

Oxidative Decarboxylation of 4-Arylmethylidene-5(4H)-oxazolones Using Cerium(IV) Ammonium Nitrate

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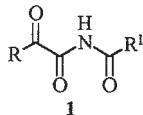
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Oxidative decarboxylation of azlactones by cerium(IV) ammonium nitrate yields 2-arylglyoxylamide in very good yields.

The chemistry of 4-arylmethylidene-5(4H)-oxazolones is of immense interest because of diverse products obtained up to heterocyclic ring cleavage.¹⁻⁷ Apart from the typical reactivity of heterocyclic ring the exocyclic double bond reacts with different reagents.

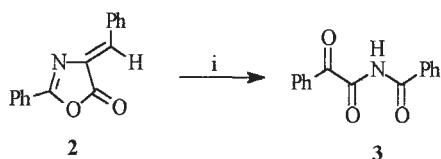
In continuation of our studies on the chemistry of azlactones,⁸⁻¹¹ the reaction of cerium(IV) ammonium nitrate has been investigated. When 4-arylmethylidene-5(4H)-oxazolones were treated with cerium(IV) ammonium nitrate the oxazolone ring was cleaved to furnish *N*-acyl-2-arylglyoxylamide (**1**).



However, the oxidative cleavages of azlactones are scarcely reported in literature. Bisson et al. reported that in the presence of mild base, azlactones rapidly absorb oxygen to afford amides with the loss of CO₂.¹² Bates et al. reported that the oxidative cleavage of saturated analogues of azlactones in the presence of oxygen over Pd/C resulted in the formation of amides.¹³ Both the methods proceeded via peroxide formation.

We reported herein the new synthesis of α -oxocarboxamides by oxidative cleavage of azlactones using CAN. To our knowledge this result is the first observation of oxidative decarboxylation of 4-methylidene-5(4H)-oxazolones affording α -oxocarboxamides. Moreover, the resulting 2-arylglyoxylamides are potentially valuable synthetic building blocks in the preparation of various heterocyclic ring systems of biological interest.¹⁴⁻¹⁹

Treatment of oxazolone **2** with CAN (CH₃CN/H₂O, 5 : 1) at ambient temperature afforded *N*-benzoyl-2-phenyl-glyoxylamide **3** in 70% yield (Scheme 1) after chromatographic purification. The structure of product **3** was established by ¹H NMR and Mass spectral data. To our knowledge this type of oxidative decarboxylation of 4-methylidene-5(4H)-oxazolones is hitherto unreported. Incidentally formation of this compound **3** was described earlier by the oxidation of 2,5-diphenyloxazole²⁰ and in the photodissociation of peroxy pyrazin-2(1*H*)-one



Scheme 1.

derivatives.²¹

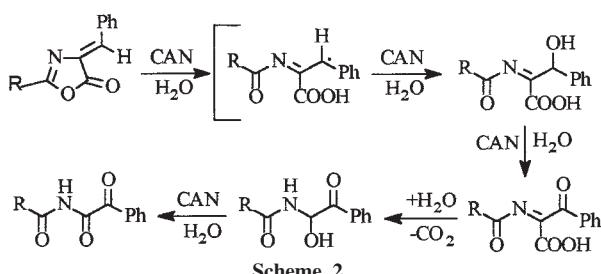
Reagents and conditions: (i) CAN (4 mol amt.), CH₃CN/H₂O (5 : 1), R.T. 6 h.

The generality of this reaction is shown in the table giving different *N*-aryl-2-acylglyoxylamides (Table, entries 1 to 8).²¹ Substitution on the benzylidene ring appears to have no influence

Table 1. *N*-Acyl-2-arylglyoxylamide

Entry	Substrate	Product	Mp / °C	Yield / %
1)			138	70
2)			152	66
3)			115	72
4)			162	75
5)			160	69
6)			121	68
7)			140	50
8)			186	65

on oxidation. Replacement of 4-benzylidene group by furfurylidene (entry 8) and that of 2-phenyl group by methyl (entry 3) did not alter the reaction and gave the glyoxylamide in good yields. The 4-arylmethylene or heteroaryl methylene group is important from the mechanistic view point. The formation of 2-phenyl-glyoxylamide may be visualized as the initial formation of 3-hydroxy-2-iminodihydrocinnamic acid intermediate which can be oxidized to a 2-imino-3-oxodihydrocinnamic acid that can eventually be converted to the product through decarboxylation and subsequent oxidation (Scheme 2). In summary, cerium(IV) ammonium nitrate effected an oxidative decarboxylation of azlactones to give arylglyoxalamide. This method is inexpensive and quite easy to conduct and readily provides access to potential structural building blocks for biologically important molecules.



¹H and ¹³C NMR spectra were recorded on a Varian FT 200 MHz (Gemini) spectrometer in CDCl₃/DMSO-d₆ with TMS as internal standard. FABMS spectra were obtained on a VG AUTOSPEC M Mass spectrometer. IR spectra were obtained on a Perkin-Elmer 1310 spectrophotometer. Elemental analyses were made by using a VARIO-EL ELEMENTAR (Germany). The oxazolones were prepared by Erlenmeyer's azlactone synthesis.²²

Typical experimental procedure is as follows: To a solution of oxazolone **2** (1 mmol) in acetonitrile and water (20 ml, 5 : 1) at room temperature was added cerium(IV) ammonium nitrate (4 molar amounts) and the reaction mixture was stirred until the complete consumption of the starting material had occurred (monitored by TLC). Acetonitrile was removed under reduced pressure. The reaction mixture was neutralized with aqueous NaHCO₃ and extracted with dichloromethane. The organic layer was dried (MgSO₄) and the solvent was removed in vacuum to afford crude solid **3**, which was purified by column chromatography (silica gel, hexane-ethylacetate, 9 : 1) in isolated yield of 70%.

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- 22 *N*-Benzoyl-2-phenyl-2-glyoxylamide-(Entry 1): mp 138 °C (lit., 145 °C); IR (KBr): ν 3264, 1712, 1680, 1472, 1328 and 1200 cm⁻¹; ¹H NMR (CDCl₃ + DMSO-d₆): δ 7.40–7.65 (m, 6H), 7.85 (d, 2H), 9.0–9.05 (d, 2H), 12.20 (br, NH, D₂O exchangeable); ¹³C NMR (CDCl₃): δ 128.5, 128.89, 129.06, 130.01, 130.92, 132.39, 133.95, 134.61, 165.43, 166.5 and 176.67; MS *m/z* (%): 148 (20), 105 (100), 77 (80), 51 (40), FABMS *m/z* (%): 254 [(M + 1)⁺, (4)], 105 (100). Anal. Calcd for C₁₅H₁₁NO₃: C, 71.15; H, 4.35; N, 5.53%. Found: C, 71.09; H, 4.28; N, 5.49%. (Entry 2): mp 152 °C; IR (KBr): ν 3280, 2432, 1712, 1664, 1456, 1312, 1216 and 640 cm⁻¹; ¹H NMR (CDCl₃ + DMSO-d₆): δ 2.40 (s, 3H), 7.25–7.35 (d, 2H), 7.40–7.70 (m, 3H), 7.80–7.90 (d, 2H), 8.0–8.10 (d, 2H), 11.90 (br, NH, D₂O exchangeable); ¹³C NMR (CDCl₃): δ 21.70, 128.07, 128.38, 128.66, 129.04, 129.81, 130.26, 133.12, 144.49, 166.59, 170.54, 186.76; FABMS *m/z* (%): 268 [(M + 1)⁺, 100], 119 (70), 105 (65). Anal. Calcd for C₁₆H₁₃NO₃: C, 71.90; H, 4.87; N, 5.24%. Found: C, 71.86; H, 4.82; N, 5.21%. Entry 3: mp 115 °C; IR (KBr): ν 3120, 2896, 1712, 1504, 1344, 1200 and 720 cm⁻¹; ¹H NMR (CDCl₃ + DMSO-d₆): δ 2.55 (s, 3H), 7.50–7.60 (t, 2H), 7.65–7.70 (d, 1H), 8.30–8.35 (d, 2H), 9.25–9.35 (br, NH, D₂O exchangeable); FABMS *m/z* (%): 192 [(M + 1)⁺, (59)], 150 (32), 105 (100). Anal. Calcd for C₁₀H₉NO₃: C, 62.83; H, 4.71; N, 7.33%. Found: C, 62.79; H, 4.68; N, 7.31%. Entry 4: mp 162 °C; IR (KBr): ν 3280, 1712, 1696, 1664, 1472, 1328, 1232 and 769 cm⁻¹; ¹H NMR (CDCl₃ + DMSO-d₆): δ 6.95–7.65 (m, 12H), 8.0–8.10 (d, 2H), 12.10–12.15 (br, NH, D₂O exchangeable); MS *m/z* (%): 345 [(M⁺, 20)], 240 (5), 196 (100), 169 (10), 141 (24), 105 (60), 77 (50). Anal. Calcd for C₂₁H₁₅NO₃: C, 73.04; H, 4.35; N, 4.06%. Found: C, 73.01; H, 4.38; N, 4.03%. Entry 5: mp 160 °C; IR (KBr): ν 3264, 1712, 1680, 1584, 1456, 1344, 1200 and 704 cm⁻¹; ¹H NMR (CDCl₃ + DMSO-d₆): δ 7.40–7.70 (m, 5H), 7.80–8.00 (d, 2H), 9.0–9.20 (d, 2H), 12.02 (br, NH, D₂O exchangeable); MS *m/z* (%): 287 [(M⁺, 2)], 244 (15), 182 (7), 139 (100), 105 (70), 77 (40). Anal. Calcd for C₁₅H₁₀ClNO₃: C, 62.72; H, 3.48; N, 4.88%. Found: C, 62.38; H, 3.29; N, 4.82%. Entry 6: mp 121 °C; IR (KBr): ν 1612, 1580, 1440, 1296, 944 and 720 cm⁻¹; ¹H NMR (CDCl₃ + DMSO-d₆): δ 3.9 (s, 3H), 6.70–7.05 (m, 3H), 7.40–7.60 (m, 2H), 7.90–8.10 (m, 2H), 8.10–8.20 (d, 2H); MS *m/z* (%): 283 [(M⁺, 10)], 136 (20), 121 (100), 105 (65), 77 (70). Anal. Calcd for C₁₆H₁₃NO₄: C, 67.83; H, 4.59; N, 4.95%. Found: C, 67.65; H, 4.33; N, 4.91%. Entry 7: mp 140 °C; IR (KBr): ν 3040, 2944, 1712, 1632, 1472, 960, 768, 672 and 560 cm⁻¹; ¹H NMR (CDCl₃ + DMSO-d₆): δ 3.15 (s, 6H), 6.90–7.00 (d, 1H), 7.50–8.75 (m, 6H), 9.90 (br, NH, D₂O exchangeable); MS *m/z* (%): 296 (5), 105 (100). Anal. Calcd for C₁₇H₁₆N₂O₃: C, 68.92; H, 5.41; N, 9.46%. Found: C, 68.69; H, 5.39; N, 9.42%. Entry 8: mp 186 °C; IR (KBr): ν 3456, 3296, 1712, 1664, 1536, 1472, 1344, 1248 and 704 cm⁻¹; ¹H NMR (CDCl₃ + DMSO-d₆): δ 6.30 (d, 1H), 6.40 (d, 1H), 7.2–7.6 (m, 4H), 7.70 (d, 2H), 8.60 (br, NH, D₂O exchangeable). MS *m/z* (%): 243 [(M⁺, 10)], 121 (80), 105 (100), 77 (90). Anal. Calcd for C₁₃H₉NO₄: C, 64.20; H, 3.70; N, 5.76%. Found: C, 64.23; H, 3.62; N, 5.59%.
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