Synthesis of Unsymmetrical Bis(imidoyl)dichlorides of Oxalic Acid

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Unsymmetrical oxalic acid-bis(imidoyl)dichlorides were prepared from ethyl 2-chloro-2-oxoacetate in three steps.

Key words: Imidoyl Chlorides, Oxalyl Derivatives, Pigments

Oxalic acid bis(imidoyl)dichlorides have been first reported by Wallach in 1879 [1]. After initial studies of the reactivity of these compounds [2, 3], Beckert and coworkers reported on the synthesis of a great variety of symmetrical, aryl-substituted derivatives based on the work of Wallach [4]. The synthesis of alkyl-substituted bis(imidoyl)dichlorides is problematic, due to their unstable nature. Beckert and our group reported on cyclization reactions of symmetrical bis(imidoyl)dichlorides with a variety of bis(nucleophiles) [5]. Recently, the first examples of unsymmetrical oxalic acid bis(imidoyl)dichlorides have been reported by Beckert [6] and by our group [7]. Herein, we wish to report full details of our approach to unsymmetrical bis(imidoyl)dichlorides based on a three-step synthesis starting with ethyl 2-chloro-2-oxoacetate.

The reaction of ethyl 2-chloro-2-oxoacetate with a number of anilines 1 gave the ethyl 2-oxo-2-(arylamino)acetates 2 (Scheme 1) [8]. The reaction of 2 with a variety of anilines afforded the novel unsymmetrical oxalamides 3a – j (42 – 83%). Reflux of a toluene solution of oxalamides 3 with phosphorus pentachloride (PCl₅) afforded, after recrystallization from n-heptane, the unsymmetrical oxalic acid bis(imidoyl) dichlorides 4a – j (23 – 77%). During the optimization of this transformation, the quality of PCl₅, the reaction time (1 h, reflux), the absence of water and the conditions for recrystallization (n-heptane) proved to play an important role.

Table 1. Products and yields.

<table>
<thead>
<tr>
<th>3a–j</th>
<th>Ar¹</th>
<th>Ar²</th>
<th>% (3a)</th>
<th>% (4a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>C₆H₅</td>
<td>2-(MeO)C₆H₅</td>
<td>78, 70</td>
<td>60</td>
</tr>
<tr>
<td>b</td>
<td>..</td>
<td>4-(MeO)C₆H₅</td>
<td>85, 85</td>
<td>56</td>
</tr>
<tr>
<td>c</td>
<td>..</td>
<td>2,4-Me₂C₆H₃</td>
<td>63</td>
<td>65</td>
</tr>
<tr>
<td>d</td>
<td>..</td>
<td>3,5-Me₂C₆H₃</td>
<td>56</td>
<td>65</td>
</tr>
<tr>
<td>e</td>
<td>..</td>
<td>1-Naphthyl</td>
<td>65</td>
<td>56</td>
</tr>
<tr>
<td>f</td>
<td>4-MeC₆H₄</td>
<td>4-(MeO)C₆H₄</td>
<td>42</td>
<td>59</td>
</tr>
<tr>
<td>g</td>
<td>..</td>
<td>3,5-Me₂C₆H₃</td>
<td>51</td>
<td>77</td>
</tr>
<tr>
<td>h</td>
<td>4-(MeO)C₆H₄</td>
<td>2,4-Me₂C₆H₃</td>
<td>60</td>
<td>65</td>
</tr>
<tr>
<td>i</td>
<td>..</td>
<td>3,5-Me₂C₆H₃</td>
<td>50</td>
<td>57</td>
</tr>
<tr>
<td>j</td>
<td>4-(O₂N)C₆H₄</td>
<td>4-(MeO)C₆H₄</td>
<td>83</td>
<td>23</td>
</tr>
</tbody>
</table>

a Yields of isolated products; b prepared from ethyl 2-oxo-2-(phenylamino)acetate and o-anisidine; c prepared from ethyl 2-oxo-2-(o-methoxyphenyl)acetate and aniline; d prepared from ethyl 2-oxo-2-(phenylamino)acetate and p-anisidine; e prepared from ethyl 2-oxo-2-(p-methoxyphenyl)acetate and aniline.

Scheme 1. Synthesis of unsymmetrical oxalic acid bis(imidoyl)dichlorides 4a – j: i, NEt₃, THF, 0 – 20 °C; ii, toluene, reflux, 6 – 8 h; iii, PCl₅, toluene, reflux, 1 h.

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Experimental Section

General procedure for the synthesis of oxalamides

To a toluene solution (10 ml) of the corresponding amine (10 mmol) was added the ethyl 2-oxo-2-(arylamino)acetate 2 (10 mmol) and the mixture was refluxed for 6–8 h. The product was isolated by filtration and washing with ethanol.

\[ \text{N-}(o\text{-Methoxyphenyl)}\text{)-N'-phenyl-oxalamide (3a)} \]

Starting with ethyl 2-oxo-2-(o-methoxyphenyl)arninoacetate (2.23 g, 10 mmol) and aniline (0.93 g, 10 mmol), 3a (1.90 g, 70%) was isolated as a colourless solid, m. p. 179 °C. Starting with ethyl 2-oxo-2-(phenyl)arninoacetate (1.93 g, 10 mmol) and o-anisidine (1.32 g, 10 mmol), 3a (2.10 g, 78%) was isolated. M. p. 178 °C.

\[ 1\text{H NMR (200 MHz, [D}_6\text{]DMSO):} \delta = 9.67 \text{ (s, 3 H, OCH}_3\text{),} 7.02 – 7.05 \text{ (d, 1 H, Ar),} 7.08 \text{ (s, 1 H, Ar),} 7.13 – 7.18 \text{ (t, 1 H, Ar),} 7.34 – 7.40 \text{ (m, 3 H, Ar),} 7.86 – 7.88 \text{ (d, 2 H, Ar).} \]

\[ 1\text{H NMR (200 MHz, [D}_6\text{]DMSO):} \delta = 2.21 \text{ (s, 3 H, CH}_3\text{),} 2.27 \text{ (s, 3 H, CH}_2\text{),} 7.02 – 7.05 \text{ (d, 1 H, Ar),} 7.08 \text{ (s, 1 H, Ar),} 7.13 – 7.18 \text{ (t, 1 H, Ar),} 7.34 – 7.40 \text{ (m, 3 H, Ar),} 7.86 – 7.88 \text{ (d, 2 H, Ar).} \]

Synthesis of Unsymmetrical Bis(imidoyl)dichlorides of Oxalic Acid 1193

Experimental Section

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Starting with ethyl 2-oxo-2-((p-Methoxyphenyl)-N-((p-Tolyl)-N'-phenyl-oxalamide (3d)

Starting with ethyl 2-oxo-2-(phenylamino)acetate (1.90 g, 10 mmol) and 3,50-xylidine (1.20 g, 10 mmol), 3d (1.50 g, 56%) was isolated as a colourless solid. M. p. 180 °C.

\[ 1\text{H NMR (200 MHz, [D}_6\text{]DMSO):} \delta = 2.50 \text{ (s, 3 H, OCH}_3\text{),} 7.02 – 7.05 \text{ (d, 1 H, Ar),} 7.10 – 7.18 \text{ (t, 1 H, Ar),} 7.34 – 7.40 \text{ (m, 3 H, Ar),} 7.86 – 7.88 \text{ (d, 2 H, Ar).} \]

\[ 1\text{H NMR (200 MHz, [D}_6\text{]DMSO):} \delta = 2.51 \text{ (s, 3 H, OCH}_3\text{),} 7.02 – 7.05 \text{ (d, 1 H, Ar),} 7.10 – 7.18 \text{ (t, 1 H, Ar),} 7.34 – 7.40 \text{ (m, 3 H, Ar),} 7.86 – 7.88 \text{ (d, 2 H, Ar).} \]

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3.75 (s, 3 H, OCH3), 6.93–6.96 (d, 2 H, Ar), 7.16–7.19 (d, 2 H, Ar), 7.73–7.80 (q, 4 H, Ar), 10.71 (s, 2 H, NH). – 13C NMR (50 MHz, [D6]DMSO): δ = 20.44, 55.11, 113.78, 120.29, 121.80, 129.04, 133.58, 135.07, 156.05, 158.12, 158.45. – MS (EI, 70 eV): m/z (%) = 284 ([M]+, 80), 123 (41), 106 (100), 77 (15). – C13H12Cl2N2O2 (282.33): calcld. C 57.16, H 4.12, N 13.32; found C 57.80, H 4.22, N 13.46.

N-(3,5-Dimethylphenyl)-N'-(p-tolylo)-oxalamide (3g)

Starting with ethyl 2-oxo-2-(p-tolylo)acetate (2.00 g, 10 mmol) and 3,5-xylene (1.20 g, 10 mmol), 3g (1.45 g, 51%) was isolated as a colourless solid. M. p. 193 °C. – IR (KBr): ν = 807 (m), 1184 (m), 1246 (s), 1523 (s), 1662 (s), 3299 (s) cm−1. – 1H NMR (200 MHz, [D6]DMSO): δ = 2.15 (s, 3 H, OCH3), 2.27 (s, 3 H, CH3), 3.75 (s, 3 H, OCH3), 6.91–7.25 (m, 3 H, Ar), 7.35–7.38 (d, 1 H, Ar), 7.50–7.60 (d, 2 H, Ar), 7.77–7.82 (d, 2 H, Ar), 10.20 (s, 1 H, NH), 10.75 (s, 1 H, NH). – 13C NMR (50 MHz, [D6]DMSO): δ = 17.45, 20.44, 55.11, 113.77, 121.86, 124.64, 126.61, 128.12, 128.82, 130.43, 130.63, 132.00, 132.44, 135.27, 156.08, 158.07, 158.58, 167.8. – MS (EI, 70 eV): m/z (%) = 284 ([M]+, 100), 148 (37), 123 (91), 77 (25), 28 (43). – C13H12Cl2N2O2 (282.33): calcld. C 56.87, H 0.63, N 3.99; found C 56.73, H 0.57, N 8.91.

N-(3,5-Dimethylphenyl)-N'-(p-nitrophenyl)-oxalamide (3i)

Starting with ethyl 2-oxo-2-(p-nitrophenyl)acetate (2.38 g, 10 mmol) and p-anisidine (1.23 g, 10 mmol), 3i (2.68 g, 83%) was isolated as a colourless solid. M. p. 174–175 °C. – IR (KBr): ν = 744 (w), 832 (w), 1243 (m), 1340 (s), 1410 (m), 1526 (s), 1603 (m), 1675 (s), 2935 (s) cm−1. – 1H NMR (200 MHz, [D6]DMSO): δ = 3.75 (s, 3 H, OCH3), 6.92–6.98 (d, 2 H, Ar), 7.73–7.80 (d, 2 H, Ar), 8.12–8.32 (q, 4 H, Ar), 10.77 (s, 1 H, NH). – 13C NMR (50 MHz, [D6]DMSO): δ = 56.65, 113.89, 120.39, 121.99, 124.75, 139.59, 143.86, 156.18, 157.45, 159.59. – MS (EI, 70 eV): m/z (%) = 315 ([M]+, 100), 300 (50), 149 (90), 108 (45). – C15H13N3O5 (315.27): calcld. C 57.60, H 4.22, N 13.32; found C 57.80, H 4.22, N 13.23.

General procedure for the synthesis of oxalimidoyl dichlorides

A toluene solution (60 ml) of oxamide 3 (10 mmol) and PCl5 (20 mmol) was refluxed for 1 h under exclusion of moisture. The solution was concentrated (30 ml) in vacuo to give a precipitate upon standing at −20 °C. The solid was filtered off and recrystallized (n-heptane).

N-(p-Methoxyphenyl)-N'-phenyl-oxalimidoyl dichloride (4b)

Starting with 3b (2.70 g, 10 mmol) and PCl5 (4.16 g, 20 mmol), 4b (1.70 g, 56%) was isolated as a yellow solid. M. p. 203 °C. – IR (KBr): ν = 751 (w), 831 (w), 1030 (w), 1250 (s), 1445 (m), 1528 (s), 1662 (s), 2399 (s), 3414 (w) cm−1. – 1H NMR (200 MHz, CDCl3): δ = 3.80 (s, 3 H, OCH3), 6.94–6.97 (d, 2 H, Ar), 7.05–7.09 (d, 1 H, Ar), 7.21–7.68 (m, 6 H, Ar). – 13C NMR (50 MHz, CDCl3): δ = 55.35, 114.01, 114.04, 120.21, 123.69, 123.96, 126.29, 128.86, 129.12, 137.67, 137.99, 158.71, 158.94. – MS (EI, 70 eV): m/z (%) = 307 ([M]+, 45) 271 (14), 168 (100), 138 (64), 77 (86), 28 (24). – C9H7Cl2N2O2 (307.16): calcld. C 58.67, H 3.90, N 9.11; found C 58.70, H 4.02, N 8.97.

N-(2,4-Dimethylphenyl)-N'-phenyl-oxalimidoyl dichloride (4c)

Starting with 3c (2.68 g, 10 mmol) and PCl5 (4.16 g, 20 mmol), 4c (2.0 g, 65%) was isolated as a yellow solid.
Starting with 3d (2.60 g, 10 mmol) and PCl₅ (4.16 g, 20 mmol), 4d was isolated as a yellow solid. - 1H NMR (200 MHz, CDCl₃): δ = 2.31 (s, 6 H, 2 × CH₃), 6.71 (s, 2 H, Ar), 6.86 (s, 1 H, Ar), 7.06-7.10 (d, 2 H, Ar), 7.19-7.24 (s, 1 H, Ar), 7.36-7.42 (t, 1 H, Ar), 7.50-7.64 (m, 4 H, Ar) - 13C NMR (50 MHz, CDCl₃): δ = 21.17, 22.56, 117.74, 119.58, 120.21, 126.48, 128.04, 128.83, 129.02, 138.55, 145.53, 145.63, C₁₆H₁₄Cl₂N₂.

N-(1-Naphthyl)-N'-phenyl-oxaldiimidoyl dichloride (4e)

Starting with 3e (2.90 g, 10 mmol) and PCl₅ (4.16 g, 20 mmol), 4e was isolated as a yellow solid. - IR (KBr): ν = 492 (w), 793 (m), 1445 (s), 1501 (s), 1526 (s), 1682 (s), 3268 (s). - 1H NMR (200 MHz, CDCl₃): δ = 7.15-7.17 (d, 1 H, Ar), 7.22-7.33 (m, 3 H, Ar), 7.43-7.45 (d, 1 H, Ar), 7.48-7.62 (m, 4 H, Ar), 7.76-7.78 (d, 1 H, Ar), 7.81-7.89 (m, 1 H, Ar), 7.96-8.05 (m, 1 H, Ar). - 13C NMR (50 MHz, CDCl₃): δ = 115.03, 115.16, 120.34, 120.46, 123.25, 123.32, 125.27, 126.47, 126.66, 127.05, 127.97, 129.00, 133.91, 133.94, 138.64, 138.97, 141.77, 145.72 - C₁₆H₁₄Cl₂N₂ (327.19): calc. C 66.09, H 3.66, found: C 65.52, H 3.83, N 4.89.

N-(3,5-Dimethylphenyl)-N'-phenyl-oxaldiimidoyl dichloride (4f)

Starting with 3f (2.85 g, 10 mmol) and PCl₅ (4.16 g, 20 mmol), 4f was isolated as a yellow solid. - IR (KBr): ν = 793 (m), 1445 (s), 1501 (s), 1526 (s), 1682 (s), 3268 (s). - 1H NMR (200 MHz, CDCl₃): δ = 2.38 (s, 3 H, CH₃), 3.84 (s, 3 H, OCH₃), 6.95-7.07 (m, 4 H, Ar), 7.22-7.31 (m, 4 H, Ar). - 13C NMR (50 MHz, CDCl₃): δ = 21.11, 55.44, 114.09, 127.70, 120.82, 123.73, 123.85, 129.50, 129.74, 136.59, 137.92, 138.11, 143.19, 158.77, 158.89 - MS (EI, 70 eV): m/z (%) = 321 ([M⁺]², 42), 285 (16), 168 (98), 151 (100), 91 (71). - C₁₈H₁₈Cl₂N₂O (321.19): calc. C 59.85, H 4.36, N 8.72; found: C 59.21, H 4.61, N 8.60.

N-(3,5-Dimethylphenyl)-N'-tolyloxaldiimidoyl dichloride (4g)

Starting with 3g (10 mmol) and PCl₅ (4.16 g, 20 mmol), 4g was isolated as a yellow solid. - 1H NMR (200 MHz, CDCl₃): δ = 2.42 (s, 3 H, CH₃), 2.44 (s, 3 H, CH₃), 2.48 (s, 3 H, CH₃), 6.82 (s, 2 H, Ar), 6.96 (s, 1 H, Ar), 7.16-7.19 (d, 2 H, Ar), 7.29-7.32 (d, 2 H, Ar). - 13C NMR (50 MHz, CDCl₃): δ = 20.91, 21.12, 22.53, 117.68, 119.98, 120.77, 127.95, 129.34, 129.41, 136.58, 136.81, 137.83, 138.46, 142.75, 145.59, C₁₇H₁₆Cl₂N₂.

N-(2,4-Dimethylphenyl)-N'-ethyl-oxaldiimidoyl dichloride (4h)

Starting with 3h (2.90 g, 10 mmol) and PCl₅ (4.16 g, 20 mmol), 4h was isolated as a yellow solid. - IR (KBr): ν = 303 (s), 1032 (m), 1249 (s), 1523 (s), 1597 (m), 1665 (s), 3302 (s). - 1H NMR (200 MHz, CDCl₃): δ = 2.05 (s, 3 H, CH₃), 2.33 (s, 3 H, CH₃), 3.83 (s, 3 H, OCH₃), 6.90-7.08 (m, 5 H, Ar), 7.23-7.33 (d, 2 H, Ar). - 13C NMR (50 MHz, CDCl₃): δ = 17.79, 20.98, 55.41, 114.06, 118.61, 123.92, 126.70, 129.41, 131.18, 136.25, 137.83, 137.95, 138.07, 142.28, 158.75, 158.89 - MS (EI, 70 eV): m/z (%) = 335 [M⁺], 59, 300 (41), 168 (1009, 77 (81), 28 (89). - C₁₇H₁₆Cl₂N₂ (335.22): calc. C 59.60, H 4.79, N 8.35; found C 59.60, H 4.79, N 8.38.

N-(3,5-Dimethylphenyl)-N'-methyl-oxaldiimidoyl dichloride (4i)

Starting with 3i (2.90 g, 10 mmol) and PCl₅ (4.16 g, 20 mmol), 4i was isolated as a yellow solid. - IR (KBr): ν = 793 (m), 1445 (s), 1501 (s), 1526 (s), 1682 (s), 3268 (s). - 1H NMR (200 MHz, CDCl₃): δ = 2.32-2.34 (s, 6 H, 2 × CH₃), 3.84 (s, 3 H, OCH₃), 6.70 (s, 2 H, Ar), 6.95 (s, 1 H, Ar), 6.97-6.98 (d, 2 H, Ar), 7.29-7.30 (d, 2 H, Ar). - 13C NMR (50 MHz, CDCl₃): δ = 20.81, 21.30, 55.43, 114.08, 117.74, 120.19, 124.03, 127.98, 128.53, 138.66, 138.66, 145.92, 158.91 - MS (EI, 70 eV): m/z (%) = 335 [M⁺], 25, 299 (15), 168 (100), 77 (81). - C₁₇H₁₆Cl₂N₂O (335.22): calc. C 59.60, H 4.77, N 8.35; found C 59.60, H 4.44, N 8.01.

N-(3,5-Dimethylphenyl)-N'-methyl-oxaldiimidoyl dichloride (4j)

Starting with 3j (3.15 g, 10 mmol) and PCl₅ (4.18 g, 20 mmol), 4j was isolated as a yellow solid. - IR (KBr): ν = 778 (m), 860 (m), 1110 (w), 1251 (s), 1345 (s), 1505 (s), 1665 (s). - 1H NMR (200 MHz, CDCl₃): δ = 3.85 (s, 3 H, OCH₃), 6.98-7.00 (d, 2 H, Ar), 7.12-7.14 (d, 2 H, Ar), 7.39-7.40 (d, 2 H, Ar), 8.33-8.34 (d, 2 H, Ar). - 13C NMR (50 MHz,
CDCl$_3$: $\delta = 55.45, 114.02, 114.15, 120.17, 123.66, 124.68, 124.92, 125.54, 137.06, 142.53, 145.44, 151.74, 159.56.$


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