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Cerium(IV) Mediated Oxygenation of Dialkyl Malonates: A Novel Synthesis of Tartronic Acid Derivatives.

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Abstract: A novel Cerium(IV) mediated oxygenation of dialkyl malonates leading to a direct synthesis of tartronic acid derivatives is described. © 1998 Elsevier Science Ltd. All rights reserved.

Carbon-carbon bond formation involving radicals generated by Cerium(IV) ammonium nitrate (CAN) has been the subject of a number of investigations recently.¹ Our own studies have shown that in intermolecular carbon-carbon bond forming reactions CAN offers a number of advantages over the more commonly used Mn(III)acetate.^{2,3} As a logical extension of this work, it was decided to investigate the use of CAN in intramolecular reactions.⁴ In an initial experiment, cinnamyl methyl malonate 1 on treatment with CAN in methanol afforded a product which was characterized as the hydroxylated product 2 and not the expected lactone (Scheme 1).⁵



The product 2 was purified by chromatography on silica gel column using hexane-ethylacetate as eluent and was characterized by spectroscopic and analytical methods.⁶ The IR spectrum of 2 showed the hydroxyl group absorption at 3432 cm⁻¹. The ¹³C NMR spectrum displayed a signal at δ 90.7 characteristic for a methine bearing the –OH group. In order to probe the generality of the reaction, the investigation was extended to a number of substrates and the results are summarized in Table 1. In all cases the oxygenated product was obtained in fair to good yield.

| Entry | Ester | Time | Product | Yield(%)* |
|-------|-------------------|---------------|-------------------------|-----------|
| 1 | Ph Ph 7 | 4hr | O O OH Ph Ph 8 | 60 |
| 2 | O O Ph 9 | 6hr | O O O Ph OH 10 | 62 |
| 3 | | 0.5 hr | O O O N OH 12 | 69 |
| 4 | OMe 13 | 3hr | O O OH OH 14 | 23 |
| 5 | OMe 0 15 | 3hr | O O OH 16 | 25 |

Table 1. Hydroxylation of β -keto esters with CAN

*Isolated yield. Reaction Conditions : 2.3 equivalents CAN, MeOH, O °C - RT.

In the light of the recent elucidation of the mechanism of oxidation of malonic acid by Cerium(IV),⁷ the oxygenation observed may be rationalized as follows (Scheme 2). The proposed mechanism invokes the formation of the peroxy intermediate 4 derived from the reaction of atmospheric oxygen with the malonyl radical.⁸



In conclusion, we have encountered a facile oxygenation of malonates which offers a novel synthetic route to tartronic acid derivatives.

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- 5. Typical experimental procedure: The ester 1 (2.5 mmol) was dissolved in methanol (30 mL) at 0 °C and treated with CAN (5.75 mmol) in methanol (40 mL). The reaction mixture was gradually brought to room temperature and stirred for 6 h. It was then diluted with water (100 mL) and extracted with dichloromethane(4 x 20 mL). The solvent was evaporated and purified by column chromatography (10% ethyl acetate in hexane as eluent) to afford 2.
- 6. Spectral Data for 2 : IR (neat) v_{max} : 3432, 2962, 1760, 1739, 1450 cm⁻¹. ¹H NMR(CDCl₃): δ 7.55-7.25 (m, 5H, ArH), 6.81-6.10 (m, 2H, olefinic), 5.12-4.50 (m, 4H), 3.86 (s, 3H, -COOCH₃). ¹³C NMR (CDCl₃) : δ 168.5, 167.9, 135.6, 128.4, 128.1, 126.5, 121.3, 90.7, 67.3, 53.6. GCMS, *m/z* : 248 (M⁺-2, 5), 192 (2), 175(3), 161(6), 117(100). For **8:** IR (neat) v_{max} : 3461, 2962, 1748, 1458 cm⁻¹. ¹H NMR (CDCl₃): δ 7.35-7.23 (m, 10H, ArH), 5.29-5.10 (m, 4H), 4.82 (brs, 2H). ¹³C NMR(CDCl₃): δ 168.10, 134.10, 128.67, 128.61, 128.27, 90.30, 68.90, 68.40, 66.40, 53.89. Analysis calculated for C₁₇H₁₆O₅: C, 67.99%; H, 5.37%. Found: C, 68.20%; H, 5.48%.
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