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**DIELS-ALDER REACTIONS BETWEEN ACROLEIN  
*N,N*-DIMETHYLHYDRAZONE AND *N*-BENZYLATED  
BENZOTRIAZOLE-, INDAZOLE- OR INDOLE-4,7-DIONES**

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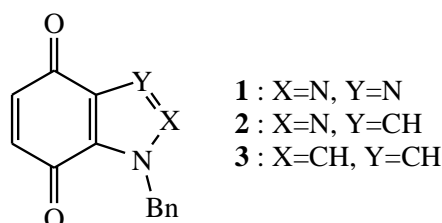
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**Abstract** – Diels-Alder reactions between acrolein *N,N*-dimethylhydrazone **4** and *N*-benzylated benzotriazole, indazole and indole-4,7-diones **1**, **2** and **3** afforded new heterotricyclic quinones **5**, **7** and **9** including from 2 to 4 intracyclic nitrogen atoms. A structural assignment of all new compounds was achieved using 2D NMR <sup>1</sup>H-<sup>13</sup>C HMBC correlations. The single 1,8- regioisomer was isolated starting from benzotriazole or indazole quinones, while a mixture of the 1,5- and 1,8- regioisomers was obtained from an indole-4,7-dione derivative. In all cases, the observed regiochemistry was in agreement with FMO calculation.

## INTRODUCTION

Heterocyclic *para*-quinones containing a nitrogen atom have been reported to possess various pharmacological properties.<sup>1,2</sup> Structure-activity relationship studies showed the importance of the number and the position of the nitrogen atom for cytotoxicity.<sup>2</sup>

In order to quantify these parameters, we recently<sup>3</sup> reported the synthesis of heterobicyclic quinones **1-3** (Figure 1). In this paper, we describe a supplementary work which consisted in introducing an additional pyridine ring.



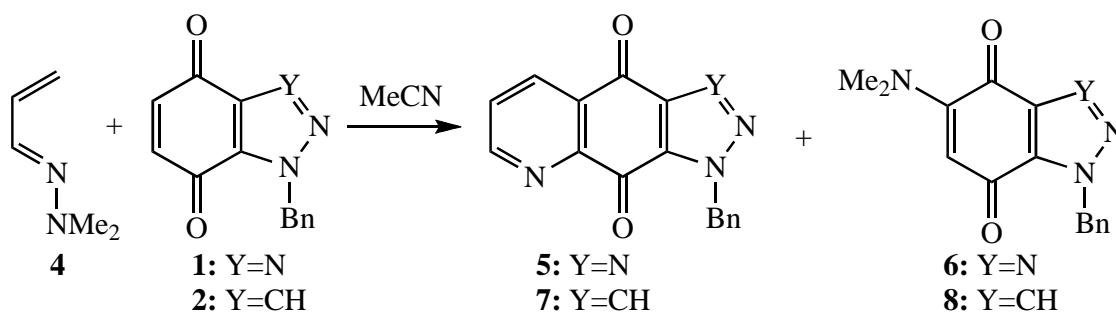
**Figure 1.** *N*-benzylated benzotriazole-, indazole-, indole-4,7-diones

The most widely methodology used<sup>4</sup> to build a pyridine ring in one step is the [4+2] cycloaddition reaction using  $\alpha,\beta$ -unsaturated dialkylhydrazones as dienes. Among them, we chose acrolein *N,N*-dimethylhydrazone **4**<sup>5</sup> in order to obtain an unsubstituted pyridine ring. This strategy led to tricyclic quinones, two of which were new original frameworks: the triazolo- and pyrazolo[4,5-*g*]quinoline-4,9-diones. To our knowledge, these skeletons have not been referenced so far.

## RESULTS AND DISCUSSION

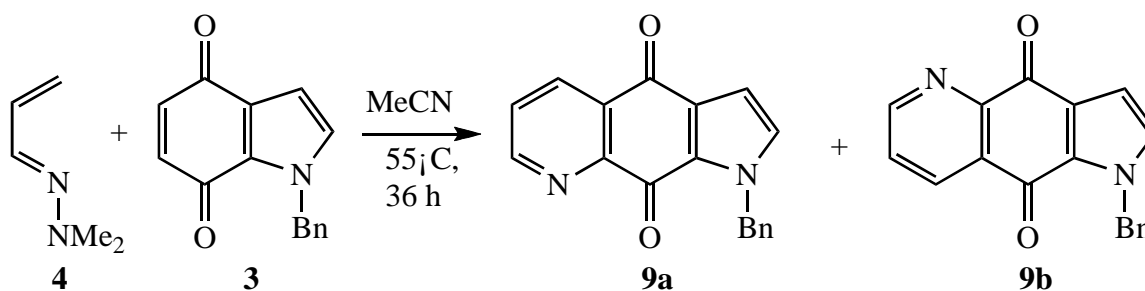
### 1. CHEMISTRY

There is no example of Diels-Alder reactions between  $\alpha,\beta$ -unsaturated dialkylhydrazones and benzotriazole- or indazole-4,7-dione derivatives. The best conditions we found for the reactions described in Scheme 1 were a heating at 50-60 °C in acetonitrile for one or two days. Tricyclic quinones **5** or **7** were then regioselectively obtained in 85 and 84% yield respectively, along with byproducts **6** or **8** (6% and 13% yield respectively). The latter ones result from the addition to the starting quinones of dimethylamine, which is released during the oxidative process of the primary cycloadduct. Attempts to minimize this addition pathway by adding acetic<sup>6</sup> anhydride in the reaction mixture failed.



**Scheme 1.**

Pyrrolo[4,5-*g*]quinoline-4,9-dione derivatives<sup>7,8</sup> are more described, due to their great biological activities.<sup>9</sup> Only one synthesis of this skeleton was described using a hetero-Diels-Alder reaction<sup>8</sup> although few examples<sup>10</sup> of [4+2] cycloadditions of indolo-4,7-diones with  $\alpha,\beta$ -unsaturated dialkylhydrazones are reported in the literature. In all cases, a mixture of 1,5- and 1,8- regioisomers was obtained in moderated overall yields. The 1,5-/1,8- ratio varies according to the nature of the substituent on the nitrogen atom of the starting quinone. The reaction described in Scheme 2 was carried out in acetonitrile at 50 °C for 36 hours and afforded a mixture of the regioisomers **9a** and **9b** (ratio **9a/9b**: 58/42) with 55% overall yield.



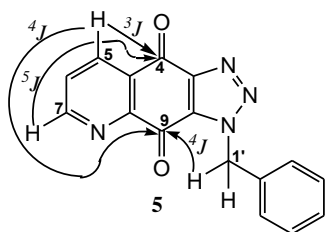
**Scheme 2.**

## 2. STRUCTURAL ANALYSIS

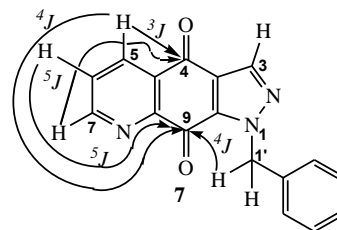
Assignment of regiochemistry was established for each compound by 2D NMR HSQC and  $^1\text{H}$ - $^{13}\text{C}$  HMBC correlations, using the characteristic long-range  $^3J$ ,  $^4J$  and  $^5J$  couplings. All of the cross couplings observed are reported in a table, and the decisive correlations for the structural assignment are summarized in the corresponding figure. For every compound, the carbonyls C-4 and C-9 (or C-7) were firstly attributed due to the  $^4J$  coupling between the methylene protons 1'-H and C-9 (or C-7). Then, couplings between the pyridine protons and the carbonyls were analyzed.

For compound **5** (Table 1), the 5-H proton showed couplings with C-4 ( $^3J_{\text{H,C}}$ ) and C-9 ( $^4J_{\text{H,C}}$ ), while the 7-H proton correlated only with C-4 ( $^5J_{\text{H,C}}$ ). These data allowed us to determine the regiochemistry of **5**.

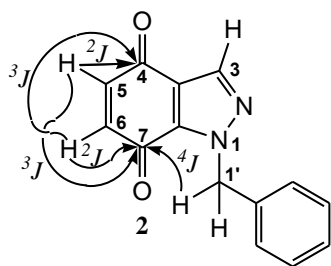
Surprisingly, for quinone **7** (Table 2), no correlation was observed between the proton 3-H and the carbon of the carbonyl groups in spite of additional NMR experiments. NMR studies of the starting indazole-4,7-dione **2** showed the same phenomenon (Table 3), which is related for several quinones linked to a pyrrolo<sup>11</sup> or pyrazolo<sup>12</sup> ring. However, as for compound **5**, the spectrum showed the same couplings between the 5-H proton with C-4 ( $^3J_{\text{H,C}}$ ) and C-9 ( $^4J_{\text{H,C}}$ ) and the 7-H proton with C-4 ( $^5J_{\text{H,C}}$ ). On the other hand, the 6-H proton correlated with C-9 ( $^5J_{\text{H,C}}$ ). So the comparative study with NMR data obtained from compound **5** led us to hypothesize a similar regiochemistry.

**Table 1.** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC correlations of **5** (DMSO, 500.13 MHz)

Atom	$^{13}\text{C}$	$^1\text{H}$	HMBC [ $J(\text{C},\text{H})$ ]				
			$^1J$	$^2J$	$^3J$	$^4J$	$^5J$
<b>3a</b>	145.5						
<b>4</b>	177.1				5-H		7-H
<b>4a</b>	131.4			5-H	6-H	7-H	
<b>5</b>	135.9	8.60	5-H	6-H	7-H		
<b>6</b>	129.3	7.95	6-H	5-H,			
<b>7</b>	154.9	9.00	7-H	6-H	5-H		
<b>8a</b>	149.8			5-H,	6-H		
<b>9</b>	174.1			5-H,	6-H		
<b>9a</b>	135.6			1'-H			
<b>1'</b>	53.7	6.10	1'-H				
<b>2'</b>	135.3						
<b>3'</b>	129.6		3'-H				
<b>4'</b>	128.7		4'-H				
<b>5'</b>	129.2		5'-H				

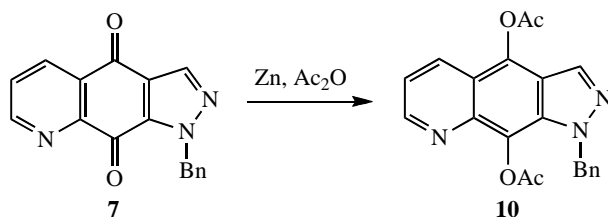
**Table 2.** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC correlations of **7** (DMSO, 500.13 MHz)

Atom	$^{13}\text{C}$	$^1\text{H}$	HMBC [ $J(\text{C},\text{H})$ ]				
			$^1J$	$^2J$	$^3J$	$^4J$	$^5J$
<b>3</b>	138.5	8.34	3-H				
<b>3a</b>	123.4			3-H			
<b>4</b>	179.0				5-H		7-H
<b>4a</b>	131.4				6-H	7-H	
<b>5</b>	135.5	8.53	5-H	6-H	7-H		
<b>6</b>	128.8	7.91	6-H	5-H, 7-H			
<b>7</b>	154.7	9.00	7-H	6-H	5-H		
<b>8a</b>	149.9				5-H, 7-H	6-H	
<b>9</b>	174.5				5-H, 1'-H	6-H	
<b>9a</b>	138.2				3-H, 1'-H		
<b>1'</b>	55.3	5.92	1'-H				
<b>2'</b>	136.8						
<b>3'</b>	128.6		3'-H				
<b>4'</b>	129.5		4'-H				
<b>5'</b>	128.9		5'-H				

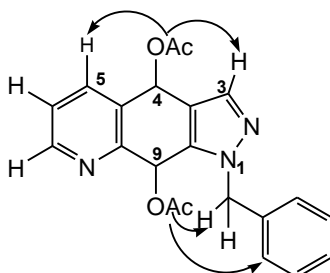
**Table 3.** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC correlations of **2** (DMSO, 500.13 MHz)

Atom	$^{13}\text{C}$	$^1\text{H}$	HMBC [ $J(\text{C},\text{H})$ ]				
			$^1J$	$^2J$	$^3J$	$^4J$	$^5J$
<b>3</b>	137.3	8.31	3-H				5-H
<b>3a</b>	122.0			3-H	5-H	6-H,	
<b>4</b>	182.4			5-H	6-H		7-H
<b>5</b>	139.3	6.84	5-H	6-H			
<b>6</b>	138.1	6.90	6-H	5-H			1'-H
<b>7</b>	178.5			6-H	5-H	1'-H	
<b>7a</b>	136.7				3-H, 5-H		
<b>1'</b>	54.9	5.92	1'-H				
<b>2'</b>	136.6						
<b>3'</b>	128.6		3'-H				
<b>4'</b>	128.9		4'-H				
<b>5'</b>	129.5		5'-H				

In order to confirm this hypothesis, a reductive acetylation of quinone **7** was carried out, following a known procedure,<sup>13</sup> to afford the diacetate **10** in 27 % yield (scheme 3).

**Scheme 3.**

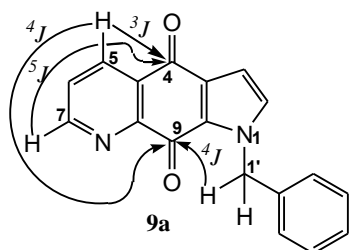
The cross couplings (Figure 2) found in the NOESY spectrum agreed with the proposed regiochemistry, confirming unambiguously the assignment of **7**.



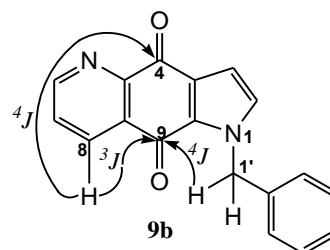
**Figure 2.** NOESY interactions for **10**

Finally, a comparative study of the spectra (Tables 4 and 5) of the pyrrolo derivatives **9a** and **9b** allowed us to determine the structure of each regioisomer. Indeed, they showed differences in the couplings between the proton opposite to the N atom of the pyridine ring ( ${}^4J_{\text{H,C-9}}$  and  ${}^3J_{\text{H,C-4}}$  for the major isomer **9a**, the reverse for the minor isomer **9b**:  ${}^4J_{\text{H,C-4}}$  and  ${}^3J_{\text{H,C-9}}$ ) and the coupling between the proton next to the same N atom ( ${}^5J_{\text{H,C-4}}$  for regioisomer **9a**, not seen for **9b**).

**Table 4.** 2D  ${}^1\text{H}$ - ${}^{13}\text{C}$  HMBC correlations for **9a** ( $\text{CDCl}_3$ , 500.13 MHz)



**Table 5.** 2D  ${}^1\text{H}$ - ${}^{13}\text{C}$  HMBC correlations for **9b** ( $\text{CDCl}_3$ , 500.13 MHz)



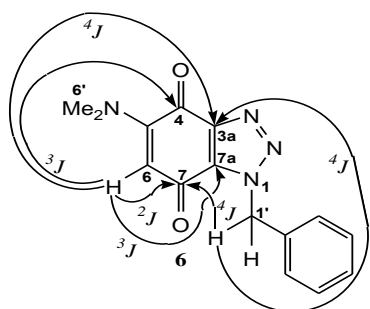
Atom	${}^{13}\text{C}$	${}^1\text{H}$	HMBC [ $J(\text{C,H})$ ]				
			${}^1J$	${}^2J$	${}^3J$	${}^4J$	${}^5J$
<b>2</b>	129.2	7.04	2-H				
<b>3</b>	128.1		3-H				
<b>3a</b>	113.6				2-H		
<b>4</b>	178.3				5-H	2-H	7-H
<b>4a</b>	130.4				6-H	7-H	
<b>5</b>	134.8	8.50	5-H	6-H	7-H		
<b>6</b>	127.2	7.63	6-H	7-H			
<b>7</b>	153.8	8.97	7-H	6-H	5-H		
<b>8a</b>	149.1				5-H,	6-H	2-H
<b>9</b>	173.7					2-H, 5-H,	
<b>9a</b>	123.1				2-H		
<b>1'</b>	53.0	5.70	1'-H				
<b>2'</b>	135.2						
<b>3'</b>	129.1		3'-H				
<b>4'</b>	128.3		4'-H				
<b>5'</b>	128.7		5'-H				

Atom	${}^{13}\text{C}$	${}^1\text{H}$	HMBC [ $J(\text{C,H})$ ]			
			${}^1J$	${}^2J$	${}^3J$	${}^4J$
<b>2</b>	129.4	6.97	2-H			
<b>3</b>	128.7		3-H			
<b>3a</b>	114.3					
<b>4</b>	177.5					2-H,
<b>4a</b>	149.2				6-H,8-H	7-H
<b>6</b>	153.9	8.94	6-H	7-H	8-H	
<b>7</b>	126.9	7.56	7-H	6-H		
<b>8</b>	134.7	8.40	8-H	7-H	6-H	
<b>8a</b>	130.3				7-H	6-H
<b>9</b>	174.5				8-H	2-H,
<b>9a</b>	123.9				2-H	
<b>1'</b>	52.8	5.61	1'-H			
<b>2'</b>	135.2					
<b>3'</b>	129.1		3'-H			
<b>4'</b>	127.8		4'-H			
<b>5'</b>	129.0		5'-H			

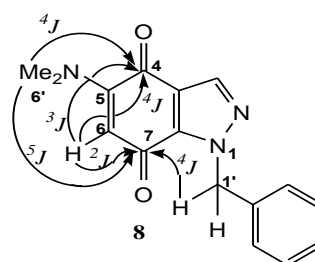
Assignment of regiochemistry was also established for by-products **6** and **8** by 2D NMR  $^1\text{H}$ - $^{13}\text{C}$  HMBC correlations (Tables 6 and 7).

For compound **6**, the 1'-H protons correlated with C-7a ( $^3J_{\text{H,C}}$ ), C-3a and C-7 ( $^4J_{\text{H,C}}$ ). Moreover, the 6-H proton showed couplings with C-5, C-7 ( $^2J_{\text{H,C}}$ ), C-4 and C-7a ( $^3J_{\text{H,C}}$ ). These data allowed us to determine the structure of **6**.

**Table 6.** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC correlations for **6** (CDCl<sub>3</sub>, 500.13 MHz)



**Table 7.** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC correlations for **8** (CDCl<sub>3</sub>, 500.13 MHz)



Atom	$^{13}\text{C}$	$^1\text{H}$	HMBC [ $J(\text{C,H})$ ]				
			$^1J$	$^2J$	$^3J$	$^4J$	$^5J$
<b>3a</b>	143.5					6-H,	
<b>4</b>	176.6				6-H		1'-H
<b>5</b>	153.2			6-H	6'-H		
<b>6</b>	104.7	5.54	6-H				6'-H
<b>7</b>	174.0			6-H			1'-H
<b>7a</b>	133.4				6-H,		
<b>1'</b>	53.3	5.89	1'-H				
<b>2'</b>	134.7						
<b>3'</b>	129.3		3'-H				
<b>4'</b>	129.1		4'-H				
<b>5'</b>	129.2		5'-H				
<b>6'</b>	44.1	3.28	6'-H				

Atom	$^{13}\text{C}$	$^1\text{H}$	HMBC [ $J(\text{C,H})$ ]				
			$^1J$	$^2J$	$^3J$	$^4J$	$^5J$
<b>3</b>	137.9	7,86	3-H				
<b>3a</b>	121.1			3-H			6'-H
<b>4</b>	179.2				3-H, 6-H		6'-H
<b>5</b>	153.6			6-H	6'-H		
<b>6</b>	105.1	5,49	6-H				6'-H
<b>7</b>	176.0			6-H			3-H, 6'-H
<b>7a</b>	137.5				3-H,		
<b>1'</b>	54.7	5,77	1'-H				
<b>2'</b>	136.2						
<b>3'</b>	129.1		3'-H				
<b>4'</b>	128.9		4'-H				
<b>5'</b>	128.6		5'-H				
<b>6'</b>	43.8	3.24	6'-H				

For derivative **8**, correlations between the 6'-H protons and C-5 ( $^3J_{\text{H,C}}$ ), C-4, C-6 ( $^4J_{\text{H,C}}$ ), C-3a and C-7 ( $^5J_{\text{H,C}}$ ) were observed. On the other hand, the 6-H proton showed couplings with C-5, C-7 ( $^2J_{\text{H,C}}$ ), C-4, C-7a ( $^3J_{\text{H,C}}$ ) and C-3a ( $^4J_{\text{H,C}}$ ). So these facts are in favour of the proposed structure.

### 3. FRONTIER MOLECULAR ORBITAL CONSIDERATIONS

In order to confirm the above assignments, quantum chemistry calculations were performed using the SYBYL suite of programs (by Tripos, Inc.). The geometry of the molecule and the energy were computed using Gaussian 98 version A10 program (Gaussian Inc.). First, the geometry of each molecule was optimized using Density Functional Theory (DFT)<sup>14</sup> with the B3LYP<sup>15</sup> method for the molecule using 6-31G\*\* for the atomic basis set. The partial charges were extracted. The coefficient of the atoms of the

HOMO orbital for **diene** compound and LUMO orbital for **dienophile** compound were sums. These values give in absolute value information about the electron density of these atoms (Table 8).

**Table 8.** Frontier molecular orbital coefficients and partial charge

compound	atom	orbital coefficient	partial charge
acrolein <i>N,N</i> -dimethylhydrazone <b>4</b>	N (HOMO)	0.36409	-0.2576
	C-4 (HOMO)	0.46505	-0.2360
1-benzyl-1 <i>H</i> -benzo triazole-4,7-dione <b>1</b>	C-5 (LUMO)	0.40701	-0.1122
	C-6 (LUMO)	0.34507	-0.1119
1-benzyl-1 <i>H</i> -indazole-4,7-dione <b>2</b>	C-5 (LUMO)	0.41498	-0.1047
	C-6 (LUMO)	0.36234	-0.1162
1-benzyl-1 <i>H</i> -indole-4,7-dione <b>3</b>	C-5 (LUMO)	0.51284	-0.1043
	C-6 (LUMO)	0.48579	-0.1111

The calculations (Table 8) indicate that for acrolein *N,N*-dimethylhydrazone **4** the largest coefficient is located at the carbon C-4, while for the quinones it is always situated at C-5. So the major regioisomers should result from the attack of the C-4 diene to the C-5 of the different quinones. Regioselectivities should be important, due to the large difference of the coefficient values, except perhaps for the indole-4,7-dione derivative **3**. Finally, these predictions agree with the observed regiochemistry for each cycloaddition: the 1,8-regioisomer is the single or the major product formed.

Moreover, the theoretical calculations can also be used to estimate the regiochemistry of by-products **6** and **8**. Even if partial charge calculations show no or only minor difference between C-5 and C-6 (Table 8), the electronic density, smaller in the largest HOMO, would promote the attack on this location. These predictions agree with the established regiochemistry too.

## CONCLUSION

We synthesized from a short process new heterocyclic derivatives including a *para* quinoline moiety. Assignment of all isolated regioisomers were achieved using 2D NMR  $^1\text{H}$ - $^{13}\text{C}$  HMBC correlations. Evaluation of antiparasitic and antitumoral potential of all compounds is currently underway.

## EXPERIMENTAL

### 1. GENERAL PROCEDURES

Melting points were measured with a Büchi apparatus (capillary tube). The  $^1\text{H}$ - (300 MHz) and  $^{13}\text{C}$ -NMR (75 MHz) spectra were recorded on a Bruker DRX 300 spectrometer. The 2D NMR experiments were

recorded on a Bruker DRX 500 spectrometer.  $^1\text{H}$ - $^{13}\text{C}$  HSQC and HMBC and NOESY experiments used gradients for better coherence selection. The chemical shifts are reported in ppm ( $\delta$ ) using tetramethylsilane (TMS) as an internal reference.  $J$  values are given in Hz. The infrared spectra were recorded with a Perkin-Elmer 1310 spectrometer. Mass spectra (EI) were recorded with a GC/MS Nermag R10-10 spectrometer. Elemental analyses were performed at the Centre de Microanalyse du CNRS at Solaize (France). Column chromatography were carried out with Matrex (60 Å, 35-70  $\mu\text{m}$ ) acidic silica gel. Acrolein *N,N*-dimethylhydrazone **4**,<sup>5</sup> benzotriazole-4,7-dione **1**, indazole-4,7-dione **2** and indole-4,7-dione **3**<sup>3</sup> were prepared according the procedures described in the literature.

## 2. [4+2] CYCLOADDITIONS

**3-Benzyl-3H-[1,2,3]triazolo[4,5-g]quinoline-4,9-dione (5) 5-(Dimethylamino)benzotriazole-4,7-dione (6):** To a solution of benzotriazole-4,7-dione **1** (150 mg, 0.63 mmol) in MeCN (5 mL), was added the acrolein *N,N*-dimethylhydrazone **4** (74 mg, 0.75 mmol) in MeCN (2 mL). After stirring for 24 h at 50 °C, the mixture was cooled and the solvent evaporated to dryness under vacuum. The crude residue was then crystallized with Et<sub>2</sub>O at 0 °C and the quinolinedione filtered **5** (140 mg, 0.47 mmol, 75%). The filtrate was evaporated under vacuum and the residue purified by column chromatography (AcOEt/petroleum ether, 1/1) to lead to **6** (10 mg, 0.035 mmol, 6%) and **5** (19 mg, 0.065 mmol, 10 %). (**5**): brown crystals;  $R_f$  = 0.18 (AcOEt/petroleum ether, 1/1); mp 133 °C; IR(KBr) 1686, 1574, 1483  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$  6.10 (2H, s, CH<sub>2</sub>-Ph), 7.37-7.48 (5H, m, H Ph), 7.95 (1H, dd,  $J_1$  = 7.9 Hz,  $J_2$  = 4.7 Hz, H-6), 8.60 (1H, dd,  $J_1$  = 7.9 Hz,  $J_2$  = 1.5 Hz, H-5), 9.00 (1H, dd,  $J_1$  = 4.7 Hz,  $J_2$  = 1.5 Hz, H-7);  $^{13}\text{C}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$  52.8, 128.7 (2C), 128.9, 129.2, 129.6 (2C), 131.4, 134.6, 135.3, 135.9, 145.5, 149.8, 159.8, 174.1, 177.1. HRMS calcd for C<sub>16</sub>H<sub>11</sub>N<sub>4</sub>O<sub>2</sub>: 291.0882 [M+H]<sup>+</sup>, found: 291.08816. (**6**): red powder;  $R_f$  = 0.55 (AcOEt/petroleum ether, 1.5/1); mp 189 °C; IR(KBr) 1702, 1618, 1541  $\text{cm}^{-1}$ ;  $^1\text{H}$  RMN (CDCl<sub>3</sub>)  $\delta$  3.28 (6H, s, 2CH<sub>3</sub>), 5.54 (1H, s, H-5), 5.89 (2H, s, CH<sub>2</sub>-Ph), 7.30-7.38 (3H, m, H Ph), 7.44-7.53 (2H, m, H Ph);  $^{13}\text{C}$  RMN (CDCl<sub>3</sub>)  $\delta$  44.1 (2C), 53.3, 104.7, 129.1 (2C), 129.2, 129.3 (2C), 133.4, 134.7, 143.5, 153.2, 174.0, 176.6; HRMS calcd for C<sub>15</sub>H<sub>15</sub>N<sub>4</sub>O<sub>2</sub>: 283.1195 [M+H]<sup>+</sup>, found: 283.1198.

**1-Benzyl-1H-pyrazolo[4,5-g]quinoline-4,9-dione (7) and 5-(Dimethylamino)indazole-4,7-dione (8):** To a solution of indazole-4,7-dione **2** (150 mg, 0.66 mmol) in MeCN (5 mL), was added **4** (78 mg, 0.80 mmol) in MeCN (2 mL). After stirring for 48 h at 60 °C, the mixture was cooled and the solvent evaporated to dryness under vacuum. The crude residue was then crystallized with Et<sub>2</sub>O at 0 °C and the quinolinedione **7** filtered (115 mg, 0.40 mmol, 63%). The filtrate was evaporated under vacuum and the

residue purified by column chromatography (AcOEt/petroleum ether, 1/1) led to **8** (red, 23 mg, 0.082 mmol, 13%) and **7** (38 mg, 0.013 mmol, 21%). (**7**): pink crystals;  $R_f = 0.14$  (AcOEt/petroleum ether, 1/1); mp 177 °C; IR(KBr) 1687, 1673, 1532  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  5.92 (2H, s,  $\text{CH}_2\text{-Ph}$ ), 7.25-7.43 (5H, m, H Ph), 7.91 (1H, dd,  $J_1 = 7.9$  Hz,  $J_2 = 4.7$  Hz, H-6), 8.34 (1H, s, H-3), 8.53 (1H, dd,  $J_1 = 7.7$  Hz,  $J_2 = 1.5$  Hz, H-5), 9.08 (1H, dd,  $J_1 = 4.5$  Hz,  $J_2 = 1.5$  Hz, H-7);  $^{13}\text{C}$  NMR (DMSO- $d_6$ )  $\delta$  55.3, 123.4, 128.6 (2C), 128.8 (2C), 128.9, 129.5, 131.4, 135.5, 136.8, 138.2, 138.5, 149.9, 154.7, 174.5, 179.0; Anal. Calcd for  $\text{C}_{17}\text{H}_{11}\text{N}_3\text{O}_2$ : C, 70.58; H, 3.83; N, 14.53; O, 11.06. Found: C, 70.27; H, 4.02; N, 14.17; O, 10.95. (**8**):  $R_f = 0.72$  (AcOEt/petroleum ether, 1.5/1); mp 119 °C; IR(KBr) 1677, 1619, 1535  $\text{cm}^{-1}$ ;  $^1\text{H}$  RMN ( $\text{CDCl}_3$ )  $\delta$  3.24 (6H, s, 2 $\text{CH}_3$ ), 5.49 (1H, s, H-6), 5.77 (2H, s,  $\text{CH}_3\text{-Ph}$ ), 7.19-7.45 (5H, m, H Ph), 7.86 (1H, s, H-3);  $^{13}\text{C}$  RMN ( $\text{CDCl}_3$ )  $\delta$  43.8 (2C), 54.7, 105.1, 121.1, 128.6, 128.9 (2C), 129.1 (2C), 136.2, 137.5, 137.9, 153.6, 176.0, 179.2; HRMS calcd for  $\text{C}_{16}\text{H}_{16}\text{N}_3\text{O}_2$ : 282.1243  $[\text{M}+\text{H}]^+$ , found: 282.1247.

**1-Benzyl-1*H*-pyrrolo[4,5-*g*]quinoline-4,9-dione (9)**: To a solution of indole-4,7-dione **3** (140 mg, 0.59 mmol) in MeCN (13 mL), was added **4** (48 mg, 0.42 mmol) in MeCN (4 mL). After stirring for 36 h at 50 °C, the mixture was evaporated and the crude purified by column chromatography (AcOEt/petroleum ether, 2/1) then ( $\text{CHCl}_3$ /acetone/ $\text{NH}_4\text{OH}$ , 150/5/1) to lead to **9a** (54 mg, 0.19 mmol, 32 %) and **9b** (39 mg, 0.135 mmol, 23 %).

(**9a**): yellow crystals;  $R_f = 0.86$  ( $\text{CHCl}_3$ /acetone/ $\text{NH}_4\text{OH}$ , 100/20/5); mp 158 °C; IR(KBr) 1673, 1666, 1496  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  5.70 (2H, s,  $\text{CH}_2\text{-Ph}$ ), 7.04 (1H, s, H-2); 7.29-7.40 (6H, m, H-3 + H Ph), 7.63 (1H, dd,  $J_1 = 7.9$  Hz,  $J_2 = 4.7$  Hz, H-6), 8.50 (1H, dd,  $J_1 = 7.9$  Hz,  $J_2 = 1.7$  Hz, H-5), 8.97 (1H, dd,  $J_1 = 4.7$  Hz,  $J_2 = 1.5$  Hz, H-7);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  53.0, 113.6, 123.1, 127.2, 128.1, 128.3 (2C), 128.7, 129.1 (2C), 129.2, 130.4, 134.8, 135.2, 149.1, 153.8, 173.7, 178.3; HRMS calcd for  $\text{C}_{18}\text{H}_{13}\text{N}_2\text{O}_2$ : 289.0977  $[\text{M}+\text{H}]^+$ , found: 289.09769.

(**9b**): yellow crystals;  $R_f = 0.78$  ( $\text{CHCl}_3$ /acetone/ $\text{NH}_4\text{OH}$ , 100/20/5); mp 178 °C; IR(KBr) 1687, 1661, 1491  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  5.61 (2H, s,  $\text{CH}_2\text{-Ph}$ ), 6.97 (1H, s, H-2); 7.14-7.34 (6H, m, H-3 + H Ph), 7.56 (1H, dd,  $J_1 = 7.7$  Hz,  $J_2 = 4.5$  Hz, H-7), 8.40 (1H, dd,  $J_1 = 7.7$  Hz,  $J_2 = 1.5$  Hz, H-6), 8.94 (1H, dd,  $J_1 = 4.5$  Hz,  $J_2 = 1.5$  Hz, H-8);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  52.8, 114.3, 123.9, 126.9, 127.8 (2C), 128.7, 129.0, 129.1 (2C), 129.4, 130.3, 134.7, 135.2, 149.2, 153.9, 174.5, 177.5; HRMS calcd for  $\text{C}_{18}\text{H}_{13}\text{N}_2\text{O}_2$ : 289.0977  $[\text{M}+\text{H}]^+$ , found: 289.09769.

### 3. REDUCTIVE ACETYLATION

**4-(Acetyloxy)-1-benzyl-1*H*-pyrazolo[4,5-*g*]quinolin-9-yl acetate (10)**: A mixture of **2** (50 mg, 0.17 mmol), zinc powder (255 mg, 3.91 mmol), sodium acetate (89 mg, 1.08 mmol) and acetic anhydride (24

mL) was stirred for 22 h. The mixture was then diluted with CH<sub>2</sub>Cl<sub>2</sub> (100 mL) and filtered. The filtrate was evaporated and purified by column chromatography (AcOEt/petroleum ether, 1.5/1) then (CH<sub>2</sub>Cl<sub>2</sub>/AcOEt, 4/1) to give **10** (17 mg, 0.045 mmol, 27%). (**10**): pale yellow powder; R<sub>f</sub> = 0.54 (CH<sub>2</sub>Cl<sub>2</sub>/AcOEt, 2/1); mp degradation >143 °C; IR(KBr) 1755, 1642, 1196 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.30 (3H, s, CH<sub>3</sub>), 2.50 (3H, s, CH<sub>3</sub>), 5.76 (2H, s, CH<sub>2</sub>-Ph), 7.06-7.30 (5H, m, H Ph), 8.10 (1H, s, H-3), 8.22 (1H, dd, J<sub>1</sub> = 8.7 Hz, J<sub>2</sub> = 1.5 Hz, H-5), 8.82 (1H, dd, J<sub>1</sub> = 3.8 Hz, J<sub>2</sub> = 1.5 Hz, H-7); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 54.8, 20.8, 20.9, 54.8, 116.7, 119.4, 120.4, 126.7 (2C), 127.2, 127.9, 128.8 (2C), 128.9, 130.9, 132.0, 132.9, 135.3, 137.4, 137.7, 151.6, 168.6, 168.9; HRMS calcd for C<sub>21</sub>H<sub>18</sub>N<sub>3</sub>O<sub>4</sub>: 376.1297 [M+H]<sup>+</sup>, found: 376.1298.

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