

Nesrine Louhichi, Amel Houas, Naoufel Ben Hamadi,\* and Moncef Msaddek

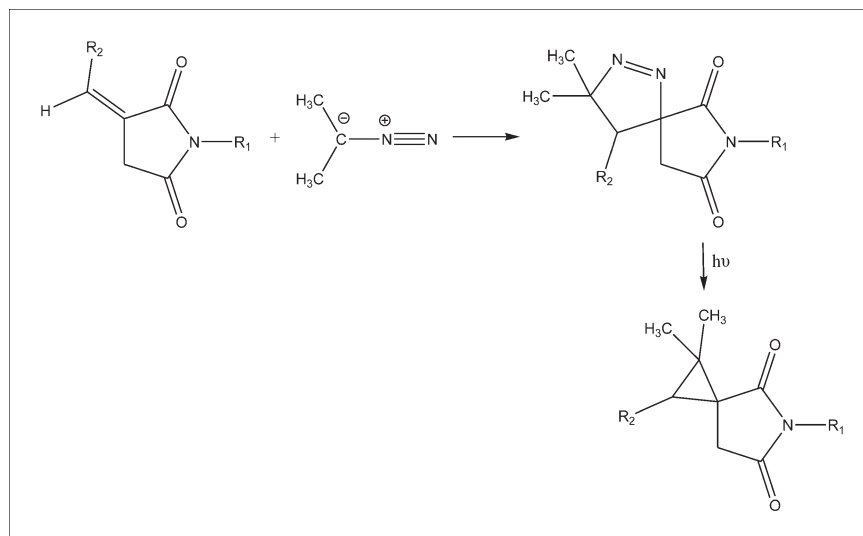
Department of Chemistry, Faculty of Sciences of Monastir, Laboratory of Synthesis Heterocyclic and Natural Substances, Boulevard of Environment, 5000 Monastir, Tunisia

\*E-mail: bh\_naoufel@yahoo.fr

Received October 24, 2010

DOI 10.1002/jhet.827

Published online 11 November 2011 in Wiley Online Library (wileyonlinelibrary.com).



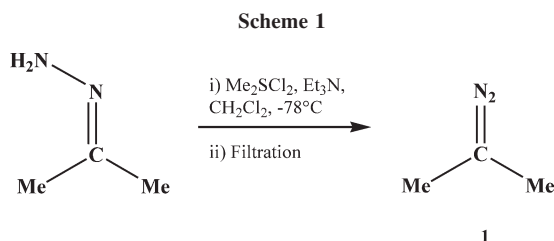
In explorations of syntheses and chemistry of spiroheterocycles, we found that the reaction of 2-diazopropane with (*E*)- $\alpha$ -arylidene-pyrrolin-2-one, (*E*)- $\alpha$ -arylidene- $\gamma$ -butyrolactone, and (*E*)-arylidene-*N*-aryl-succinimide derivatives produced spiro- $\Delta^1$ -pyrazolines. The photolysis of  $\Delta^1$ -pyrazolines has led to cyclopropanes. The structures of the obtained adducts have been assigned by means of spectroscopic measurements.

*J. Heterocyclic Chem.*, **49**, 267 (2012).

## INTRODUCTION

In recent years, there has been an increasing interest in the chemistry of heterocyclic compounds containing nitrogen atom because of their biological significance. Many of them show antibacterial [1], antidepressant [2], anticonvulsant [3], antiparkinsonian [4], antitumor [5], antimicrobial [6], and anti-inflammatory activities [7]. Pyrazolines present an interesting group of compounds, many of which possess widespread pharmacological properties such as analgesic, antipyretic, and antirheumatic activities [8]. These derivatives are also well known for their pronounced anti-inflammatory properties [9] and are used as potent antidiabetic agents [10]. In addition, the pharmacological and antitumor activities of many compounds containing pyrazoline rings have been reviewed [11]. Recent progressive interest was directed toward nanocrystal investigation of 1,3,5-triaryl-2-pyrazoline derivatives [12] due to their well-known fluorescence properties with high quantum yield useful as whitening or brightening agents for textile fibre, plastic and paper industries [13]. Many efforts have been also directed toward use of this behavior for construction of

organic electroluminescence devices with a multilayer structure and as fluorescence probes in some elaborated chemosensors [14]. On the other hand, heterocycles containing the cyclopropane ring also exhibit various pharmacological activities [15]. Recently, much attention has been focused on amino acids containing conformationally constrained cyclopropane rings due to their important biological activities. For example,  $\beta$ -cyclopropylalanine is a potent antagonist to *E. coli* American Type Culture Collection (ATCC) 9723 [16] and inhibits spore germination of *Pyricularia oryzae* Cav., the causative agent of rice blast disease [17]. Pyrazolines are also synthetically useful scaffolds in organic chemistry [18]. The reaction of 1,3-dipolar cycloadditions (1,3-DCs) is a classical and widely used method for the construction of pyrazolines [19]. The general concept of 1,3-DCs was introduced by Huisgen and co-workers in the early 1960. The work of Huisgen stated the basis for the understanding of the mechanism of concerted or stepwise cycloaddition reactions [20]. In continuation to our work on the synthesis of heterocycles *via* 1,3-DCs and evolution of cycloadducts [21], we report that in the previous papers we have



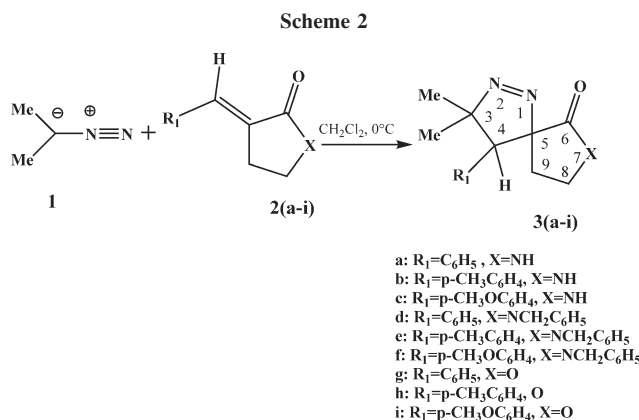
described the development of 1,3-DCs of 2-diazopropane. These compounds are converted to cyclopropanes.

## RESULTS AND DISCUSSION

The starting materials 2 and 4 were prepared by condensation of pyrrolin-2-one,  $\gamma$ -butyrolactone, and *N*-phenylmaleimide, respectively, with aldehydes as described in the literature [22]. Diazopropane 1 was prepared according to the literature procedure and conserved at  $-78^\circ\text{C}$  [23]. When a solution of hydrazone in  $\text{CH}_2\text{Cl}_2$  containing 2.5 equiv. of triethylamine was added to a  $-78^\circ\text{C}$  solution of chlorodimethylsulfonium chloride in  $\text{CH}_2\text{Cl}_2$ , the color of the reaction immediately changed to dark red (Scheme 1).

Addition of 2-diazopropane 1 to a solution of 2 in dichloromethane at  $0^\circ\text{C}$  until 2 was consumed followed by warming to room temperature gave monoadducts spiro- $\Delta^1$ -pyrazolines 3 in good yield (Scheme 2). The spiro adducts 3a–i were purified and characterized.

The 1,3-DCs of 2-diazopropane is, in each case, regiospecific. The chemical shifts of  $\text{C}_5$  [ $^{13}\text{C}$ -nuclear magnetic resonance (NMR)] are in excellent agreement with those usually obtained when this quaternary carbon is attached to nitrogen atom [24]. In a similar manner,

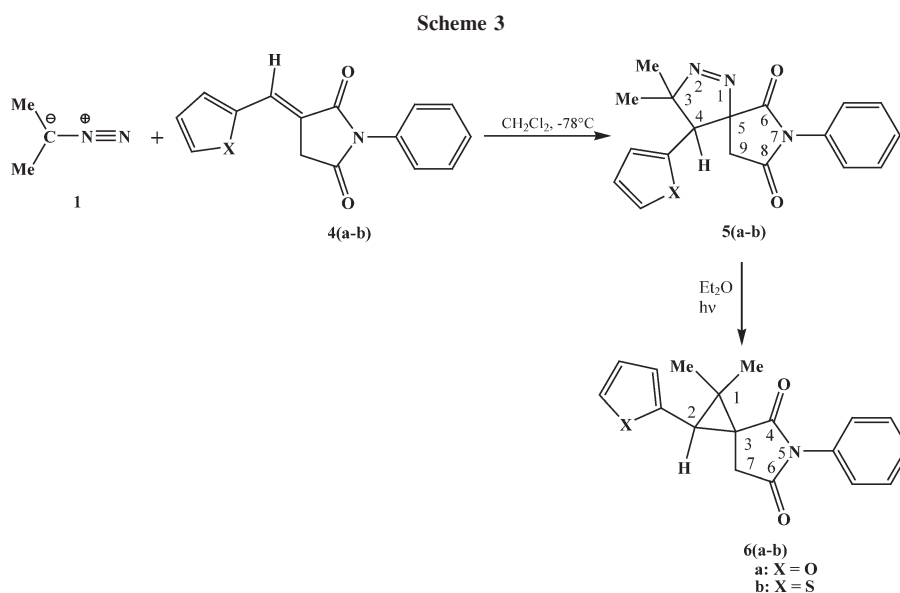


the 1,3-DCs reaction of ethereal 2-diazopropane to a solution of 3-methylene-*N*-phenylpyrrolidine-2,5-dione derivatives 4 in dichloromethane at  $-78^\circ\text{C}$  leads to the corresponding spiro- $\Delta^1$ -pyrazolines 5 in good yield. Irradiation of an ethereal solution of the  $\Delta^1$ -pyrazolines 5 through Pyrex with a high-pressure mercury arc lamp (Philips HPK 125 W) at  $0$ – $5^\circ\text{C}$  led to exclusive formation of *gem*-dimethylcyclopropanes [25] (Scheme 3). Its spectroscopic data (NMR) fit perfectly with those of product 6.

In summary, the reaction of 2-diazopropane with (*E*)- $\alpha$ -arylidene-pyrrolin-2-one, (*E*)- $\alpha$ -arylidene- $\gamma$ -butyrolactone, and (*E*)-arylidene-*N*-arylsuccinimide derivatives is regiospecific. Photolysis of the initially formed spiro- $\Delta^1$ -pyrazoline 5 afforded *gem*-dimethylcyclopropanes 6.

## EXPERIMENTAL

**Generalities.** Infrared spectra were recorded on Perkin-Elmer IR-197 infrared spectrometer. Mass spectra were



determined on a Nierjohnson MS80RF spectrometer. Melting points were determined on a Buchi-510 capillary melting point apparatus. Thin layer chromatography (TLC) was performed on silica gel 254 plates (Merck) with UV (254 nm) visualisation whereas chromatographic separations were conducted on silica gel Si-60-7734 Merck using water-Jacketed columns.  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra were recorded at 300 and 75.47 MHz, respectively. Coupling constants are given in Hz. Elemental analyses were performed on a Perkin-Elmer 240B microanalyzer. Diethyl ether was freshly distilled over sodium wire with a trace of benzophenone. Dichloromethane was distilled from calcium hydride.

**General procedure for trapping of 2-diazopropane 1 with alkenes.** A stirred solution of 2 and 4 (5 mmol) in dry dichloromethane (150 mL) was cooled to  $-78^\circ\text{C}$  and treated with an ethereal solution of 2-diazopropane. The mixture was monitored by TLC, and the addition of 2-diazopropane was ceased when no starting material was present. The mixture was allowed to warm to room temperature for 3 h and concentrated to give the crude reaction product. Recrystallization from ethanol.

**4-Phenyl-3,3-dimethyl-1,2,7-triazaspiro[4.4]non-1-ene-6-one (3a).** By the above method, (*E*)-3-benzylidenepyrrolidin-2-one 2a (0.865 g, 5 mmol) gave white crystals (0.972 g, 80%). mp  $170\text{--}171^\circ\text{C}$  [ethanol]. IR:  $\text{N}=\text{N}$  1540,  $\text{C}=\text{O}$  1670  $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.15 (s, 3H,  $\text{CH}_3$ ), 1.58 (s, 3H,  $\text{CH}_3$ ), 2.00 and 2.28 (m, 2H,  $\text{H}_9$ ), 3.23 and 3.74 (m, 2H,  $\text{H}_8$ ), 3.30 (s, 1H,  $\text{H}_4$ ), 6.57 (s, 1H, NH), 6.89–7.25 (m, 5H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 24.2 and 28.7 ( $\text{CH}_3$ ), 31.3 ( $\text{C}_9$ ), 40.3 ( $\text{C}_8$ ), 52.7 ( $\text{C}_4$ ), 94.9 ( $\text{C}_5$ ), 100.2 ( $\text{C}_3$ ), 127.5–136.8 ( $\text{C}_{\text{arom}}$ ), 173.9 ( $\text{C}_6$ ). Anal. Calcd. For  $\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}$ : C, 69.11; H, 7.04; N, 17.27%; Found: C, 69.14; H, 7.11; N, 17.05%.

**4-Tolyl-3,3-dimethyl-1,2,7-triazaspiro[4.4]non-1-ene-6-one (3b).** By the above method, (*E*)-3-tolylidenepyrrolidin-2-one 2b (0.935 g, 5 mmol) gave white crystals (0.617 g, 48%). mp  $160\text{--}161^\circ\text{C}$  [ethanol]. IR:  $\text{N}=\text{N}$  1540,  $\text{C}=\text{O}$  1670  $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.21 (s, 3H,  $\text{CH}_3$ ), 1.63 (s, 3H,  $\text{CH}_3$ ), 2.05 and 2.34 (m, 2H,  $\text{H}_9$ ), 2.32 (s, 3H,  $\text{CH}_3$ ), 3.28 and 3.79 (m, 2H,  $\text{H}_8$ ), 3.31 (s, 1H,  $\text{H}_4$ ), 6.72 (s, 1H, NH), 6.85 and 7.08 (d, 4H,  $\text{H}_{\text{arom}}$ ,  $J = 8.1$  Hz).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 21.0; 23.8 and 28.2 ( $\text{CH}_3$ ), 30.8 ( $\text{C}_9$ ), 40.0 ( $\text{C}_8$ ), 51.9 ( $\text{C}_4$ ), 94.3 ( $\text{C}_5$ ), 99.7 ( $\text{C}_3$ ), 128.9–136.9 ( $\text{C}_{\text{arom}}$ ), 173.7 ( $\text{C}_6$ ). Anal. Calcd. For  $\text{C}_{15}\text{H}_{19}\text{N}_3\text{O}$ : C, 70.01; H, 7.44; N, 16.33%; Found: C, 70.03; H, 7.46; N, 16.40%.

**4-Anisyl-3,3-dimethyl-1,2,7-triazaspiro[4.4]non-1-ene-6-one (3c).** By the above method, (*E*)-3-anisylidenepyrrolidin-2-one 2c (1.01 g, 5 mmol) gave white crystals (1.02 g, 75%). mp  $110\text{--}111^\circ\text{C}$  [ethanol]. IR:  $\text{N}=\text{N}$  1535,  $\text{C}=\text{O}$  1675  $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.21 (s, 3H,  $\text{CH}_3$ ), 1.63 (s, 3H,  $\text{CH}_3$ ), 2.10 and 2.32 (m, 2H,  $\text{H}_9$ ), 3.29 and 3.81 (m, 2H,  $\text{H}_8$ ), 3.32 (s, 1H,  $\text{H}_4$ ), 3.79 (s, 3H,  $\text{OCH}_3$ ), 6.13 (s, 1H, NH), 6.81 and 6.87 (d, 4H,  $\text{H}_{\text{arom}}$ ,  $J = 9$  Hz).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 23.8 and 28.2 ( $\text{CH}_3$ ), 30.8 ( $\text{C}_9$ ), 39.8 ( $\text{C}_8$ ), 51.5 ( $\text{C}_4$ ), 55.2 ( $\text{OCH}_3$ ), 94.3 ( $\text{C}_5$ ), 99.5 ( $\text{C}_3$ ), 113.6–158.7 ( $\text{C}_{\text{arom}}$ ), 173.3 ( $\text{C}_6$ ). Anal. Calcd. For  $\text{C}_{15}\text{H}_{19}\text{N}_3\text{O}_2$ : C, 65.91; H, 7.01; N, 15.37%; Found: C, 69.99; H, 7.03; N, 15.42%.

**7-Benzyl-4-phenyl-3,3-dimethyl-1,2,7-triazaspiro[4.4]non-1-ene-6-one (3d).** By the above method, (*E*)-*N*-benzyl-3-benzylidenepyrrolidin-2-one 2d (1.31 g, 5 mmol) gave white crystals (1.33 g, 80%). mp  $139\text{--}140^\circ\text{C}$  [ethanol]. IR:  $\text{N}=\text{N}$  1545,  $\text{C}=\text{O}$  1670  $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.52 (s, 3H,

$\text{CH}_3$ ), 1.63 (s, 3H,  $\text{CH}_3$ ), 1.85 and 2.20 (m, 2H,  $\text{H}_9$ ), 3.05 and 3.65 (m, 2H,  $\text{H}_8$ ), 3.39 (s, 1H,  $\text{H}_4$ ), 4.38 and 4.42 (d, 2H,  $\text{CH}_2$ ,  $J = 16.5$  Hz), 6.88–7.27 (m, 10H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 24.3 and 28.8 ( $\text{CH}_3$ ), 29.0 ( $\text{C}_9$ ), 44.8 ( $\text{C}_8$ ), 48.0 ( $\text{CH}_2$ ), 53.1 ( $\text{C}_4$ ), 95.1 ( $\text{C}_3$ ), 101.4 ( $\text{C}_5$ ), 127.5–136.9 ( $\text{C}_{\text{arom}}$ ), 170.8 ( $\text{C}_6$ ). Anal. Calcd. For  $\text{C}_{21}\text{H}_{23}\text{N}_3\text{O}$ : C, 75.65; H, 6.95; N, 12.60%; Found: C, 75.34; H, 6.80; N, 12.55%.

**7-Benzyl-4-tolyl-3,3-dimethyl-1,2,7-triazaspiro[4.4]non-1-ene-6-one (3e).** By the above method, (*E*)-*N*-benzyl-3-tolylidenepyrrolidin-2-one 2e (1.385 g, 5 mmol) gave white crystals (1.179 g, 68%). mp  $116\text{--}117^\circ\text{C}$  [ethanol]. IR:  $\text{N}=\text{N}$  1540,  $\text{C}=\text{O}$  1680.  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.53 (s, 3H,  $\text{CH}_3$ ), 1.59 (s, 3H,  $\text{CH}_3$ ), 2.25 (s, 3H,  $\text{CH}_3$ ), 1.87 and 2.22 (m, 2H,  $\text{H}_9$ ), 3.06 and 3.58 (m, 2H,  $\text{H}_8$ ), 3.36 (s, 1H,  $\text{H}_4$ ), 4.37 and 4.41 (d, 2H,  $\text{CH}_2$ ,  $J = 16.5$  Hz), 6.98–7.68 (m, 9H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 22.0, 24.3, and 27.7 ( $\text{CH}_3$ ), 29.0 ( $\text{C}_9$ ), 44.8 ( $\text{C}_8$ ), 48.1 ( $\text{CH}_2$ ), 53.2 ( $\text{C}_4$ ), 95.0 ( $\text{C}_3$ ), 101.4 ( $\text{C}_5$ ), 124.4–142.4 ( $\text{C}_{\text{arom}}$ ), 171.0 ( $\text{C}_6$ ). Anal. Calcd. For  $\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}$ : C, 76.05; H, 7.25; N, 12.09%; Found: C, 76.43; H, 7.40; N, 12.14%.

**7-Benzyl-4-anisyl-3,3-dimethyl-1,2,7-triazaspiro[4.4]non-1-ene-6-one (3f).** By the above method, (*E*)-*N*-benzyl-3-anisylidenepyrrolidin-2-one 2f (1.46 g, 5 mmol) gave white crystals (0.998 g, 55%). mp  $113\text{--}114^\circ\text{C}$  [ethanol]. IR:  $\text{N}=\text{N}$  1535,  $\text{C}=\text{O}$  1670  $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.49 (s, 3H,  $\text{CH}_3$ ), 1.55 (s, 3H,  $\text{CH}_3$ ), 1.85 and 2.25 (m, 2H,  $\text{H}_9$ ), 3.03 and 3.49 (m, 2H,  $\text{H}_8$ ), 3.29 (s, 1H,  $\text{H}_4$ ), 3.88 (s, 3H,  $\text{OCH}_3$ ), 4.39 and 4.42 (d, 2H,  $\text{CH}_2$ ,  $J = 16.5$  Hz), 6.79–7.54 (m, 9H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 24.4 and 28.0 ( $\text{CH}_3$ ), 29.2 ( $\text{C}_9$ ), 44.8 ( $\text{C}_8$ ), 47.9 ( $\text{CH}_2$ ), 54.0 ( $\text{C}_4$ ), 55.7 ( $\text{OCH}_3$ ), 95.0 ( $\text{C}_3$ ), 101.4 ( $\text{C}_5$ ), 126.4–159.0 ( $\text{C}_{\text{arom}}$ ), 170.8 ( $\text{C}_6$ ). Anal. Calcd. For  $\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}_2$ : C, 72.70; H, 6.93; N, 11.56%; Found: C, 72.71; H, 6.78; N, 11.39%.

**4-Phenyl-3,3-dimethyl-1,2-diaza-7-oxospiro[4.4]non-1-ene-6-one (3g).** By the above method, (*E*)- $\alpha$ -benzylidene- $\gamma$ -butyrolactone 2g (0.87 g, 5 mmol) gave white crystals (1.25 g, 61%). mp  $105\text{--}106^\circ\text{C}$  [ethanol]. IR:  $\text{N}=\text{N}$  1540,  $\text{C}=\text{O}$  1680  $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.18 (s, 3H,  $\text{CH}_3$ ), 1.58 (s, 3H,  $\text{CH}_3$ ), 2.15 (m, 1H,  $\text{H}_9$ ), 2.45 (m, 1H,  $\text{H}_9$ ), 3.31 (s, 1H,  $\text{H}_4$ ), 4.35 (m, 1H,  $\text{H}_8$ ), 4.75 (m, 1H,  $\text{H}_8$ ), 6.84–7.27 (m, 5H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 24.1 and 28.8 ( $\text{CH}_3$ ), 32.6 ( $\text{C}_9$ ), 53.6 ( $\text{C}_4$ ), 67.2 ( $\text{C}_8$ ), 96.2 ( $\text{C}_3$ ), 99.2 ( $\text{C}_5$ ), 128.0–136.1 ( $\text{C}_{\text{arom}}$ ), 174.0 ( $\text{C}_6$ ). Anal. Calcd. For  $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_2$ : C, 68.83; H, 6.60; N, 11.47%; Found: C, 68.78; H, 6.55; N, 11.41%.

**4-Tolyl-3,3-dimethyl-1,2-diaza-7-oxospiro[4.4]non-1-ene-6-one (3h).** By the above method, (*E*)- $\alpha$ -tolylidene- $\gamma$ -butyrolactone 2h (0.94 g, 5 mmol) gave white crystals (1.26 g, 65%). mp  $94\text{--}95^\circ\text{C}$  [ethanol]. IR:  $\text{N}=\text{N}$  1540,  $\text{C}=\text{O}$  1675  $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.08 (s, 3H,  $\text{CH}_3$ ), 1.74 (s, 3H,  $\text{CH}_3$ ), 2.04 (m, 1H,  $\text{H}_9$ ), 2.16 (s, 3H,  $\text{CH}_3$ ), 2.33 (m, 1H,  $\text{H}_9$ ), 3.18 (s, 1H,  $\text{H}_4$ ), 4.22 (m, 1H,  $\text{H}_8$ ), 4.64 (m, 1H,  $\text{H}_8$ ), 6.65; 6.94 ( $\text{AA'BB'}$ ,  $\text{H}_{\text{arom}}$ ,  $J_{\text{AA'BB'}}$  = 8.1 Hz),  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 22.6, 27.3, 23.7, and 28.4 ( $\text{CH}_3$ ), 32.2 ( $\text{C}_9$ ), 53.0 ( $\text{C}_4$ ), 66.8 ( $\text{C}_8$ ), 95.6 ( $\text{C}_3$ ), 98.7 ( $\text{C}_5$ ), 129.2–137.4 ( $\text{C}_{\text{arom}}$ ), 173.7 ( $\text{C}_6$ ). Anal. Calcd. For  $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_2$ : C, 69.74; H, 7.02; N, 10.84%; Found: C, 69.63; H, 6.92; N, 10.71%.

**4-Anisyl-3,3-dimethyl-1,2-diaza-7-oxospiro[4.4]non-1-ene-6-one (3i).** By the above method, (*E*)- $\alpha$ -anisylidene- $\gamma$ -butyrolactone 2i (1.02 g, 5 mmol) to give white crystals (0.894 g,

49%). mp 64–65°C [ethanol]. IR: N=N 1535, C=O 1670  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.24 (s, 3H,  $\text{CH}_3$ ), 1.63 (s, 3H,  $\text{CH}_3$ ), 2.15 (m, 1H,  $\text{H}_6$ ), 2.41 (m, 1H,  $\text{H}_9$ ), 3.27 (s, 1H,  $\text{H}_4$ ), 3.73 (s, 3H,  $\text{OCH}_3$ ), 4.33 (m, 1H,  $\text{H}_8$ ), 4.74 (m, 1H,  $\text{H}_8$ ), 6.74–7.2 (m, 4H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 22.6 and 27.3 ( $\text{CH}_3$ ), 31.1 ( $\text{C}_9$ ), 51.5 ( $\text{C}_4$ ), 54.2 ( $\text{OCH}_3$ ), 65.7 ( $\text{C}_8$ ), 94.5 ( $\text{C}_3$ ), 97.6 ( $\text{C}_5$ ), 112.8–157.9 ( $\text{C}_{\text{arom}}$ ), 172.7 ( $\text{C}_6$ ). Anal. Calcd. For  $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_3$ : C, 65.68; H, 6.61; N, 10.21%; Found: C, 65.59; H, 6.56; N, 10.17%.

**4-Furfuryl-3,3-dimethyl-7-phenyl-1,2,7-triazaspiro[4.4]non-1-ene-6,8-one (5a).** By the above method, furfurylidene-*N*-phenylsuccinimide 4a (1.26 g, 5 mmol) to give a white crystals (0.807 g, 50%). mp 154–155°C. IR: N=N 1530  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.28 (s, 3H,  $\text{CH}_3$ ), 1.67 (s, 3H,  $\text{CH}_3$ ), 2.81 and 3.13 (d, 2H,  $\text{H}_9$ ,  $J = 18.3$  Hz), 3.77 (s, 1H,  $\text{H}_4$ ), 6.91–7.39 (m, 8H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 22.9 and 25.9 ( $\text{CH}_3$ ), 36.2 ( $\text{C}_9$ ), 47.9 ( $\text{C}_4$ ), 94.1 ( $\text{C}_3$ ), 97.0 ( $\text{C}_5$ ), 127.6–133.0 ( $\text{C}_{\text{arom}}$ ), 172.1 and 174.5 ( $\text{C}_{6,8}$ ). Anal. Calcd. For  $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_3$ : C, 66.86; H, 5.30; N, 13.00%; Found: C, 66.80; H, 5.27; N, 13.09%.

**3,3-Dimethyl-7-phenyl-4-thiophenyl-1,2,7-triazaspiro[4.4]non-1-ene-6,8-one (5b).** By the above method, (2-thiophenyl)methylene-*N*-phenylsuccinimide 4b (1.34 g, 5 mmol) to give white crystals (1.02 g, 60%). mp 173–174°C. IR: N=N 1540  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.35 (s, 3H,  $\text{CH}_3$ ), 1.74 (s, 3H,  $\text{CH}_3$ ), 2.93 and 3.16 (d, 2H,  $\text{H}_9$ ,  $J = 18.3$  Hz), 3.98 (s, 1H,  $\text{H}_4$ ), 6.87–7.54 (m, 8H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 23.2 and 26.6 ( $\text{CH}_3$ ), 36.2 ( $\text{C}_9$ ), 48.8 ( $\text{C}_4$ ), 94.1 ( $\text{C}_3$ ), 96.4 ( $\text{C}_5$ ), 126.5–134.9 ( $\text{C}_{\text{arom}}$ ), 173.1 and 173.6 ( $\text{C}_{6,8}$ ). Anal. Calcd. For  $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$ : C, 63.70; H, 5.05; N, 12.38%; Found: C, 63.71; H, 5.08; N, 12.25%.

**General procedure for the irradiation of the spiro- $\Delta^1$ -pyrazolines (5a–b).** All irradiations were carried out using similar conditions. The derivative was dissolved in ether [pretreated by stirring with solid ( $\text{NaCO}_3$ ), filtered and flushed with argon] and irradiated at 5°C for a total of 1 h or until the starting material was consumed (TLC). After this period, the solvent was removed in a vacuum without heating to give brown oil, which was subjected to rapid silica filtration. Recrystallization from dichloromethane/light petroleum.

**2-Furfuryl-1,1-dimethyl-5-phenyl-5-azabicyclo[4.2]-4,6-dione (6a).** By the above method, pyrazoline 5a (1.61 g, 5 mmol) to give a white solid (0.737 g, 50%). mp 180–181°C.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.21 (s, 3H,  $\text{CH}_3$ ), 1.63 (s, 3H,  $\text{CH}_3$ ), 2.66 and 2.80 (d, 2H,  $\text{H}_7$ ,  $J = 19.2$  Hz), 3.03 (s, 1H,  $\text{H}_2$ ), 6.97–7.33 (m, 8H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 20.71 and 20.80 ( $\text{CH}_3$ ), 31.22 ( $\text{C}_7$ ), 31.85 ( $\text{C}_1$ ), 34.00 ( $\text{C}_3$ ), 40.23 ( $\text{C}_2$ ), 126.96–133.01 ( $\text{C}_{\text{arom}}$ ), 175.15 and 176.84 ( $\text{C}_{4,6}$ ). Anal. Calcd. For  $\text{C}_{18}\text{H}_{17}\text{NO}_3$ : C, 73.20; H, 5.80; N, 4.74%; Found: C, 73.25; H, 5.76; N, 4.65%.

**1,1-Dimethyl-5-phenyl-2-thiophenyl-5-azabicyclo[4.2]-4,6-dione (6b).** By the above method, pyrazoline 5b (1.69 g, 5 mmol) to give a white solid (1.24 g, 80%). mp 149–150°C.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$ : 1.22 (s, 3H,  $\text{CH}_3$ ), 1.52 (s, 3H,  $\text{CH}_3$ ), 2.64 and 2.73 (d, 2H,  $\text{H}_7$ ,  $J = 19.2$  Hz), 2.97 (s, 1H,  $\text{H}_2$ ), 6.79–7.44 (m, 8H,  $\text{H}_{\text{arom}}$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ; 75.47 MHz)  $\delta$ : 20.25 and 20.99 ( $\text{CH}_3$ ), 31.35 ( $\text{C}_7$ ), 31.41 ( $\text{C}_1$ ), 33.71 ( $\text{C}_3$ ), 40.11 ( $\text{C}_2$ ), 123.75–134.63 ( $\text{C}_{\text{arom}}$ ), 174.66 and 175.16 ( $\text{C}_{4,6}$ ). Anal. Calcd. For  $\text{C}_{18}\text{H}_{17}\text{NO}_2\text{S}$ : C, 69.43; H, 5.50; N, 4.50%; Found: C, 69.40; H, 5.46; N, 4.39%.

## REFERENCES AND NOTES

- [1] (a) Lange, J. H. M.; Coolen, H. K. A. C.; vanStuivenberg, H. H.; Dijkman, J. A. R.; Herremans, A. H. J.; Ronken, E.; Keizer, H. G.; Tipker, K.; McCreary, A. C.; Veerman, W.; Wals, H. C.; Stork, B.; Verveer, P. C.; Denhartog, A. P.; deJong, N. M. J.; Adolfs, T. J. P.; Hoogendoorn, J.; Kruse, C. G. *J Med Chem* 2004, 47, 627; (b) Chimentì, F.; Bolasco, A.; Manna, F.; Secci, D.; Chimentì, P.; Befani, O.; Turini, P.; Giovannini, V.; Mondovi, B.; Cirilli, R.; La Torre, F. *J Med Chem* 2004, 47, 2071; (c) Camacho, M. E.; Leon, J.; Entrena, A.; Velasco, G.; Carrion, M. D.; Escames, G.; Vivo, A.; Acuna-Castroviejo, D.; Gallo, M. A.; Espinosa, A. *J Med Chem* 2004, 47, 5641; (d) Rajendra Prasad, Y.; Lakshmana Rao, A.; Prasanna, L.; Murali, K.; Ravi Kumar, P. *Bioorg Med Chem Lett* 2005, 15, 5030; (e) Cox, C. D.; Torrent, M.; Breslin, M. J.; Mariano, B. J.; Whitman, D. B.; Coleman, P. J.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Schaber, M. D.; Lobell, R. B.; Tao, W.; South, V. J.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Prueksaritanont, T.; Slaughter, D. E.; Li, C.; Mahan, E.; Lu, B.; Hartman, G. D. *Bioorg Med Chem Lett* 2006, 16, 3175; (f) Goodell, J. R.; Puig-Basagoiti, F.; Forshey, B. M.; Shi, P. Y.; Ferguson, D. M. *J Med Chem* 2006, 49, 2127.
- [2] (a) Bilgin, A.; Palaska, E.; Sunal, R.; Gumusel, B. *Pharmazie* 1994, 49, 67; (b) Bilgin, A.; Palaska, E.; Sunal, R. *Arzneimittel-forschung/Drug Res* 1993, 43, 1041; (c) Bilgin, A.; Yesilada, A.; Palaska, E.; Sunal, R. *Arzneimittel-forschung/Drug Res* 1992, 42, 1271.
- [3] Gokhan, N.; Yesilada, A.; Ucar, G.; Erol, K.; Bilgin, A. *Arch Pharm Med Chem* 2003, 336, 362.
- [4] Amr, A. E.; Hegab, M. I.; Ibrahim, A. A.; Abdallah, M. M. *Monatshefte fur Chemie* 2003, 134, 1395.
- [5] (a) Amr, A. E.; Abou-Ghaila, M. H. *Amino Acids* 2004, 26, 283; (b) Brana, M. F.; Castellano, J. M.; Mpran, M.; Perez de Vega, M. J.; Gian, X. D.; Romerdahl, C. A.; Keihauer, G.; *Eur Med Chem* 1995, 30, 235.
- [6] (a) Amr, A. E.; Mohamed, A. M.; Ibrahim, A. A. Z. *Naturforsch* 2003, 58b, 861; (b) Amr, A. E.; Abdel-Salam, O. I.; Attia, A.; Stibor, I. *Collect Czech Commun* 1999, 64, 288.
- [7] (a) Fahmy, H. H.; El-Eraay, W. *Arch Pharm Res* 2001, 24, 171; (b) Abou-Ghaila, M. H.; Amr, A. E.; Abdallah, M. M. *Z Naturforsch* 2003, 58b, 903.
- [8] (a) Hukki, J.; Laitinen, P.; Alberty, J. E. *Pharm Acta Helv* 1968, 43, 704; (b) Jung, J. C.; Watkins, E. B.; Avery, M. A. *Heterocycles* 2005, 65, 77.
- [9] (a) Bansal, E.; Srivastava, V. K.; Kumar, A. *Eur J Med Chem* 2001, 36, 81; (b) Udupi, R. H.; Rao, S. N.; Bhat, A. R. *Indian J Heterocycl Chem* 1998, 7, 217.
- [10] (a) Ahn, J. H.; Kim, H. M.; Jung, S. H.; Kang, S. K.; Kim, K. R.; Rhee, S. D.; Yong, S. D.; Cheon, H. G.; Kim, S. S. *Bioorg Med Chem Lett* 2004, 14, 4461; (b) Villhauer, E. B.; Brinkman, J. A.; Naderi, C. B.; Dunning, B. E.; Mangold, B. L.; Mone, M. D.; Russell, M. E.; Weldon, S. C.; Hughes, T. E. *J Med Chem* 2002, 45, 2362.
- [11] (a) Amr, A. E. *Indian J Heterocycl Chem* 2000, 10, 49; (b) Hammam, A. G.; Fahmy, A. F. M.; Amr, A. E.; Mohamed, A. M. *Indian J Chem* 2003, 42B, 1985; (c) Hammam, A. G.; Abdel Hafez, N. A.; Midura, W. H.; Mikolajczyk, M. Z. *Naturforsch* 2000, 55b, 417.
- [12] (a) Oh, S. W.; Kang, Y. S. *Colloids Surf A: Physicochem Eng Aspects* 2005, 415, 257; (b) Oh, S. W.; Zhang, D. R.; Kang, Y. S. *Mater Sci Eng C* 2004, 24, 131; (c) Fu, H. B.; Wang, Y. Q.; Yao, J. N. *J Am Chem Soc* 2001, 123, 1434; (d) Fu, H. B.; Wang, Y. Q.; Yao, J. N. *Chem Phys Lett* 2000, 322, 327; (e) Fu, H. B.; Xie, R. M.; Wang, Y. Q.; Yao, J. N. *Colloids Surf A: Physicochem Eng Aspects* 2000, 174, 367.
- [13] (a) Wagner, A.; Schellhammer, C. W.; Petersen, S. *Angew Chem Int Ed Engl* 1966, 5, 699; (b) Wang, P.; Komatsuzaki, N. O.; Himeda, Y.; Sugihara, H.; Arakawa, H.; Kasuga, K. *Tetrahedron Lett* 2001, 42, 9199.

- [14] Jin, M.; Liang, Y. J.; Lu, R.; Chuai, X. H.; Yi, Z. H.; Zhao, Y. Y.; Zhang, H. J. *Synth Met* 2004, 140, 37.
- [15] Argyropoulou, E. C.; Pilanidou, P.; *Tetrahedron Lett* 2003, 44, 3755.
- [16] Meek, J. S.; Rowe, J. W. *J Am Chem Soc* 1955, 77, 6675.
- [17] Ohta, T.; Nakajima, S.; Sato, Z.; Aoki, T.; Hatanaka, S.; Nozoe, S. *Chem Lett* 1986, 4, 511.
- [18] Di, M.; Rein, K.; *Tetrahedron Lett* 2004, 45, 4705.
- [19] Garcia Ruano, J. L.; Alonso de Diego, S. A.; Blanco, D.; Martin Castro, A. M.; Rosario Martin, M.; Rodríguez Ramos, J. H. *Org Lett* 2001, 3, 3173.
- [20] Huisgen, R. *Pure Appl Chem* 1981, 53, 171.
- [21] Ben Hamadi, N.; Msaddek, M. *J Chem Res* 2007, 2, 121.
- [22] (a) Zimmer, H.; Armbruster, D. C.; Trauth, L. J. *J Heterocyclic Chem* 1965, 2, 171; (b) Hedaya, E.; Theodoropoulos, S. *Tetrahedron* 1968, 24, 2241.
- [23] Muhammad, J.; Matthias, B. *Org Lett* 2007, 9, 1789.
- [24] Fathi, T.; Dinh, N. A.; Schmitt, G.; Cerutti, E.; Laude, B. *Tetrahedron* 1988, 44, 4527.
- [25] (a) Andrews, S. D.; Day, A. C.; Raymond, P.; Whiting, M. C. *Org Synth* 1970, 50, 27; (b) Donaldson, W. A. *Tetrahedron* 2001, 57, 8589, and references therein.