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LETTERS

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.**

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]

Scheme 1

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 ^{13}C NMR spectrum displayed a signal at δ 90.7 characteristic for a methine bearing the –OH group.

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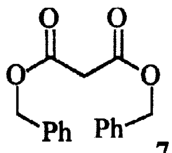
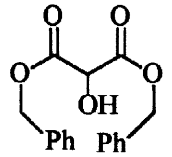
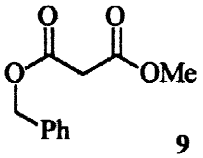
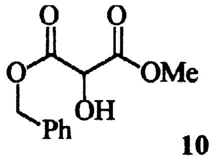
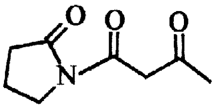
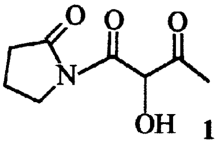
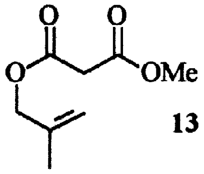
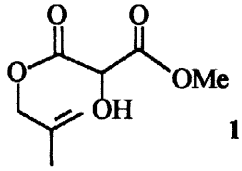
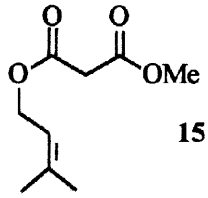
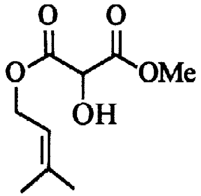
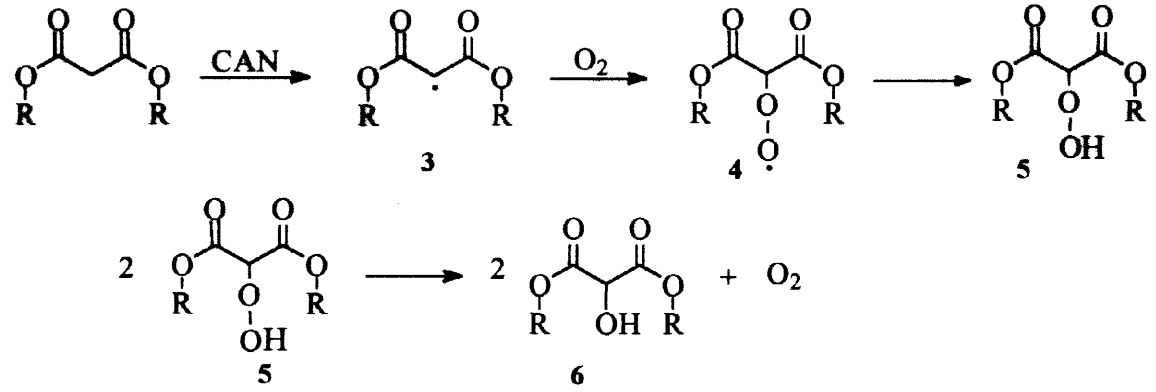
In order to probe the generality of the reaction, the investigation was extended to a number of substrates and the results are summarized in Table 1. In all cases the oxygenated product was obtained in fair to good yield.

Table 1. Hydroxylation of β-keto esters with CAN

Entry	Ester	Time	Product	Yield(%)*
1	 7	4hr	 8	60
2	 9	6hr	 10	62
3	 11	0.5hr	 12	69
4	 13	3hr	 14	23
5	 15	3hr	 16	25

*Isolated yield.
Reaction Conditions : 2.3 equivalents CAN, MeOH, 0 °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]



Scheme 2

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

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References and notes

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3. Nair, V.; Mathew, J.; Prabhakaran J. *Chem. Soc. Rev.;* **1997**, 127 and references sited therein.
4. Except for two isolated reports, there has been no information on the use of CAN in intramolecular reactions.
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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) ν_{max} : 3432, 2962, 1760, 1739, 1450 cm^{-1}. ^{1}H NMR($CDCl_3$): 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, -$COOCH_3$). ^{13}C NMR ($CDCl_3$) : 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) ν_{max}: 3461, 2962, 1748, 1458 cm^{-1}.

   ^{1}H NMR ($CDCl_3$): δ 7.35-7.23 (m, 10H, ArH), 5.29-5.10 (m, 4H), 4.82 (brs, 2H). ^{13}C NMR($CDCl_3$): δ 168.10, 134.10, 128.67, 128.61, 128.27, 90.30, 68.90, 68.40, 66.40, 53.89. Analysis calculated for $C_{17}H_{16}O_5$: C , 67.99%; H , 5.37%. Found: C , 68.20%; H , 5.48%.

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8. A similar Mn(III) induced reaction of α-allyl β-keto esters with molecular oxygen has been reported: Ohshima, T.;Sodeoka, M.; Shibasaki, M. *Tetrahedron. Lett.*, **1993**, *52*, 8509.