiff base **5**. The addition of Schiff base to cyclohexane-1,3-dione compounds, then after elimination furnished the intermediate product **8**. Then the addition of 2-aminobenzimidazole to **8** gave the intermediate product **9**, which upon intermolecular cyclization and dehydration gave rise to **4**.

To test the proposed mechanism, we carried out the synthesis of **4a** in two steps, first of which was to get the pure Schiffe base **5**, which was characterized by IR and ^{1}H NMR spectral data, and then reacted with **3** under similar conditions. The target compound of **4a** was obtained with yield similar to the one-pot reaction. That fact supported the proposed mechanism (Scheme 3).

In this study, all the products were characterized by melting point, ir and ^{1}H nmr spectral data, as well as elemental analyses.

In conclusion, we have developed a three-component reaction of aldehyde, cyclohexane-1,3-dione compound and 2-aminobenzimidazole in water under microwave irradiation conditions for the synthesis of triaza-benzo[*b*]fluoren-6-one derivatives. Particularly valuable features of this method include excellent yields of the products, shorter reaction time, reduced environmental impact, and straightforward procedure.

EXPERIMENTAL

Microwave irradiation was carried out in a monomodal Emrys™ Creator from Personal Chemistry, Uppsala, Sweden. Melting points were determined in open capillaries and are uncorrected. ir spectra were recorded on a TENSOR 27 spectrometer in KBr. ^{1}H nmr spectra were measured on a DPX 400 spectrometer operating at 400 MHz, using DMSO-d_6 as solvent and TMS as internal standard. Elemental analyses were determined by using a Perkin-Elmer 240c elemental analysis instrument.

General Procedure for the synthesis of triaza-benzo[*b*]fluoren-6-one derivatives (4a-4y). In a 10-mL Emrys™ reaction vial, aldehyde (1 mmol), cyclic β-dicarbonyl compound (1 mmol), 2-aminobenzimidazole (1 mmol) and water (2 mL) were mixed and then capped. After irradiation for 2-4 min, the reaction mixture was cooled to room temperature. After pouring the liquid (water), the mixture was further purified by crystallized from 95% EtOH.

5-(4-Chloro-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4a). This compound was obtained according to above general procedure; ir (potassium bromide):

3225, 3041, 2950, 2890, 1674, 1569, 1187, 977, 834, 747 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.16 (s, 1H, NH), 7.39-7.29 (m, 6H, ArH), 7.06 (t, 1H, J = 7.2 Hz, ArH), 6.96 (t, 1H, J = 7.6 Hz, ArH), 6.45 (s, 1H, CH), 2.69-2.67 (m, 2H, CH_2), 2.33-2.20 (m, 2H, CH_2), 1.97-1.85 (m, 2H, CH_2). *Anal* calcd. for $C_{20}H_{16}ClN_3O$: C, 68.67; H, 4.61; N, 12.01. Found: C, 68.69; H, 4.60; N, 12.00.

5-(4-Bromo-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4b). This compound was obtained according to above general procedure; ir (potassium bromide): 3222, 3093, 2952, 1644, 1436, 1072, 884, 748 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.18 (s, 1H, NH), 7.44 (d, 2H, J = 8.0 Hz, ArH), 7.38 (d, 1H, J = 8.0 Hz, ArH), 7.29 (d, 2H, J = 8.4 Hz, ArH), 7.23 (d, 1H, J = 8.0 Hz, ArH), 7.06 (t, 1H, J = 8.0 Hz, ArH) , 6.96 (t, 1H, J = 7.6 Hz, ArH), 6.44 (s, 1H, CH), 2.69-2.67 (m, 2H, CH_2), 2.30-2.21 (m, 2H, CH_2), 1.99-1.83 (m, 2H, CH_2). *Anal* calcd. for $C_{20}H_{16}BrN_3O$: C, 60.93; H, 4.09; N, 10.66. Found: C, 60.94; H, 4.09; N, 10.68.

5-Benzo[*d*][1,3]dioxol-5-yl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4c). This compound was obtained according to above general procedure; ir (potassium bromide): 3224, 3095, 2942, 2831, 1642, 1360, 785 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.11 (s, 1H, NH), 7.38 (d, 1H, J = 7.6 Hz, ArH), 7.36 (d, 1H, J = 7.6 Hz, ArH), 7.07 (t, 1H, J = 7.6 Hz, ArH), 6.98 (t, 1H, J = 8.0 Hz, ArH), 6.87 (s, 1H, ArH), 6.82-6.75(m, 2H, ArH), 6.36 (s, 1H, CH), 5.92 (d, 2H, J = 8.4 Hz, OCH_2O), 2.70-2.69 (m, 2H, CH_2), 2.27-2.25 (m, 2H, CH_2), 1.88-1.86 (m, 2H, CH_2). *Anal* calcd. for $C_{21}H_{17}N_3O_3$: C, 70.18; H, 4.77; N, 11.69. Found: C, 70.16; H, 4.78; N, 11.70.

5-Butyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]-fluoren-6-one (4d). This compound was obtained according to above general procedure; ir (potassium bromide): 3100, 2955, 2868, 1655, 1132, 739 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.77 (s, 1H, NH), 7.48 (d, 1H, J = 7.2 Hz, ArH), 7.40 (d, 1H, J = 6.8 Hz, ArH), 7.13-7.07 (m, 2H, ArH), 5.60 (s, 1H, CH), 2.62-2.60 (m, 2H, CH_2), 2.35-2.33 (m, 2H, CH_2), 2.01-1.92 (m, 3H, CH), 1.75-1.67 (m, 1H, CH), 1.06-1.03 (m, 3H, CH), 0.68-0.65 (m, 4H, CH). *Anal* calcd. for $C_{18}H_{21}N_3O$: C, 73.19; H, 7.17; N, 14.23. Found: C, 73.21; H, 7.16; N, 14.22.

5-(2-Chloro-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4e). This compound was obtained according to above general procedure; ir (potassium bromide): 3222, 3093, 2952, 1644, 884, 748 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.24 (s, 1H, NH), 7.52-7.51 (m, 1H, ArH), 7.39-7.32 (m, 2H, ArH), 7.27 (t, 1H, J = 7.6 Hz, ArH), 7.21 (t, 1H, J = 7.6 Hz, ArH), 7.10-7.03 (m, 2H, ArH), 6.95 (t, 1H, J = 7.6 Hz, ArH), 6.66 (s, 1H, CH), 2.71-2.68 (m, 2H, CH_2), 2.29-2.18 (m, 2H, CH_2), 2.01-1.83 (m, 2H, CH_2). *Anal* calcd. for $C_{20}H_{16}ClN_3O$: C, 68.67; H, 4.61; N, 12.01. Found: C, 68.69; H, 4.60; N, 12.02.

5-Phenyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo-[*b*]fluoren-6-one (4f). This compound was obtained according to above general procedure; ir (potassium bromide): 3226, 3029, 2957, 1653, 885, 749 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.10 (s, 1H, NH), 7.38-7.31 (m, 3H, ArH), 7.25-7.22 (m, 3H, ArH), 7.15 (t, 1H, J = 7.6 Hz, ArH), 7.04 (t, 1H, J = 7.6 Hz, ArH), 6.95 (t, 1H, J = 7.6 Hz, ArH), 6.42 (s, 1H, CH), 2.71-2.70 (m, 2H, CH_2), 2.32-2.20 (m, 2H, CH_2), 2.00-1.86 (m, 2H, CH_2). *Anal* calcd. for $C_{20}H_{17}N_3O$: C, 76.17; H, 5.43; N, 13.32. Found: C, 76.16; H, 5.44; N, 13.33.

5-(4-Fluoro-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4g). This compound was obtained according to above general procedure; ir (potassium bromide): 3227, 3043, 2956, 1644, 1510, 890, 759 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.10 (s, 1H, NH), 7.34-7.31 (m, 3H, ArH), 7.20 (d, 1H, J = 7.6 Hz, ArH), 7.04-6.99 (m, 3H, ArH), 6.92 (t, 1H, J = 7.2 Hz, ArH), 6.41 (s, 1H, CH), 2.65-2.63 (m, 2H, CH_2), 2.31-2.15 (m, 2H, CH_2), 1.97-1.83 (m, 2H, CH_2). *Anal* calcd. for $C_{20}H_{16}FN_3O$: C, 72.06; H, 4.84; N, 12.61. Found: C, 72.08; H, 4.83; N,12.60.

5-(4-Dimethylamino-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4h). This compound was obtained according to above general procedure; ir (potassium bromide): 3224, 3043, 2995, 1645, 1522, 949, 820 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.96 (s, 1H, NH), 7.30 (d, 1H, J = 4.0 Hz, ArH), 7.21 (d, 1H, J = 8.0 Hz, ArH), 7.07 (d, 2H, J = 8.8 Hz, ArH), 6.99 (t, 1H, J = 7.2 Hz, ArH), 6.91 (t, 1H, J = 7.2 Hz, ArH), 6.50 (d, 2H, J = 8.8 Hz, ArH), 6.25 (s, 1H, CH), 2.75 (s, 6H, $2CH_3$), 2.65-2.63 (m, 2H, CH_2), 2.29-2.15 (m, 2H, CH_2), 1.95-1.90 (m, 2H, CH_2). *Anal* calcd. for $C_{22}H_{22}N_4O$: C, 73.72; H, 6.19; N, 15.63. Found: C, 73.74; H, 6.18; N, 15.62.

5-(3-Bromo-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4i). This compound was obtained according to above general procedure; ir (potassium bromide): 3220, 3048, 2891, 1647, 1571, 996, 890 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.16 (s, 1H, NH), 7.55 (s, 1H, ArH), 7.36-7.31 (m, 2H, ArH), 7.24-7.13 (m, 3H, ArH), 7.02 (t, 1H, J = 7.6 Hz, ArH), 6.94 (t, 1H, J = 7.6 Hz, ArH), 6.41 (s, 1H, CH), 2.66-2.63 (m, 2H, CH_2), 2.28-2.18 (m, 2H, CH_2), 1.95-1.80 (m, 2H, CH_2). *Anal* calcd. for $C_{20}H_{16}BrN_3O$: C, 60.93; H, 4.09; N, 10.66. Found: C, 60.92; H, 4.10; N, 10.65.

5-(4-Nitro-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4j). This compound was obtained according to above general procedure; ir (potassium bromide): 3223, 3040, 2949, 1646, 1515, 898, 822 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.25 (s, 1H, NH), 8.06 (d, 2H, J = 8.8 Hz, ArH), 7.56 (d, 2H, J = 8.8 Hz, ArH), 7.35 (d, 1H, J = 8.0 Hz, ArH), 7.17 (d, 1H, J = 7.6 Hz, ArH), 7.02 (t, 1H, J = 7.2 Hz, ArH), 6.92 (t, 1H, J = 8.0 Hz, ArH), 6.59 (s, 1H, CH), 2.68-2.65 (m, 2H, CH_2), 2.31-2.15 (m, 2H, CH_2), 1.97-1.80 (m, 2H, CH_2). *Anal* calcd. for $C_{20}H_{16}N_4O_3$: C, 66.66; H, 4.48; N, 15.55. Found: C, 66.68; H, 4.47; N, 15.56.

5-*p*-Tolyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo-[*b*]fluoren-6-one (4k). This compound was obtained according to above general procedure; ir (potassium bromide): 3224, 3038, 2950, 1645, 1514, 977, 829 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.04 (s, 1H, NH), 7.31 (d, 1H, J = 7.6Hz, ArH), 7.20-7.14 (m, 3H, ArH), 7.01-6.98 (m, 3H, ArH), 6.90 (t, 1H, J = 7.6 Hz, ArH), 6.33 (s, 1H, CH), 2.65-2.64 (m, 2H, CH_2), 2.29-2.19 (m, 2H, CH_2), 2.17 (s, 3H, CH_3), 1.93-1.80 (m, 2H, CH_2). *Anal* calcd. for $C_{21}H_{19}N_3O$: C, 76.57; H, 5.81; N, 12.76. Found: C, 76.55; H, 5.80; N, 12.77.

5-(3-Nitro-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4l). This compound was obtained according to above general procedure; ir (potassium bromide): 3220, 3040, 2950, 1652, 1514, 1020, 744 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.30 (s, 1H, NH), 8.27 (s, 1H, ArH), 8.04(d, 1H, J = 8.4 Hz, ArH), 7.70 (d, 1H, J = 7.6 Hz, ArH), 7.55 (t, 1H, J = 8.0 Hz, ArH), 7.40 (d, 1H, J = 7.6 Hz, ArH), 7.27 (d, 1H, J = 7.6 Hz, ArH), 7.06 (t, 1H, J = 7.2 Hz, ArH), 6.96 (t, 1H, J = 7.6 Hz, ArH), 6.67 (s, 1H, CH), 2.73-2.70 (m, 2H, CH_2), 2.36-2.19 (m, 2H, CH_2), 1.99-1.85 (m, 2H, CH_2). *Anal* calcd. for $C_{20}H_{16}N_4O_3$: C, 66.66; H, 4.48; N, 15.55. Found: C, 66.69; H, 4.49; N, 15.54.

5-(4-Methoxy-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4m). This compound was obtained according to above general procedure; ir (potassium bromide): 3226, 3040, 2955, 1655, 1514, 1038, 748 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.09 (s, 1H, NH), 7.36 (d, 1H, J = 7.6 Hz,

ArH), 7.26-7.23 (m, 3H, ArH), 7.04(t, 1H, J = 7.6 Hz, ArH), 6.95(t, 1H, J = 7.6 Hz, ArH), 6.78 (d, 2H, J = 7.6 Hz, ArH), 6.37 (s, 1H, CH), 3.65(s, 3H, OCH_3), 2.70-2.69 (m, 2H, CH_2), 2.31-2.20 (m, 2H, CH_2), 1.99-1.85 (m, 2H, CH_2). *Anal* calcd. for $C_{21}H_{19}N_3O_2$: C, 73.03; H, 5.54; N, 12.17. Found: C, 73.05; H, 5.53; N, 12.18.

5-(3,4-Dimethoxy-phenyl)-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4n). This compound was obtained according to above general procedure; ir (potassium bromide): 3226, 3095, 2904, 1654, 1516, 888, 738 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.08 (s, 1H, NH), 7.35 (t, 2H, J = 7.6 Hz, ArH), 7.06-7.03 (m, 2H, ArH), 6.97 (t, 1H, J = 7.6 Hz, ArH), 6.79-6.70(m, 2H, ArH), 6.38 (s, 1H, CH), 3.70(s, 3H, OCH_3), 3.64(s, 3H, OCH_3), 2.69-2.67 (m, 2H, CH_2), 2.32-2.20 (m, 2H, CH_2), 2.06-1.86 (m, 2H, CH_2). *Anal* calcd. for $C_{22}H_{21}N_3O_3$: C, 70.38; H, 5.64; N, 11.19. Found: C, 70.36; H, 5.65; N, 11.20.

5-(4-Chloro-phenyl)-8, 8-dimethyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4o). This compound was obtained according to above general procedure; ir (potassium bromide): 3232, 3050, 2963, 2866, 1660, 1106, 890, 776 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.19 (s, 1H, NH), 7.39-7.31 (m, 5H, ArH), 7.25 (d, 1H, J = 8.4 Hz, ArH), 7.07 (t, 1H, J = 7.6 Hz, ArH), 6.98 (t, 1H, J = 7.6 Hz, ArH), 6.45 (s, 1H, CH), 2.67-2.51 (m, 2H, CH_2), 2.29-2.04 (m, 2H, CH_2), 1.07 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). *Anal* calcd. for $C_{22}H_{20}ClN_3O$: C, 69.93; H, 5.33; N, 11.12. Found: C, 69.92; H, 5.33; N, 11.13.

8,8-Dimethyl-5-phenyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4p). This compound was obtained according to above general procedure; ir (potassium bromide): 3228, 2956, 891, 838, 759 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.13 (s, 1H, NH), 7.38-7.33 (m, 3H, ArH), 7.28-7.23 (m, 3H, ArH), 7.18-7.14 (m, 1H, ArH), 7.05 (t, 1H, J = 8.0 Hz, ArH), 6.96 (t, 1H, J = 7.6 Hz, ArH), 6.42 (s, 1H, CH), 2.67-2.50 (m, 2H, CH_2), 2.29-2.04 (m, 2H, CH_2), 1.06 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). *Anal* calcd. for $C_{22}H_{21}N_3O$: C, 76.94; H, 6.16; N, 12.24. Found: C, 76.93; H, 6.15; N, 12.25.

5-(4-Bromo-phenyl)-8,8-dimethyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4q). This compound was obtained according to above general procedure; ir (potassium bromide): 3232, 3048, 2932, 1648, 891, 740 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.17 (s, 1H, NH), 7.47-7.37 (m, 2H, ArH), 7.30-7.24 (m, 4H, ArH), 7.07 (t, 1H, J = 8.0 Hz, ArH), 6.97 (t, 1H, J = 8.0 Hz, ArH), 6.43 (s, 1H, CH), 2.67-2.66 (m, 2H, CH_2), 2.28-2.04 (m, 2H, CH_2), 1.06 (s, 3H, CH_3), 0.93(s, 3H, CH_3). *Anal* calcd. for $C_{22}H_{20}BrN_3O$: C, 62.57; H, 4.77; N, 9.95. Found: C, 62.59; H, 4.78; N, 9.96.

5-(2-Chloro-phenyl)-8,8-dimethyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4r). This compound was obtained according to above general procedure; ir (potassium bromide): 3227, 3094, 2953, 1655, 890, 756 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.20 (s, 1H, NH), 7.39-7.09 (m, 6H, ArH), 7.06 (t, 1H, J = 7.6 Hz, ArH), 6.96 (t, 1H, J = 7.2 Hz, ArH), 6.67 (s, 1H, CH), 2.66-2.51 (m, 2H, CH_2), 2.27-2.02 (m, 2H, CH_2), 1.07 (s, 3H, CH_3), 0.97 (s, 3H, CH_3). *Anal* calcd. for $C_{22}H_{20}ClN_3O$: C, 69.93; H, 5.33; N, 11.12. Found: C, 69.92; H, 5.34; N, 11.10.

5-(4-Methoxy-phenyl)-8,8-dimethyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4s). This compound was obtained according to above general procedure; ir (potassium bromide): 3231, 3099, 2957, 2866, 1645, 838,737 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.08 (s, 1H, NH), 7.36 (d, 1H, J = 7.6 Hz, ArH), 7.28-7.24 (m, 3H, ArH), 7.04 (t, 1H, J = 7.6 Hz, ArH), 6.96 (t, 1H, J = 8.0 Hz, ArH), 6.76 (d, 2H, J = 8.4 Hz, ArH), 6.36 (s, 1H, CH), 3.66 (s, 3H, OCH_3), 2.65-2.51 (m, 2H, CH_2) 2.28-2.03 (m, 2H, CH_2), 1.06 (s, 3H, CH_3), 0.95 (s, 3H, CH_3). *Anal* calcd. for $C_{23}H_{23}N_3O_2$: C, 73.97; H, 6.21; N, 11.25. Found: C, 73.99; H, 6.20; N, 11.24.

5-Benzo[1,3]dioxol-5-yl-8,8-dimethyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4t). This compound was obtained according to above general procedure; ir (potassium bromide): 3228, 3095, 2966, 1644, 850, 791 cm^{-1};^1H nmr (DMSO-d_6): δ 11.09 (s, 1H, NH), 7.38-7.31 (m, 2H, ArH), 7.06 (t, 1H, J = 7.2 Hz, ArH), 6.98 (t, 1H, J = 7.6 Hz, ArH), 6.89 (s, 1H, ArH),6.82-6.76 (m, 2H, ArH), 6.35 (s, 1H, CH), 5.93 (d, 2H, J = 8.0 Hz, OCH_2O), 2.64-2.53 (m, 2H, CH_2), 2.28-2.06 (m, 2H, CH_2), 1.06 (s, 3H, CH_3), 0.96 (s, 3H, CH_3). *Anal* calcd. for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85. Found: C, 71.29; H, 5.44; N, 10.86.

5-(3,4-Dimethoxy-phenyl)-8,8-dimethyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4u). This compound was obtained according to above general procedure; ir (potassium bromide): 3231, 3048, 2935, 2866, 1665, 1650, 891,759 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.04 (s, 1H, NH), 7.36 (d, 2H, J = 8.4 Hz, ArH), 7.07-6.96 (m, 3H, ArH), 6.79 (s, 2H, ArH), 6.35 (s, 1H, CH), 3.68 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 2.67-2.51 (m, 2H, CH_2), 2.30 (m, 2H, CH_2), 1.07 (s, 3H, CH_3), 0.96 (s, 3H, CH_3). *Anal* calcd. for $C_{24}H_{25}N_3O_3$: C, 71.44; H, 6.25; N, 10.41. Found: C, 71.46; H, 6.24; N, 10.42.

5-(3,4-Dichloro-phenyl)-8,8-dimethyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4v). This compound was obtained according to above general procedure; ir (potassium bromide): 3234, 3060, 2962, 1650, 891, 758 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.25 (s, 1H, NH), 7.51-7.38 (m, 4H, ArH), 7.09-6.90 (m, 3H, ArH), 6.67 (s, 1H, CH), 2.62-2.33 (m, 2H, CH_2), 2.27-2.02(m, 2H, CH_2), 1.07 (s, 3H, CH_3), 0.97 (s, 3H, CH_3). *Anal* calcd. for $C_{22}H_{19}Cl_2N_3O$: C, 64.09; H, 4.64; N, 10.19. Found: C, 64.11; H, 4.63; N, 10.19.

5-(3-Bromo-phenyl)-8,8-dimethyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4w). This compound was obtained according to above general procedure; ir (potassium bromide): 3222, 3048, 2944, 1650, 887, 743 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.17 (s, 1H, NH), 7.61 (s, 1H, ArH), 7.38 (t, 2H, J = 8.0 Hz, ArH), 7.31-6.98 (m, 3H, ArH), 7.08 (t, 1H, J = 7.6 Hz, ArH), 7.00 (t, 1H, J = 7.6 Hz, ArH), 6.46 (s, 1H, CH), 2.66-2.50 (m, 2H, CH_2), 2.29-2.07 (m, 2H, CH_2), 1.07(s, 3H, CH_3), 0.94(s, 3H, CH_3). *Anal* calcd. for $C_{22}H_{20}BrN_3O$: C, 62.57; H, 4.77; N, 9.95. Found: C, 62.55; H, 4.78; N, 9.96.

5-(4-Fluoro-phenyl)-8,8-dimethyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4x). This compound was obtained according to above general procedure; ir (potassium bromide): 3225, 3041, 2954, 2895, 1645, 846,748 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.13 (s, 1H, NH), 7.40-7.36 (m, 3H, ArH), 7.26 (d, 1H, J = 7.6 Hz, ArH), 7.10-7.05 (m, 3H, ArH), 6.97 (t, 1H, J = 7.6 Hz, ArH), 6.46 (s, 1H, CH), 2.65-2.51 (m, 2H, CH_2), 2.29-2.05 (m, 2H, CH_2), 1.07(s, 3H, CH_3), 0.94(s, 3H, CH_3). *Anal* calcd. for $C_{22}H_{20}FN_3O$: C, 73.11; H, 5.58; N, 11.63. Found: C, 73.09; H, 5.57; N, 11.64.

8,8-Dimethyl-5-p-tolyl-5,8,9,10-tetrahydro-7*H*-4b,10,11-triaza-benzo[*b*]fluoren-6-one (4y). This compound was obtained according to above general procedure; ir (potassium bromide): 3232, 3049, 2958, 2895, 1647, 846,737 cm^{-1}; ^1H nmr (DMSO-d_6): δ 11.08 (s, 1H, NH), 7.36 (d, 1H, J = 8.6 Hz, ArH), 7.26-7.20 (m, 3H, ArH), 7.06-7.03 (m, 3H, ArH), 6.95 (t, 1H, J = 7.6 Hz, ArH), 6.36 (s, 1H, CH), 2.66-2.53 (m, 2H, CH_2), 2.28-

2.03 (m, 2H, CH_2), 2.10 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). *Anal* calcd. for $C_{23}H_{23}N_3O$: C, 77.28; H, 6.49; N, 11.76. Found: C, 77.27; H, 6.50; N, 11.77.

(*E*)-*N*-(4-chlorobenzylidene)-1*H*-benzo(*d*)imidazol-2-amine (Schiffe base 5). In a 10-mL Emrys™ reaction vial, 4-chlorobenzaldehyde (1 mmol), 2-aminobenzimidazole (1 mmol) and water (2 mL)were mixed and then capped. After irradiation for 1 min, the reaction mixture was cooled to room temperature. Then the mixture was filtered to give the crude product, which was further purified by recrystallization from 95% EtOH. Ir (potassium bromide): 3245, 3078, 2973, 2764, 1684, 1585, 1389, 1090, 852cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 12.74 (s, 1H, NH), 9.47 (s, 1H, CH), 8.11-8.10 (d, 2H, J = 8.0 Hz, ArH), 7.67 (d, 2H, J = 8.0 Hz, ArH), 7.61-7.59 (m, 1H, ArH), 7.46-7.45(m, 1H, ArH), 7.21-7.19(m, 2H, ArH). *.Anal.* calcd. for $C_{14}H_{10}N_3Cl$: C, 65.76; H, 3.94; N, 16.43. Found: C, 65.73; H, 3.95; N, 16.42.

Acknowledgement. We thank the National Natural Science Foundation of China (No. 20672090), the Nature Science Foundation of the Jiangsu Province (No. BK 2006033) for financial support, Six Kinds of Professional Elite Foundation of the Jiangsu Province (No. 06-A-039), and project (No. 07KJ45) supported by Xuzhou Medical College.

REFERENCES AND NOTES

[1] Anastas, P. T.; Warner, J. C. *Green Chemistry*: *Theory and Practice*; Oxford University Press: Oxford, 1998.

[2] (a) Wasserscheid, P., Welton, T., Eds.; *Ionic Liquid in Synthesis; Verlag GmbH* and Co. KGaA: Weinheim, 2003. (b) Darr, J. A.; Poliakoff, M. *Chem. Rev*. **1999**, *99*, 495. (c) Clifford, A. A.; Rayer, C. M. *Tetrahedron Lett*. **2001**, *42*, 323.

[3] (a) Kappe, C. O. *Angew. Chem., Int. Engl.* **2004**, *43*, 6250. (b) Lidstrom, P.; Tierney, J.; Wathey, B.;Westman, J. *Tetrahedron* **2001**, *57*, 9225. (c) Varma, R. S. *Green Chem*. **1999**, 1, 43. (d) Gabriel, C.; Gabriel, S.; Grant, E. H.; Halstead, B. S. J.; Mingos, D. M. P. *Chem. Soc. Rev*. **1998**, *27*, 213.

[4] (a) Varma, R. S. *Advances in Green Chemistry: Chemical Syntheses Using Microwave Irradiation*; AstraZeneca Research Foundation India: Bangalore, India, 2002. (b) Varma, R. S. *Organic Synthesis using Microwave and Supported Reagents. In Microwaves in organic Synthesis*; Loupy, A., Ed.; Wiley-VCH: Weinheim, 2002; pp 181-218. (c) Larhed, M.; Moberg, C.; Hallberg, A. *Acc. Chem. Res.* **2002**, *35*, 717. (d) Varma, R. S. *J. Heterocyclic. Chem*. **1999**, *36*, 1565. (e) Dallinger, D.; Kappe, C. O. *Chem. Rev*. **2007**, *107*, 2563.

[5] (a) Noga, E. J.; Barthalmus, G. T.; Mitchell, M. K. *Cell Biol. Int. Rep*. **1986**, *10*, 239. (b) Craig, P. N. In *Comprehensive Medicinal Chemistry*; Drayton, C. J., Ed.; Pergamon Press: NY, 1991; Vol. 8.

[6] Daidone, G.; Maggio, B.; Raffa, D.; Plescia, S.; Bajardi, M. L.; Caruso, A.; Cuttuli, V. M. C. and Amico-Roxas, M. *Eur. J. Med. Chem*., **1994**, *29*, 707

[7] Backhit, A. A. and Khalil, M. A. *Pharmazie*, **1998**, *53*, 539.

[8] Agarwal, R.; Singli, C. and Mishara, N. S. *Ind. Drugs*, **1988**, *25*, 185.

[9] Pramella, B.; Rajanarender, E. and Murty, A. K. *J. Heterocyclic. Chem*., **1992**, *2*, 115.

[10] Shyimad, M.; Kalsi, R.; Dixit, K. S. and Barthwal, J. P. *Arzeim-Forsch. Drug Res*., **1991**, *41*, 514.

[11] Shakhidoyator, Kh. M.; Eripor, E. O.; Yun, L. M.; Yamankulov, M. and Kadyrov, Ch. Sh. *Fungitsidy*, 1980, 66; *Chem. Abstr*. **1981**, *94*, 192253.

[12] Fetter, J.; Czuppon, T.; Hornyak, G. and Feller, A. *Tetrahedron*, **1997**, *34*, 247.

[13] Brana, M. F. and Perez, M. J. *J. Heterocyclic. Chem*. **1997**, *34*, 807.

[14] (a) Varma, R. S. *Microwave Technology-Chemical Applications: Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed.; John Wiley& Sons: New York, 2004. (b) Namboodiri,V. V.; Varma, R. S. *Green Chem*. **2001**, *3*, 146. (C).Tu, S. J.; Zhang, Y.; Zhang, J. Y.; Jiang, B.; Jia, R. H. *Synlett*, **2006**, *17*, 2785. (d). Tu, S. J.; Jiang, B.; Zhang, J. Y.; Jia, R. H.; Zhang, Y.; Yao, C. S. *Org. Biomol. Chem*., **2006**, *4*, 3980.

[15] (a) Li, C. J. *Chem. Rev*. **1993**, *93*, 2023. (b) Li, C. J.; Chen, T. H. *Organic Reactions in Aqueous Media*; Wiley: New York, 1997. (c) Wei, W.; Keh, C. C. K.; Li, C. J.; Varma, R. S. *Clean Technol. Environ. Policy* **2005**, *7*, 62.

[16] An, J.; Bagnell, L.; Cablewski, T.; Strauss, C. R.; Trainor, R. W. *J. Org. Chem*. **1997**, *62*, 2505.

[17] Insuasty, B.; Salcedo, A.; Quiroga, J.; Abonia, R.; Nogueras, M.; Cobo, J. and Salido, S. *Hetercyclic. Commun*., **2004**, *10*, 399.