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Mohamed Othman, Pascal Pigeon, Bernard Decroix. New fused lactones from indolizinediones via N-acyliminium ions. *Tetrahedron*, 1998, 54 (30), pp.8737-8744. 10.1016/S0040-4020(98)00468-2 . hal-01230415

**HAL Id: hal-01230415**

**<https://hal.science/hal-01230415>**

Submitted on 6 Feb 2018

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# New Fused Lactones from Indolizinediones *via* *N*-Acyliminium Ions

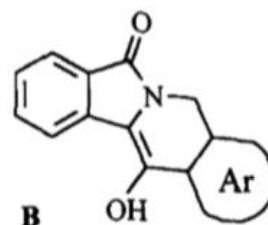
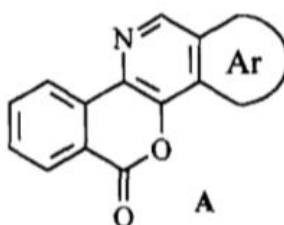
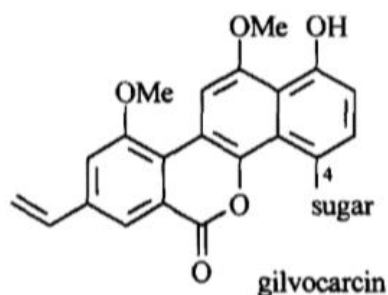
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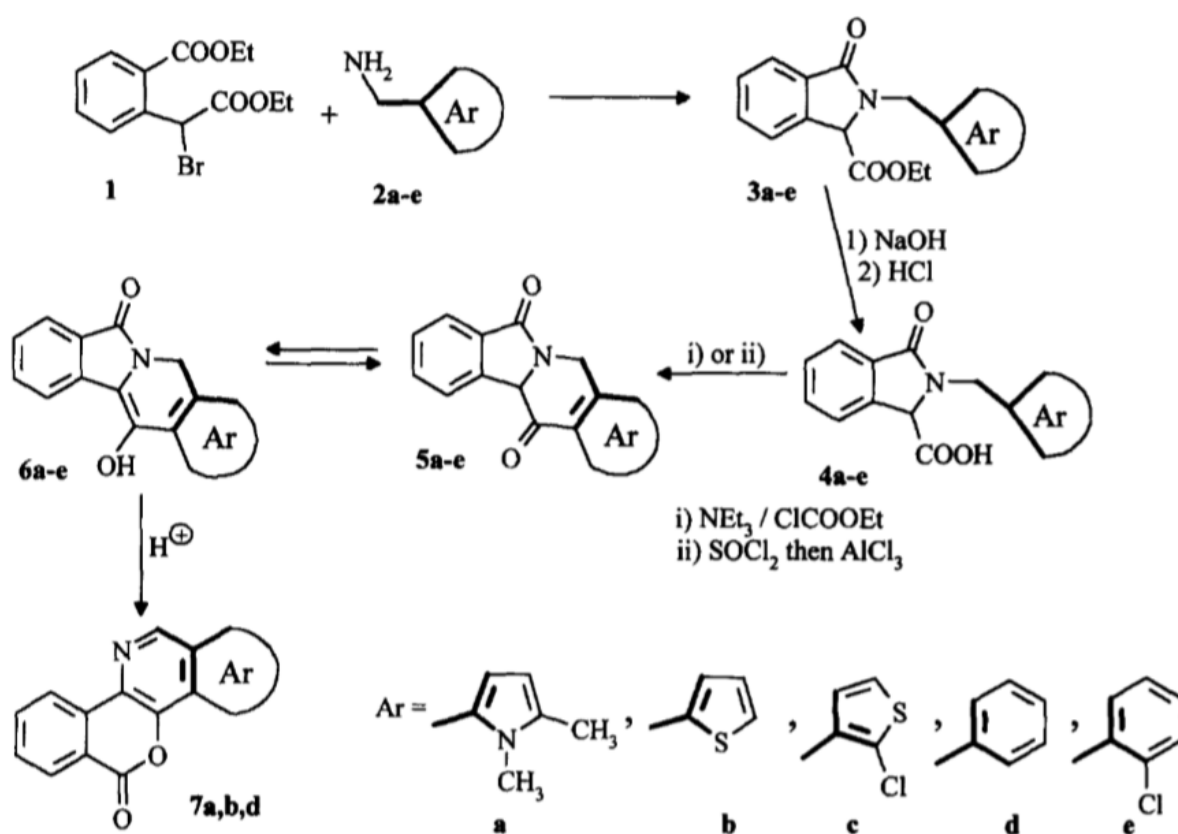
Abstract: *N*-Arylmethylphthalimidine-3-carboxylates **3** are good precursors for the synthesis of ketones **5a,b** or enols **6c-e** which upon acidic treatment led to lactones **7** via an *N*-acyliminium ion.

Gilvocarcin<sup>1</sup> and related compounds are metabolites of certain *Streptomyces* species and constitute a novel class of aryl C-glycoside antibiotics<sup>2</sup>. These compounds share a common tetracyclic aromatic nucleus, 6*H*-benzo[d]naphto[1,2-*b*]pyran-6-one to which sugars are attached at the C<sub>4</sub> position. Recently, isosteres of defucogilvocarcin have been described<sup>3</sup>, in which the vinylbenzene moiety is replaced by a benzofuran moiety. We wish to report herein our results concerning the introduction of a heterocyclic system in place of the naphthalenic system in related compounds of type **A**. Furthermore that latter species is also closely related to alkaloids possessing a benzopyranisoquinoline skeleton. Literature<sup>4-7</sup> shows a variety of examples of these types of compounds, which in many cases exhibit a remarkable physiological activity (antiinflammatory, dopaminergic, antidepressive). Finally, the synthesis of [1]benzopyran[4,3-*c*]isoquinoline derivatives have been reported<sup>8</sup> very recently by employing isoflavone as the starting material.



Ar = thiophene, pyrrole, benzene

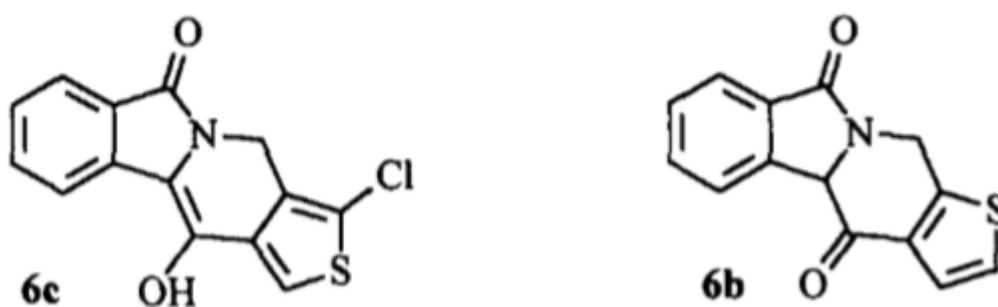
In the reported studies, the lactonization step resulted of the condensation between an acyl chloride and a phenol<sup>1</sup> or condensation of a carboxylic acid or a carboxamide with a ketal conjugated to an enone system<sup>3</sup>. For this step we propose to pursue a strategy based upon the rearrangement of isoindolones of type **B** in an acidic medium. Actually, it has been demonstrated that during the Friedel-Crafts cyclization of *N*-arylmethylpyroglutamoyl chlorides a lactone could be obtained as a by-product<sup>9</sup>. Furthermore during the treatment of a benzoindolizinedione with polyphosphoric acid dehydration occurred leading to a benzoindolizinone<sup>10</sup> via an *N*-acyliminium ion as described for other iminium salts<sup>11</sup>. From these results, compound **B** could be considered as a good precursor for the synthesis of **A**. For this purpose the lactam moiety did not possess a hydrogen atom in the 13-position of the nitrogen atom and the acyl ion resulting of the opening of the lactam function was stabilized by the benzene ring. Thus, preparation of compounds of type **B** has been undertaken (Scheme 1).



Scheme 1

Diethyl  $\alpha$ -bromohomophthalate **1**<sup>12</sup> upon treatment with arylmethyamines **2a-e** for 8 hours in acetonitrile at room temperature, afforded the isoindolones **3a-e** in good yields (84-92%). Saponification of esters **3a-e** gave the corresponding acids **4a-e** (70-82%). Cyclization of the acids **4b-e** was performed using a Friedel-Crafts reaction. As previously described in the synthesis of thienoindolizines<sup>13</sup> acids **4b-e** were treated with thionyl chloride in dichloromethane and the resulting acid chloride in the presence of aluminium trichloride of high quality as a catalyst gave the cyclic compounds **5** or **6b-e** in good yields (70-90%). The cyclization of **4a** under these conditions resulted in a complete degradation, but proceeded when acid **4a** was treated with ethyl chloroformate in the presence of triethylamine (75%)<sup>12</sup>. The pyrrole ring was sufficiently reactive and no Lewis acid was necessary whereas the other acids did not react. The ketone forms **5a,b** are stable, while in few minutes the ketones **5c-e** tautomerized into the enol forms **6c-e**.

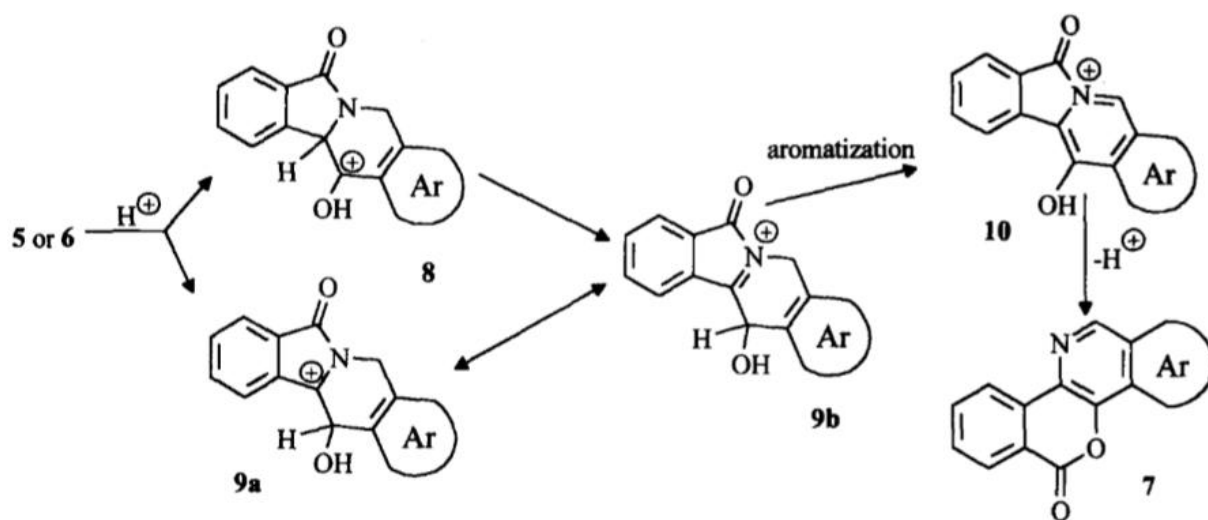
Structural assignments of compounds **5** and **6** were obtained by usual spectrometric methods (IR, <sup>1</sup>H and <sup>13</sup>C NMR). The <sup>1</sup>H NMR spectra of **5a** and **5b** exhibit an AB system for the protons of the methylene group and **6c-d** show a singlet for the corresponding methylene group and the absence of the junction proton according to our previous observation on related compounds<sup>14,15</sup>. The stable hydroxy forms **6d-e** could be due to a *s-trans* configuration not possible in the cases of **6a,b**. Actually, the synthesis of the 3,4-fused thiophene derivative **6c** supported this hypothesis since only the enol form was isolated.



**Scheme 2**

Subjected to refluxing toluene in the presence of a catalytic quantity of *p*-toluenesulfonic acid for one to three days, compounds **5a,b** or **6d** gave selectively the lactones

**7a,b,d** in good yields (72-90%). The reaction is rationalized by involving either the protonated ketone **8** which rearranges itself to the more stable iminium salt **9b** by a hydrogen shift or the protonated enol **9a** stabilized as the iminium salt **9b** (Scheme 3). An aromatization of **9b** gives the acylpyridinium intermediate **10** similar to that postulated with an amino group in place of hydroxyl group<sup>16</sup>. Rearrangement of **10**, with the loss of a proton, provides the lactones **7**. The proposed structures for compounds **7a,b,d** are supported by spectroscopic analyses. For example compound **7b** shows that the chemical shifts of the four benzenic protons (<sup>1</sup>H NMR) and the one of the carbonyl group (<sup>13</sup>C NMR) are in agreement with those reported in the literature for related compounds<sup>1,7,13</sup>. Furthermore the low-resolution mass spectrum of compound **7b** shows the molecular ion as the base peak at m/e 253 and the major ion at m/e 225 corresponds to loss of carbon monoxide. This is in agreement with the observations made by Katritzky for [2]benzopyrano[4,3-b]pyridin-6-ones<sup>18</sup> and characteristic of coumarin<sup>19</sup>. Compounds **7a,d** give similar features.



Scheme 3

In conclusion, we proposed a short access to lactone **7** via ready available phthalimidine-3-carboxylate derivatives **3**. The reaction has been applied to several different aromatic rings (thiophene, benzene, pyrrole) and will facilitate analog preparation in the search for new biologically active materials.

## Experimental

Melting points are uncorrected. The infrared spectra of solids (potassium bromide) were recorded on a Perkin Elmer FTIR paragon 1000 spectrometer. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AC-200 (200 MHz) instrument in deuteriochloroform solution and chemical shifts ( $\delta$ ) are expressed in ppm relative to internal TMS. Ascending thin layer chromatography was performed on precoated plates of silica gel 60 F 254 (Merck) and the spots visualized using an ultraviolet lamp or iodine vapor. E. Merck silica gel 60 F (70-300 mesh) was used for column chromatography. The elemental analyses were carried out by the microanalysis laboratory of INSA at Rouen, F 76130 M<sup>t</sup>. S<sup>t</sup>. Aignan, France. Amine **2a** was prepared as indicated in reference 12, amines **2b,d,e** are commercially available.

### **3-Aminomethyl-2-chlorothiophene (2c)**

To a refluxing solution of hexamethylenetetramine (7.5 g, 50 mmol) in carbon tetrachloride (60 mL) was added dropwise a solution of 3-bromomethyl-2-chlorothiophene (9.5 g, 45 mmol) in 100 mL of carbon tetrachloride. The reflux was continued for 3 h then the mixture was cooled, filtrated and the precipitate was recrystallized from ethanol to afford the intermediate salt (96%). To a suspension of this salt in anhydrous ethanol (200 mL) concentrated hydrochloric acid was carefully added. The mixture was refluxed for 4 h, cooled, then filtrated. The filtrate was concentrated under a reduced pressure and the residue was recrystallized from ethanol-ether mixture (9/1) to afford the hydrochloride of **2c**. A suspension of this hydrochloride in dichloromethane (200 mL) was basified dropwise with a 1N sodium hydroxide solution. The mixture was stirred for 4 h and then the organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure to afford the amine **1e** as an oil. Yield 66%; IR: 3100 ( $\text{NH}_2$ )  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.43 (s, 2H,  $\text{NH}_2$ ), 3.77 (s, 2H,  $\text{CH}_2$ ), 6.91 (d,  $J = 6$  Hz, 1H,  $\text{H}_{\text{thiophene}}$ ), 7.03 (d,  $J = 6$  Hz, 1H,  $\text{H}_{\text{thiophene}}$ ).

### **Ethyl 2-(arylmethyl)phthalimidine-3-carboxylates (3) : general procedure**

To an ice chilled solution of diethyl  $\alpha$ -bromohomophthalate (2 g, 6.34 mmol) in dry acetonitrile was added under an argon atmosphere the amine **2a-e** (12.7 mmol), and the resulting mixture was stirred at room temperature for 8 h. The salt that formed was removed by filtration, and the filtrate was concentrated under reduced pressure. The oily residue was

trituated in a minimum of ether at 0°C. The precipitate was separated by filtration and recrystallized from ethanol.

### **Ethyl 2-(1,5-dimethylpyrrol-2-ylmethyl)phthalimidine-3-carboxylate (3a)**

This product was prepared according to our previous work<sup>12</sup>.

### **Ethyl 2-(thien-2-ylmethyl)phthalimidine-3-carboxylate (3b)**

Yield 92%; mp 171°C; IR: 1736 (C=O), 1698 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.28 (t, J = 7 Hz, 3H, CH<sub>3</sub>), 4.21-4.27 (m, 2H, CH<sub>2</sub>), 4.53 (d, J = 16 Hz, 1H, CH<sub>2</sub>), 4.99 (s, 1H, CH), 5.55 (d, J = 16 Hz, 1H, CH<sub>2</sub>), 6.91-6.95 (m, 2H, H<sub>arom</sub>), 7.22-7.24 (m, 1H, H<sub>arom</sub>), 7.48-7.54 (m, 3H, H<sub>arom</sub>), 7.85-7.89 (m, 1H, H<sub>arom</sub>); Anal. Calcd. for C<sub>16</sub>H<sub>15</sub>NO<sub>3</sub>S: C, 63.77; H, 5.02; N, 4.65. Found: C, 63.97; H, 5.10; N, 4.97.

### **Ethyl 2-(2-chlorothien-3-ylmethyl)phthalimidine-3-carboxylate (3c)**

Yield 90%; mp 158°C; IR: 1749 (C=O), 1703 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.28 (t, J = 7 Hz, 3H, CH<sub>3</sub>), 4.18-4.30 (m, 2H, CH<sub>2</sub>), 4.42 (d, J = 15 Hz, 1H, CH<sub>2</sub>), 4.92 (s, 1H, CH), 5.23 (d, J = 15 Hz, 1H, CH<sub>2</sub>), 6.88 (d, J = 6 Hz, 1H, H<sub>thiophene</sub>), 7.03 (d, J = 6 Hz, 1H, H<sub>thiophene</sub>), 7.50-7.54 (m, 3H, H<sub>arom</sub>), 7.83 (d, J = 7 Hz, 1H, H<sub>arom</sub>); Anal. Calcd. for C<sub>16</sub>H<sub>14</sub>ClNO<sub>3</sub>S: C, 57.23; H, 4.20; N, 4.17. Found: C, 57.31; H, 4.17; N, 4.31.

### **Ethyl 2-(phenylmethyl)phthalimidine-3-carboxylate (3d)**

Yield 84%; mp 75°C; IR: 1738 (C=O), 1694 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.25 (t, J = 7 Hz, 3H, CH<sub>3</sub>), 4.17-4.29 (m, 3H, NCH<sub>2</sub> + CH<sub>2</sub>), 4.87 (s, 1H, CH), 5.45 (d, J = 16 Hz, 1H, NCH<sub>2</sub>), 7.24-7.27 (m, 4H, H<sub>arom</sub>), 7.48-7.51 (m, 4H, H<sub>arom</sub>), 7.80-7.90 (m, 1H, H<sub>arom</sub>); Anal. Calcd. for C<sub>18</sub>H<sub>17</sub>NO<sub>3</sub>: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.22; H, 5.82; N, 4.70.

### **Ethyl 2-(2-chlorophenylmethyl)phthalimidine-3-carboxylate (3e)**

Yield 88%; mp 89°C; IR: 1735 (C=O), 1694 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.26 (t, J = 7 Hz, 3H, CH<sub>3</sub>), 4.15-4.28 (m, 2H, CH<sub>2</sub>), 4.58 (d, J = 15 Hz, 1H, NCH<sub>2</sub>), 4.95 (s, 1H, CH), 5.38 (d, J = 15 Hz, 1H, NCH<sub>2</sub>), 7.17-7.21 (m, 2H, H<sub>arom</sub>), 7.30-7.37 (m, 2H, H<sub>arom</sub>), 7.48-7.60 (m, 3H, H<sub>arom</sub>), 7.71-7.82 (m, 1H, H<sub>arom</sub>); Anal. Calcd. for C<sub>18</sub>H<sub>16</sub>ClNO<sub>3</sub>: C, 65.56; H, 4.89; N, 4.25. Found: C, 65.62; H, 4.92; N, 4.34.

### **2-(Arylmethyl)phthalimidine-3-carboxylic acids (4)**

General procedure : to the esters **3b-e** (4 mmol) in 20 mL of ethanol was added sodium hydroxide solution (0.32 g, 8 mmol in 10 ml of water). The reaction mixture was stirred for 12 hours, concentrated in vacuo, diluted with water, and washed with dichloromethane. The aqueous layer was acidified with 10% hydrochloric acid solution to pH = 1, whereby a precipitate was separated to give the acids **4a-e**. These acids were very sensitive to decarboxylation on heating and were not recrystallized.

#### **2-(1,5-Dimethylpyrrol-2-ylmethyl)phthalimidine-3-carboxylic acid (4a)**

This product was prepared according to our previous work<sup>12</sup>.

#### **2-(Thien-2-ylmethyl)phthalimidine-3-carboxylic acid (4b)**

Yield 80%; mp 107°C; IR: 2884 (OH), 1731 (C=O), 1638 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 4.58 (d, J = 16 Hz, 1H, CH<sub>2</sub>), 5.09 (s, 1H, CH), 5.58 (d, J = 16 Hz, 1H, CH<sub>2</sub>), 6.88-6.98 (m, 2H, H<sub>arom</sub>), 7.19-7.23 (m, 1H, H<sub>arom</sub>), 7.46-7.54 (m, 2H, H<sub>arom</sub>), 7.65 (d, J = 7 Hz, 1H, H<sub>arom</sub>), 7.85 (d, J = 7 Hz, 1H, H<sub>arom</sub>); Anal. Calcd. for C<sub>14</sub>H<sub>11</sub>NO<sub>3</sub>S: C, 61.53; H, 4.06; N, 5.12. Found: C, 61.65; H, 4.12; N, 5.10.

#### **2-(2-Chlorothiophen-3-ylmethyl)phthalimidine-3-carboxylic acid (4c)**

Yield 76%; mp 158°C; IR: 3100 (OH), 1733 (C=O), 1641 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 4.43 (d, J = 15 Hz, 1H, CH<sub>2</sub>), 4.99 (s, 1H, CH), 5.24 (d, J = 15 Hz, 1H, CH<sub>2</sub>), 6.88 (d, J = 6 Hz, 1H, H<sub>thiophene</sub>), 7.01 (d, J = 6 Hz, 1H, H<sub>thiophene</sub>), 7.47-7.61 (m, 3H, H<sub>arom</sub>), 7.82-7.85 (m, 1H, H<sub>arom</sub>); Anal. Calcd. for C<sub>14</sub>H<sub>10</sub>ClNO<sub>3</sub>S: C, 54.64; H, 3.28; N, 4.55. Found: C, 54.80; H, 3.36; N, 4.84.

#### **2-(Phenylmethyl)phthalimidine-3-carboxylic acid (4d)**

Yield 74%; mp 139°C; IR: 2880 (OH), 1741 (C=O), 1646 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 4.27 (d, J = 15 Hz, 1H, CH<sub>2</sub>), 4.95 (s, 1H, CH), 5.50 (d, J = 15 Hz, 1H, CH<sub>2</sub>), 7.22-7.26 (m, 5H, H<sub>arom</sub>), 7.45-7.60 (m, 3H, H<sub>arom</sub>), 7.83-7.87 (m, 1H, H<sub>arom</sub>); Anal. Calcd. for C<sub>16</sub>H<sub>13</sub>NO<sub>3</sub>: C, 71.90; H, 4.90; N, 5.24. Found: C, 72.01; H, 4.85; N, 5.32.

#### **2-(2-Chlorophenylmethyl)phthalimidine-3-carboxylic acid (4e)**

Yield 70%; mp 149°C; IR: 2898 (OH), 1737 (C=O), 1645 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 4.49 (d, J = 16 Hz, 1H, CH<sub>2</sub>), 5.09 (s, 1H, CH), 5.17 (d, J = 16 Hz, 1H, CH<sub>2</sub>), 7.27-7.50 (m,



4H, H<sub>arom</sub>), 7.61-7.78 (m, 4H, H<sub>arom</sub>); Anal. Calcd. for C<sub>16</sub>H<sub>12</sub>ClNO<sub>3</sub>: C, 63.69; H, 4.01; N, 4.64. Found: C, 63.82; H, 4.10; N, 4.90.

### Synthesis of indolizines **5** or **6**

General procedure : the solution of acids **4b-e** (5 mmol), dry dichloromethane (20 mL), oxalyle chloride (0.5 mL), and dimethylformamide (one drop) was stirred for 4 hours. The solution was concentrated under reduced pressure and dry dichloromethane (20 mL) was added. This solution was added dropwise to a stirred mixture of 99.99% aluminium chloride (2 g, 15 mmol) and dry dichloromethane. The mixture was stirred for one hour, then was poured into a mixture of ice and water. The organic layer was washed with water, dried (MgSO<sub>4</sub>), then concentrated under reduced pressure. The ketone **5b** was recrystallized from ethanol and very insoluble enols **6** were washed with boiling acetone.

#### **4,10b-Dihydro-2,3-dimethylbenzo[a]pyrrolo[2,3-f]indolizine-6,11-dione (5a)**

This product was prepared according to our previous work<sup>12</sup>.

#### **4,10b-Dihydrobenzo[a]thieno[2,3-f]indolizine-6,11-dione (5b)**

Yield 90%; mp 213°C; IR: 1702 (C=O), 1672 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 4.65 (d, J = 18 Hz, 1H, CH<sub>2</sub>), 5.21 (s, 1H, CH), 5.78 (d, J = 18 Hz, 1H, CH<sub>2</sub>), 7.22 (d, J = 5 Hz, 1H, H<sub>thiophene</sub>), 7.40 (d, J = 5 Hz, 1H, H<sub>thiophene</sub>), 7.51 (t, J = 7 Hz, 1H, H<sub>arom</sub>), 7.63 (t, J = 7 Hz, 1H, H<sub>arom</sub>), 7.84 (d, J = 7 Hz, 1H, H<sub>arom</sub>), 8.00 (d, J = 7 Hz, 1H, H<sub>arom</sub>); <sup>13</sup>C NMR: δ 38.9 (CH<sub>2</sub>), 63.4 (CH), 123.5 (CH), 124.7 (CH), 124.8 (CH), 125.2 (CH), 128.9 (CH), 130.8 (C), 132.2 (CH), 135.5 (C), 139.0 (C), 152.2 (C), 167.5 (CO), 184.6 (CO); MS (IE, 70 ev) m/e: 255 (M<sup>+</sup>), 243, 124, 96; Anal. Calcd. for C<sub>14</sub>H<sub>9</sub>NO<sub>2</sub>S: C, 65.87; H, 3.55; N, 5.49. Found: C, 65.95; H, 3.68; N, 5.44.

#### **3-Chloro-11-hydroxy-5H-benzo[a]thieno[3,4-f]indolizin-6-one (6c)**

Yield 85%, mp 141°C; IR: 3100 (OH), 1629 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): δ 3.99 (s, 2H, CH<sub>2</sub>), 7.26-7.33 (m, 3H, 2H<sub>arom</sub>+H<sub>thiophene</sub>), 7.75 (d, J = 7 Hz, 1H, H<sub>arom</sub>), 7.89 (t, J = 1 Hz, 1H, H<sub>arom</sub>); Anal. Calcd. for C<sub>14</sub>H<sub>8</sub>ClNO<sub>2</sub>S: C, 58.04; H, 2.78; N, 4.83. Found: C, 58.12; H, 2.81; N, 4.75.

#### **12-Hydroxy-5H-dibenzo[a,f]indolizin-7-one (6d)**

Yield 87%; mp 158-164°C (decomp.); IR: 3100 (OH), 1638 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): δ 5.00 (s, 2H, CH<sub>2</sub>), 7.37-7.47 (m, 4H, H<sub>arom</sub>), 7.62-7.80 (m, 3H, H<sub>arom</sub>), 8.17 (d, J = 8 Hz, 1H, H<sub>arom</sub>); <sup>13</sup>C NMR: δ 42.3 (CH<sub>2</sub>), 117.2 (CH), 122.1 (CH), 122.4 (CH), 123.3 (CH), 126.8 (CH), 127.5 (CH), 127.6 (CH), 127.7 (C), 128.7 (CH), 129.3 (CH), 130.9 (C), 131.3 (CH), 133.2 (C), 136.2 (C), 163.7 (CO); Anal. Calcd. For C<sub>16</sub>H<sub>11</sub>NO<sub>2</sub>: C, 77.10; H, 4.45; N, 5.62. Found: C, 77.32; H, 4.51; N, 5.51.

#### **4-Chloro-12-hydroxy-5H-dibenzo[a,f]indolizin-7-one (6e)**

Yield 90%; mp 258°C; IR: 3051 (OH), 1643 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): δ 4.98 (s, 2H, CH<sub>2</sub>), 7.40-7.55 (m, 3H, H<sub>arom</sub>), 7.60-7.74 (m, 2H, H<sub>arom</sub>), 7.81 (d, J = 7 Hz, 1H, H<sub>arom</sub>), 8.18 (d, J = 1Hz, 1H, H<sub>arom</sub>); Anal. Calcd. for C<sub>16</sub>H<sub>10</sub>ClNO<sub>2</sub>: C, 67.74; H, 3.55; N, 4.94. Found: C, 67.70; H, 3.49; N, 4.96.

#### **Synthesis of lactones 7a,b,d**

The solution of ketone **5a,b** or enol **6d** (4 mmol) and *p*-toluenesulfonic acid (catalytic amount) in toluene (80 mL) was refluxed for 1 to 3 days (monitored by TLC). The solution was cooled, washed with 10% sodium hydrogen carbonate solution, dried (MgSO<sub>4</sub>), filtered, then concentrated under reduced pressure. The residue was chromatographed (silica gel, dichloromethane) then was recrystallized from ethanol.

#### **5H-1,2-dimethyl-[1]benzopyrano[3,2-b]pyrrolo[3,2-d]pyridin-4-one (7a)**

Yield 84%; mp 271°C; IR: 1730 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.47 (s, 3H, CH<sub>3</sub>), 3.80 (s, 3H, CH<sub>3</sub>), 6.62 (s, 1H, H<sub>pyrrole</sub>), 7.54 (t, J = 8 Hz, 1H, H<sub>arom</sub>), 7.85 (t, J = 8 Hz, 1H, H<sub>arom</sub>), 8.35 (d, J = 8 Hz, 1H, H<sub>arom</sub>), 8.60 (s, 1H, H<sub>pyridine</sub>), 8.64 (d, J = 8 Hz, 1H, H<sub>arom</sub>); <sup>13</sup>C NMR: δ 12.8 (CH<sub>3</sub>), 30.3 (CH<sub>3</sub>), 98.0 (CH), 120.8 (C), 122.3 (C), 122.9 (CH), 125.7 (C), 128.2 (CH), 128.8 (CH), 129.9 (CH), 134.9 (CH), 136.1 (C), 137.6 (C), 141.6 (2 C), 161.4 (CO); Anal. Calcd. for C<sub>16</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.81; H, 4.64; N, 10.81.

#### **5H-[1]benzopyrano[3,2-b]tbieno[3,2-d]pyridin-4-one (7b)**

Yield 90%; mp 209°C; IR: 1732 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.63 (t, J = 8 Hz, 1H, H<sub>arom</sub>), 7.79 (s, 2H, H<sub>thiophene</sub>), 7.89 (t, J = 8 Hz, 1H, H<sub>arom</sub>), 8.37 (d, J = 8 Hz, 1H, H<sub>arom</sub>), 8.68 (d, J = 8 Hz, 1H, H<sub>arom</sub>), 9.03 (s, 1H, H<sub>pyridine</sub>); <sup>13</sup>C NMR: δ 120.0 (CH), 121.5 (C), 123.4 (CH), 129.4 (C), 129.5 (CH), 130.1 (CH), 133.0 (CH), 134.6 (C), 135.3 (CH), 136.3 (C),

138.3 (C), 140.5 (CH), 142.6 (C), 160.2 (CO); MS (IE, 70 ev) m/e: 253 ( $M^+$ ), 225, 196; Anal. Calcd. for  $C_{14}H_7NO_2S$ : C, 66.39; H, 2.27; N, 5.53. Found: C, 66.30; H, 2.38; N, 5.62.

#### **5H-[1]benzopyrano[3,2-c]isoquinolin-6-one (7d)**

Yield 72%; mp 229°C; IR: 1720 (C=O)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ ):  $\delta$  7.60-7.98 (m, 4H,  $H_{arom}$ ), 8.05 (d, J = 8 Hz, 1H,  $H_{arom}$ ), 8.41 (d, J = 8 Hz, 1H,  $H_{arom}$ ), 8.50 (d, J = 8 Hz, 1H,  $H_{arom}$ ), 8.75 (d, J = 8 Hz, 1H,  $H_{arom}$ ), 9.18 (s, 1H,  $H_{pyridine}$ );  $^{13}C$  NMR:  $\delta$  121.2 (CH), 121.6 (C), 123.4 (CH), 126.3 (C), 127.5 (CH), 128.7 (CH), 129.4 (C), 129.5 (CH), 130.0 (CH), 131.2 (CH), 135.2 (CH), 136.6 (2 C), 142.7 (C), 148.8 (CH), 160.5 (CO); Anal. Calcd. for  $C_{16}H_9NO_2$ : C, 77.72; H, 3.67; N, 5.66. Found: C, 77.85; H, 3.74; N, 5.61.

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