

Cerium(IV) ammonium nitrate mediated addition of dimethyl malonate to styrene: a remarkable reaction

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Cerium(IV) ammonium nitrate mediated addition of dimethyl malonate to styrene afforded the products **3** and **4** (via **7**) along with very small amounts of **5** and **6**.

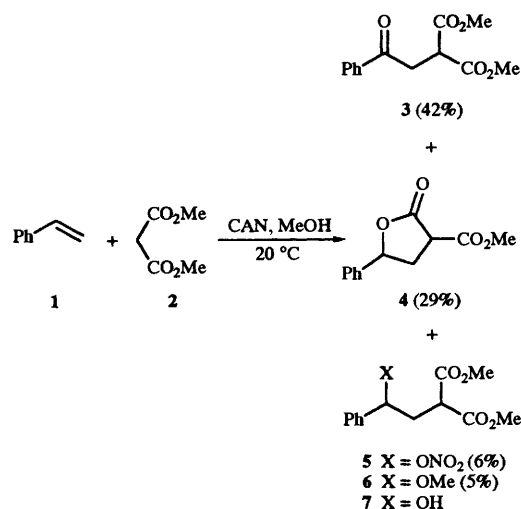
Oxidative generation¹ of carbon-centred radicals mediated by metal salts (Mn^{III}, Co^{II}, Cu^{II}, Ag^I, V^V and Ce^{IV}) is well established and in this connection recently we have shown² that cerium(IV) ammonium nitrate (CAN) is superior to Mn(OAc)₃ for the oxidative addition of 1,3-dicarbonyl compounds to unactivated alkenes. In the course of this work we were intrigued by a report³ claiming that the reaction of styrene with dimethyl malonate promoted by CAN afforded exclusively the nitrate **5** and the methyl ether **6**.[†] We have obtained results that are significantly different and these are presented here.

A solution of CAN in methanol was treated with a mixture of styrene and dimethyl malonate as reported and the reaction mixture was processed.³ HPLC and ¹H NMR analysis of the crude product revealed that it contained mainly compounds **3** and **7** and only traces of **5** and **6**. Chromatography on silica gel column afforded **3** (42%), **4** (29%, evidently formed by the lactonization[‡] of **7**), **5** (6%) and **6** (5%) (Scheme 1).

A tentative mechanism which will rationalize the results can be presented as follows: the addition of malonyl radical **8**, generated by Ce^{IV}, to styrene would give the benzylic radical **9** which is then trapped by NO₃⁻ to form the unstable radical anion **10**. The oxidative fragmentation of **10** would lead to the ketone **3**. The direct fragmentation of **10**, followed by protonation of the resulting alkoxide **11** would give the carbinol **7**, the precursor for the lactone **4**. The mechanism for the formation of nitrate **5** can involve either the oxidation of **10** or the trapping of the benzylic cation **12**, resulting from the Ce^{IV} oxidation of the radical **9**, by NO₃⁻. Similarly, **12** can be trapped by methanol to afford **6**. The formation of **6** by the solvolysis of **5** is less likely since the only product isolated in the attempted methanolysis of **5** was the lactone **4**. Although benzylic alcohols are known⁵ to undergo oxidation to ketones by Ce^{IV}, such a pathway may not be operative in the formation of **3**, as our attempts to convert the carbinol **7** into **3** by CAN have not been successful. Also, in all likelihood, the ketone **3** is not derived from **6** since attempted oxidation of **6** failed to afford **3**. The mechanistic rationale described above is illustrated in Scheme 2.

While there is no direct precedent for the mechanistic rationalization presented here it may be pointed out that the addition of nitrate to the benzylic radical produced during the CAN mediated reaction of azide with styrene is documented.⁶

Although reasonable, the mechanistic interpretations given in



Scheme 1

Scheme 2 are largely speculative and it is important to recognize that other pathways leading to the products can be invoked. For instance, the formation of **7** by the hydrolysis of **6** is a possibility and the formation of **3** from **7** by the oxidation of the latter by NO₂ or some other oxidising species derived from CAN cannot be ruled out.[¶]

We have conducted the experiment numerous times precisely under the conditions reported³ by Baciocchi *et al.* and found that our results are consistently reproducible.^{||} It is also noteworthy that the use of a large excess of styrene as reported³ is unnecessary for the completion of the reaction. For instance, when the experiment was repeated under the conditions we have described² for the addition of 1,3-dicarbonyl compounds to alkenes (dimethylmalonate : styrene: CAN, 1 : 1.2 : 2.3), the yields and the product composition were virtually unchanged.

Our preliminary results with ring substituted styrenes indicate that the reaction is general. In conclusion, we have uncovered an interesting CAN mediated reaction of dimethyl malonate to styrene which, apart from its mechanistic implication, may be potentially useful in organic synthesis. Further work is in progress.

Experimental

A solution of CAN (4.98 g, 9.1 mmol) in methanol was allowed to react with a mixture of styrene (2.08 g, 20 mmol) and dimethyl malonate (0.594 g, 4.5 mmol) as reported.³ The

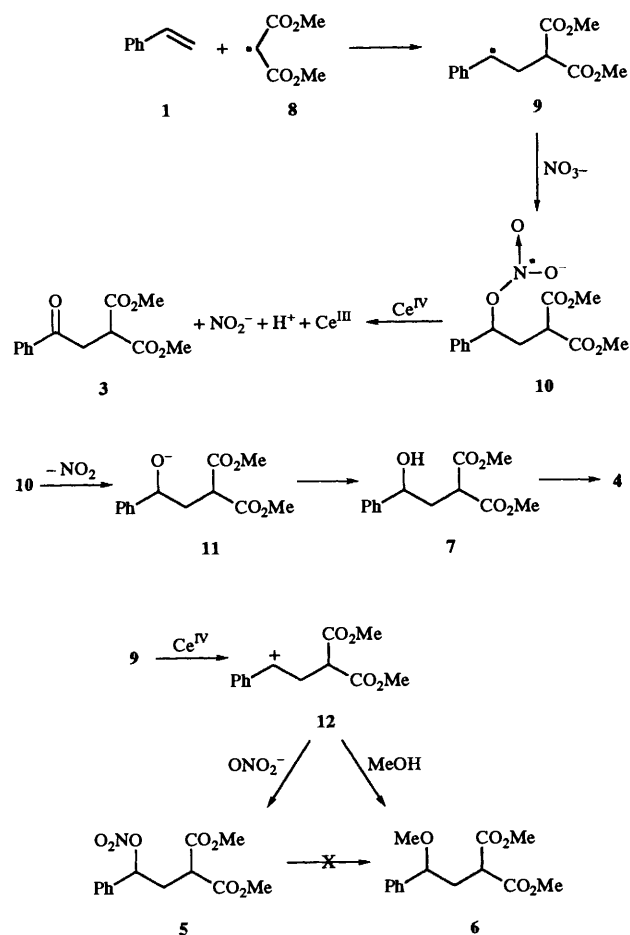
[†] The authors of ref. 3 did not isolate compounds **5** and **6**, only indirect evidence for their formation being provided.

[‡] Although quite unstable, the carbinol **7** can be isolated by rapid column chromatography. With time it undergoes lactonization to give **4**.

[§] Addition of NO₃⁻ to radicals generated by CAN to form anion radicals has been postulated.⁴

[¶] The authors gratefully acknowledge this suggestion from a referee.

^{||} We have communicated our results to Professor Baciocchi and in his response he has been unable to shed any light on the discrepancy between his reported results (ref. 3) and our findings.



Scheme 2

residue obtained on silica gel column chromatography using 5, 10 and 15% ethyl acetate in light petroleum afforded compounds **5** and **6** as a mixture and pure products **3** (0.470 g, 42%) and **4** (0.287 g, 29%), respectively. Compounds **5** (elution with dichloromethane, 0.075 g, 6%) and **6** (elution with ethyl acetate, 0.065 g, 5%) were obtained pure as pale yellow oils from their mixture by MPLC separation.

Dimethyl (2-oxo-2-phenylethyl)malonate **3** (Found: C, 62.5; H, 5.7. $C_{13}H_{14}O_5$ requires C, 62.39; H, 5.64%); $\nu_{\max}(\text{CH}_2\text{Cl}_2)/\text{cm}^{-1}$ 2960, 1749, 1689, 1443 and 1285; $\delta_{\text{H}}(90 \text{ MHz, CDCl}_3)$ 8.02–7.91 (2H, m, ArH), 7.58–7.43 (3H, m, ArH), 4.10–4.01 (1H, m, CH), 3.77 (6H, s, CO_2Me) and 3.67–3.48 (2H, m, CH_2); $\delta_{\text{C}}(22.4 \text{ MHz, CDCl}_3)$ 196.4, 169.1, 135.5, 133.2, 128.4, 127.9, 52.5, 46.2 and 37.1; m/z (GC-MS) 250 (M^+ , 5), 232 (10), 219 (6), 187 (8), 159 (7) and 105 (100).

Methyl 2-oxo-5-phenyltetrahydrofuran-3-carboxylate **4**. This product is a mixture of *cis-trans* isomers (Found: C, 65.3; H, 5.5. $C_{12}H_{12}O_4$ requires C, 65.45; H, 5.5%); $\nu_{\max}(\text{CH}_2\text{Cl}_2)/\text{cm}^{-1}$

2961, 1783, 1741 and 1459; $\delta_{\text{H}}(300 \text{ MHz, CDCl}_3)$ 7.33–7.23 (5H, m, ArH), 5.63 (t, J 7.2), 5.36 (dd, J 10.2, 6.2), 3.76 (s, CO_2Me), 3.74 (s, CO_2Me), 3.72–3.54 (1H, m, CHCO_2Me) and 3.01–2.30 (2H, m, CH_2); $\delta_{\text{C}}(22.4 \text{ MHz, CDCl}_3)$ 171.3, 167.9, 167.8, 138.4, 137.8, 128.7, 128.6, 128.5, 125.6, 125.1, 80.3, 79.8, 53.0, 52.8, 47.4, 46.6, 34.7 and 34.5; m/z (GC-MS) 220 (M^+ , 20), 192 (25), 160 (20), 145 (12), 120 (20) and 105 (70).

Dimethyl [2-nitroxy-2-phenylethyl]malonate **5**. $\nu_{\max}(\text{CH}_2\text{Cl}_2)/\text{cm}^{-1}$ 2962, 1759, 1740, 1639, 1440 and 1278; $\delta_{\text{H}}(90 \text{ MHz, CDCl}_3)$ 7.40 (5H, s, ArH), 5.93 (1H, dd, J 8.0, 6.2, CHONO_2), 3.78 (3H, s, CO_2Me), 3.77 (3H, s, CO_2Me), 3.64–3.48 (1H, m, CH), 2.64–2.45 (2H, m, CH_2); $\delta_{\text{C}}(22.4 \text{ MHz, CDCl}_3)$ 169.4, 137.1, 129.5, 129.0, 126.4, 82.9, 52.5, 48.3 and 33.6; m/z (GC-MS) 234 ($M^+ - \text{ONO}_2 - 1$, 10), 170 (60) and 129 (50).

Dimethyl (2-methoxy-2-phenylethyl)malonate **6**. $\nu_{\max}(\text{CH}_2\text{Cl}_2)/\text{cm}^{-1}$ 2957, 1755, 1743 and 1440; $\delta_{\text{H}}(90 \text{ MHz, CDCl}_3)$ 7.31–7.26 (5H, m, ArH), 4.16 (1H, dd, J 7.5, 5.9, CHOCH_3), 3.74 (3H, s, CO_2Me), 3.72 (3H, s, CO_2Me), 3.64–3.56 (1H, m, CH), 3.18 (3H, s, OMe) and 2.32–2.24 (2H, m, CH_2); $\delta_{\text{C}}(22.4 \text{ MHz, CDCl}_3)$ 169.8, 169.6, 141.0, 128.2, 127.8, 126.4, 81.3, 56.7, 52.3, 48.7 and 37.2; m/z (GC-MS) 266 (M^+ , 5), 251 (8), 235 (7) and 135 (50).

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