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Depending on the conditions, and the basicity of the amine, arylamines react with chelidonic acid to yield five different types of product: salts, *N*-arylchelidamic acids, *N*-aryl-4-pyridone-2-carboxylic acids, *N*-aryl-4-pyridones, or chelidamic acid itself.

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Reactions of aryl amines and chelidonic acid **1** have been reported to give, depending on the conditions, *N*-arylchelidamic acids **3** [1-4] or *N*-aryl-4-pyridones **5** [1,4-6], and, in one case, a salt **2** [2b]. We now find that at least two other products can result from such reactions: *N*-aryl-4-pyridone-2-carboxylic acids **4** and chelidamic acid **6** itself.

We treated a variety of aryl amines with chelidonic acid under various conditions and obtained one or other of these five different products as summarized in Table I. Table II gives the characterization of the compounds found and their spectral features are noted in Table III.

#### Salt Formation.

Aniline and *p*-methoxyaniline on heating with chelidonic acid in water followed by evaporation (Procedure A) gave simply the *bis*-anilinium chelidonates **2a** and **2b**, this formulation is supported by combustion analysis (Table II), and ir and <sup>1</sup>H nmr spectra (Table III). The same products were obtained by mixing chelidonic acid and the aromatic amine in a 1:2 ratio in water.

Salt formation of the type just mentioned is restricted to the more basic amines. Thus *o*-nitroaniline under the con-

ditions of Procedure A did not react with chelidonic acid. Lerch [2b] reported that chelidonic acid gave an ammonium salt with ammonia, and "aniline chelidonate" (no mp or analysis) with aniline.

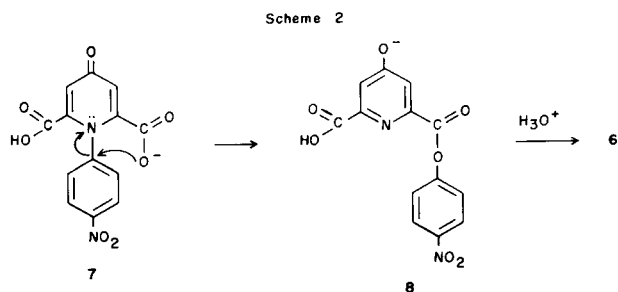
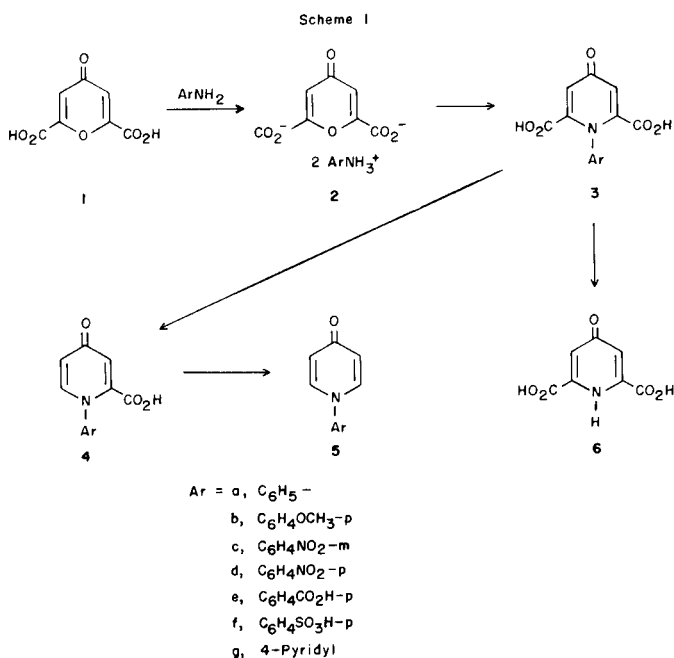
#### *N*-Arylchelidamic Acids.

There have been previous reports of the preparation of *N*-arylchelidamic acids from aryl amines and **1** by direct heating with amine [1,3] (usually such heating gives the pyridone **5**, see below), or by refluxing in water [2a,4].

The more basic amines, aniline and *p*-methoxyaniline, on refluxing with **1** in water followed by evaporation and then further heating (Procedure B) gave **3a** and **3b** respectively.

We found that long reflux with water for less basic amines often caused monocarboxylation (see below). However, that this decarboxylation was avoided by refluxing in aqueous hydrochloric acid instead of water; in this way the *N*-*m*- and *N*-*p*-nitrophenylchelidamic acids [3c,d] were obtained. The *m*-nitro derivative **3c** was also obtained (50%) by nitration of *N*-phenylchelidamic acid **3a**. Chelidamic acids **3e** and **3g** were obtained by heating gently *p*-aminobenzoic acid and 4-aminopyridine, respectively, with chelidonic acid **1**.

Apparently none of the *N*-arylchelidamic acids now prepared have previously been characterized (although *e.g.*, the *N*-phenyl derivative **3a** has been reported [2a] and postulated as an intermediate [1]. They were identified by spectral and elemental analysis: **3a** crystallized as a monohydrate, **3c** and **3e** as dihydrates, **3g** as a 2½ hydrate and **3b** in the anhydrous form. The C-3,5-*H* singlet appeared at 6.6-7.0 ppm, the ν OH at 3000-3400 cm<sup>-1</sup> (broad) and ν C=O at 1740-1700 cm<sup>-1</sup> (Table III).



*N*-Aryl-4-pyridone-2-carboxylic Acids.

*N*-Phenyl-4-pyridone-2-carboxylic acid has been previously prepared by heating aniline with 4-pyridone-2-carboxylic acid [7], but we found no reports of such compounds resulting from amines and chelidonic acid.

In our hands, several of the less basic amines induced monodecarboxylation: on prolonged reflux with **1** in water, *m*-nitro-, *p*-nitro-, and *p*-carboxy-aniline gave **4c,d**, and **4e**, respectively. Sulphanilic acid required heating with **1** to give **4f**.

Combustion analysis showed **4c** and **4d** to be anhydrous but that **4e** and **4f** formed sesquihydrates. The ir and <sup>1</sup>H nmr spectra (Table III) support the structures. In **4c** and **4d** the pyridone ring protons form an ABC pattern of which the 3*H* doublet (*J* = 3 Hz) (at 6.68 and 6.94 ppm respectively) and 5*H* double doublet (*J* = 3 Hz, 8 Hz; at 6.30 and 6.57 ppm) were clearly distinguished. In **4e** and **4f** the ABC pattern of pyridine ring protons overlap with the substituted phenyl ring protons making the spectrum more complex.

Table I  
Reaction of Arylamines with Chelidonic Acid

<i>N</i> -Aryl	No Reaction Proc [a]	Salt <b>2</b>		Chelidamic Acid <b>3</b>			4-Pyridone-2-carboxylic Acid <b>4</b> [b]		4-Pyridone <b>5</b>		Ref
		Decomp Proc [a]	Formation Proc [a]	Proc [a]	Yield %	Ref	Proc [a]	Yield %	Proc [a]	Yield %	
C <sub>6</sub> H <sub>5</sub>		D	B	A,C	65-70	[2a,b]			E,G,H	35-50	[b,1,2]
C <sub>6</sub> H <sub>4</sub> NO <sub>2</sub> - <i>o</i>	A,B,C			C	30	[b]	A	95	G	25	[3]
C <sub>6</sub> H <sub>4</sub> NO <sub>2</sub> - <i>m</i>				C	55	[b]	A	20			
C <sub>6</sub> H <sub>4</sub> NO <sub>2</sub> - <i>p</i>	F	E							G	~40	[6,3]
C <sub>6</sub> H <sub>4</sub> Cl- <i>o,m,p</i>									G	30-40	[1]
C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> - <i>o,m</i>				G	80	[1,4]					
C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> - <i>p</i>		E	B	A	95	[b]					
C <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub> - <i>p</i>									G	20	[3]
C <sub>6</sub> H <sub>4</sub> OC <sub>2</sub> H <sub>5</sub> - <i>p</i>									G	~40	[6]
C <sub>6</sub> H <sub>4</sub> Br- <i>p</i>											
C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> H- <i>p</i>	C	E		B,F	85	[b]	A	95			
C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> - <i>p</i>				A	44	[5]					
C <sub>6</sub> H <sub>4</sub> SO <sub>3</sub> H- <i>p</i>	A,F						B	50			
C <sub>6</sub> H <sub>3</sub> diCH <sub>3</sub> -2,4									G	60	[1]
4-Pyridyl	A,C	F		B	85	[b]					
1-Naphthyl									G	40	[1]

[a] Description of procedures (A-F) used in the present work are given in the experimental. Procedures G (Direct heating of chelidonic acid and aromatic amine) and H (Direct heating of aniline chelidonate) refer to literature work and are from the references quoted. [b] Present work.

Table II  
Products of Reaction of Arylamines with Chelidonic Acid [a]

Product	Procedure	Yield %	Crystal [b] Form	Mp (°C)	Required			Elemental Analysis %			
					C	H	N	Molecular Formula	C	H	N
<b>2a</b>	B	100	P	186 dec	60.2	5.0	7.4	C <sub>19</sub> H <sub>10</sub> N <sub>2</sub> O <sub>6</sub> ·½H <sub>2</sub> O	60.1	4.7	7.1
<b>2b</b>	B	100	R	192 dec	58.6	5.1	6.5	C <sub>21</sub> H <sub>22</sub> N <sub>2</sub> O <sub>8</sub>	58.2	5.2	6.4
<b>3a</b>	A,C	65-70	M	195	56.3	4.0	5.0	C <sub>13</sub> H <sub>9</sub> NO <sub>5</sub> ·H <sub>2</sub> O	56.3	4.0	5.0
<b>3b</b>	A	95	N	212	58.1	3.8	4.8	C <sub>14</sub> H <sub>11</sub> NO <sub>6</sub>	58.1	3.9	4.8
<b>3c</b>	C	30	R	186	45.9	3.5	8.2	C <sub>13</sub> H <sub>9</sub> N <sub>2</sub> O <sub>7</sub> ·2H <sub>2</sub> O	45.3	3.6	8.3
<b>3e</b>	B,F	85	N	200 dec	49.5	3.8	4.1	C <sub>14</sub> H <sub>9</sub> NO <sub>7</sub> ·2H <sub>2</sub> O	49.5	3.9	4.0
<b>3g</b>	B	85	N	234	47.4	4.3	9.2	C <sub>12</sub> H <sub>8</sub> N <sub>2</sub> O <sub>5</sub> ·2½H <sub>2</sub> O	47.6	4.0	9.3
<b>4c</b>	A	95	M	203	55.4	3.1	10.8	C <sub>12</sub> H <sub>8</sub> N <sub>2</sub> O <sub>5</sub>	55.4	3.1	10.7
<b>4d</b>	A	20	N	208	55.4	3.1	10.8	C <sub>12</sub> H <sub>8</sub> N <sub>2</sub> O <sub>5</sub>	55.0	2.9	10.4
<b>4e</b>	A	95	M	210	54.5	4.2	4.9	C <sub>13</sub> H <sub>9</sub> NO <sub>5</sub> ·1½H <sub>2</sub> O	54.3	4.3	4.9
<b>4f</b>	B	50	N	200 dec	44.7	3.7	4.3	C <sub>12</sub> H <sub>9</sub> NO <sub>6</sub> S·1½H <sub>2</sub> O	44.9	3.8	4.3
<b>5a</b>	E	50	N	70-75 [c]	63.8	6.3	6.8	C <sub>11</sub> H <sub>9</sub> NO·2H <sub>2</sub> O	63.4	6.2	6.6
<b>6</b>	C	55	N	278 [d]	41.8	3.5	7.0	C <sub>7</sub> H <sub>5</sub> NO <sub>5</sub> ·H <sub>2</sub> O	41.6	3.5	6.7

[a] Present work only. [b] All recrystallisations have been done in water; P = plates, N = needles, R = rhombs, M = Microcrystals. [c] The lit [1] mp 125°. [d] The lit mp 255-260° [A. P. Sedgwick and N. Collie, *J. Chem. Soc.*, **67**, 403 (1895)].

Table III  
IR and <sup>1</sup>H NMR Spectral Data

Compound No.	IR (cm <sup>-1</sup> ) [a]		<sup>1</sup> H NMR (δ ppm) [b]	
	ν OH, ν OH	ν C=O	Pyridone Ring	Aryl Ring
<b>2a</b>	3200 [c]	1715, 1680	7.00 (2H) s	7.15-7.65 (10H) m
<b>2b</b>	3200	1680	6.98-7.45 (10H) m	3.85 (6H) s [e]
<b>3a</b>	3150-3400 [c]	1720	6.62 (2H) s	7.50 (5H) bs
<b>3b</b>	3400	1735	6.73 (2H) s	7.32 (4H) m (AA'BB' pattern); 3.90 (3H) s
<b>3c</b>	3450 [c]	1700	6.95 (2H) s	8.04 (2H) m; 8.60 (2H) m
<b>3e</b>	3440 [c]	1740	7.10 (2H) s	6.75 (2H) dd; 7.80 (2H) dd [J = 8 Hz and 1 Hz]
<b>3g</b>	3300-3500 [c]	1730	7.02 (2H) s	6.98 (2H) d; 8.23 (2H) d [J = 7 Hz]
<b>4c</b>	3440	1720	6.30 (1H) dd [J = 3 Hz and 8 Hz]; 6.68 (1H) d [J = 3 Hz]	7.84 (3H) m; 8.29 (2H) m [d]
<b>4d</b>	3500	1700	6.57 (1H) dd [J = 3 Hz and 8 Hz]; 6.94 (1H) d [J = 3 Hz]	7.96 (3H) m (d); 8.60 (2H) m
<b>4e</b>	3440 [c]	1700	7.00 (2H) m	7.80 (3H) m; 8.30 (2H) m [d]
<b>4f</b>	3400 [c]	1710	8.70 (1H) d [J = 8 Hz]	7.10-8.20 (6H) m [d]
<b>5a</b>	3500 [c]	1640	6.38 (2H) d; 8.17 (2H) d [J = 9 Hz]	7.70 (5H) s
<b>6</b>	3420-3600 [c]	1710	7.86 (s)	

[a] All ir spectra recorded in bromoform. [b] All <sup>1</sup>H nmr spectra recorded in DMSO-d<sub>6</sub>/deuterium oxide with TMS as internal standard. (The HOD peak was around 4.50 δ ppm). [c] Overlapping water hydroxyl band. [d] One of the pyridone ring proton (C<sub>6</sub>) comes along with the *N*-aryl protons. [e] -OCH<sub>3</sub> protons. Abbreviations are s = singlet, bs = broad singlet, d = doublet, dd = double doublet, m = multiplet.

In the ir spectrum ν OH was found at 3400-3500 cm<sup>-1</sup> and ν C=O at 1700-1720 cm<sup>-1</sup>.

#### *N*-Aryl-4-pyridones.

Many previous syntheses of *N*-aryl-4-pyridones **5** have utilized chelidonic acid **1** and aromatic amines [1-6], but all have involved heating with excess amines at 160-180° or isolation of intermediate chelidamic acids. We now find that **5a** can be obtained by heating aniline and **1** directly in dimethyl sulphoxide.

#### 4-Pyridone-2,6-dicarboxylic Acid.

Refluxing *p*-nitroaniline with **1** in aqueous hydrochloric acid gave 4-pyridone-2,6-dicarboxylic acid **6**, which was identified by melting point, and ir and <sup>1</sup>H nmr spectra. It crystallized as a monohydrate. The formation of **6** from **3d** can be explained by intramolecular nucleophilic displacement of the carboxylate anion **7** to give **8** followed by hydrolysis to **6** (Scheme 2). Although there is no direct evidence for this sequence, analogous rearrangements have been observed in 2-ethoxycarbonyl-1,2'-pyridylpyridinium cations [8].

### EXPERIMENTAL

The <sup>1</sup>H nmr spectra were recorded with a Varian EM 360 L spectrometer using internal TMS as the reference. The ir spectra were obtained in a Perkin-Elmer 283B spectrophotometer. Melting points were recorded on a Bristoline hot-stage microscope and are uncorrected.

The different procedures are given here: the melting point, yield, crystallizing solvent, crystal form and combustion analysis are recorded in Table II and the ir and <sup>1</sup>H nmr spectral data in Table III.

#### Procedure A.

Chelidonic acid (0.20 g, 1 mmole) and the aromatic amine (1 mmole) were refluxed in water (10 ml) for 24 hours. The product was obtained by evaporation at 60°/20 mm Hg, followed by recrystallization.

#### Procedure B.

Chelidonic acid (0.20 g, 1 mmole) and the aromatic amine (1 mmole) were refluxed in water (10 ml) for 24 hours. Solvent was removed at 60°/15 mm Hg and heating at 60° continued for another 30 minutes. The product was then recrystallized.

#### Procedure C.

Chelidonic acid (0.20 g, 1 mmole) and the aromatic amine (1 mmole) were refluxed in 15 *M* aqueous hydrochloric acid (7.5 ml) for 24 hours. Solvent was removed at 60°/20 mm Hg, and the product recrystallized.

#### Procedure D.

Chelidonic acid (0.20 g, 1 mmole) and the aromatic amine (1 mmole) were refluxed in pyridine (10 ml) for 24 hours. The solvent was removed at 60°/20 mm Hg and the product recrystallized.

#### Procedure E.

Chelidonic acid (0.20 g, 1 mmole) and the aromatic amine (1 mmole) were refluxed in dimethyl sulfoxide (10 ml) for 1 hour. The whole was poured into water (50 ml) and the product which separated on cooling was recrystallized.

#### Procedure F.

Chelidonic acid (0.20 g, 1 mmole) and the aromatic amine (1 mmole) were mixed thoroughly and heated at 150° for 1 hour. The residue was recrystallized.

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