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Synthesis of 5-Acetoxy-2(5*H*)-Furanones through Manganese(III)-Promoted Functionalization of Arylacetylenes

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Abstract—Reaction of phenylacetylenes **1a–e** with manganese(III) triacetate in acetic acid/acetic anhydride at reflux gave the corresponding 5-acetoxy-5-phenyl-2(5*H*)-furanones **2a–e** in good yield (40–86%). Furanones **2** were derived from further oxidation of the initially formed 5-phenyl-2(3*H*)-furanones **4** which were in turn obtained through regioselective addition of carboxymethyl radicals to the alkyne **1** triple bond and subsequent oxidative cyclization of the resulting α-phenylvinyl radical **3**. In contrast, the (trimethylsilyl)alkylacetylene **1f** gave the corresponding furanone **2f** in only 25% yield, whereas alkylacetylenes **1g–h** totally failed to give the corresponding furanones **2f–h**, probably due to the incapability of the α-alkyl vinyl radical intermediates **3g–h** of undergoing oxidative cyclization. © 2000 Elsevier Science Ltd. All rights reserved.

Several methods are reported in the literature concerning the oxidative functionalization of the CC double bond.[1] In contrast, the oxidation of the CC triple bond has received much lesser attention. The hitherto known methods are mainly confined to the oxidative transformation of the CC triple bond to diketones or carboxylic acids.[1a] Recently, we have reported the DDQ-promoted oxidation of alkylacetylenes, which occurs at the propargylic carbon leading to *Z*-enynes in a stereoselective mode.[2]

In our interest in the chemistry of the CC triple bond[3] we have undertaken a study of the manganese(III) triacetate promoted oxidation of alkynes.

Manganese(III) triacetate is widely employed in organic synthesis as oxidising reagent.[4] Heiba et al.[5] reported in 1974 that β-ketoethers, and related β-dicarbonyl compounds, are oxidised to radicals at 25–70°C in acetic acid. In 1984, Corey and Kang[6] reported the cyclization of β-keto acids. Since these pioneering works, Mn(III)-based oxidative free radical cyclizations and annulations have been extensively investigated.[1,7]

Previously, the oxidative addition of acetic acid to alkenes had been reported.[8] Under these conditions Mn(III) triacetate generates carboxymethyl radicals. These add to the alkene double bond to give alkyl radicals which are further oxidised to give saturated γ-lactones. These oxidative additions have been extensively explored.[9] In contrast, the oxidative addition to the alkyne triple bond has not been explored yet, notwithstanding that it could lead to synthetically useful unsaturated γ-lactones. Unsaturated γ-lactones (the so called 'butenolides') are encountered frequently in a large number of natural products, including flavour components, insect sex pheromones and antibiotics.[10] A large variety of synthetic methods have been reported.[11]

Results and Discussion

For this work we used commercially available acetylenes **1a–h**. Reactions were carried out by heating a 0.2 M solution of the appropriate alkyne **1a–h** in a 1:1 acetic acid/acetic anhydride mixture to reflux in the presence of 4 molar equivalents of Mn(III) triacetate. With anhydrous Mn(III) triacetate all the reactions were completed in 20 min. Within this time the deep brown colour faded and a white precipitate of Mn(II) acetate was formed. GC-MS analysis showed the disappearance of starting alkyne **1**. Reactions carried out with the commercial dihydrate salt required a longer time; the disappearance of starting alkyne **1** occurred in 4–5 h.

Phenylacetylenes **1a–c**,**e** gave, after work up, the corresponding crude 5-acetoxy-2(5*H*)-furanones **2a–c**,**e** (Scheme 1). Subsequent purification on silica gel column gave these products in good yields (78–86%). Similar results were obtained for diphenylacetylene **1d**, but the corresponding furanone **2d** was recovered, after flash chromatography, only in 40% yield.

The formation of 5-acetoxy-2-(5*H*)-furanones **2a–d** can be explained by the reaction mechanism shown in Scheme 2.

Keywords: manganese triacetate; alkynes; radical addition; furanone; γ-butenolide.

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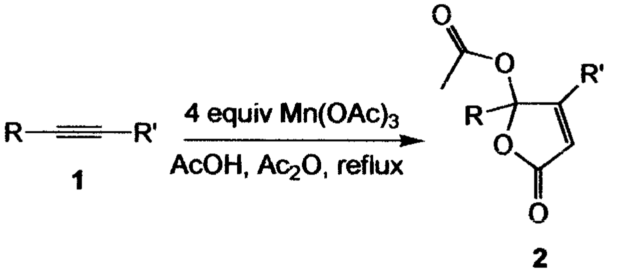


Scheme 1. **a**: R=Ph, R′=H; **b**: R=Ph, R′=Me; **c**: R=Ph, R′=propyl; **d**: R=R′=Ph; **e**: R=Ph, R′=$SiMe_3$; **f**: R=$SiMe_3$, R′=butyl; **g**: R=R′=propyl; **h**: R=octyl; R′=H.

Regioselective addition[12] of carboxymethyl radicals to the CC triple bond gives vinyl radicals **3a–d**, which afford 2(3*H*)-furanones **4** through oxidative cyclization onto the oxygen atom. In turn, furanones **4** undergo a further two-electron oxidation to allyl cations **5**, with formation of furanones **2** through regioselective trapping by the acetoxy counterion at the benzylic position. The overall reaction leading to **2** from **1** is a 4 electron oxidation process, and 4 molar equivalents of Mn(III) triacetate are required. When the reaction of **1a–d** was carried out with less than 4 molar equivalents of Mn(III), unreacted alkyne was found, and no traces of the possible furanone **4** intermediate was detected. This finding indicates that the oxidation of **4** to **2** is a fast process.

Furanone **2d** has already been prepared in 12% yield by Oishi and Kurosawa[13] through Mn(III) triacetate oxidation of α-acetoxystilbene. In this case it was also suggested that furanone **4d** was an intermediate derived from initial carboxymethyl radical addition to the alkene double bond, followed by oxidative cyclization of the ensuing alkyl radical.

Structural assignment to the hitherto unknown furanones **2a–c**,**e** came from ^1H and ^{13}C NMR, IR and MS spectra and elemental analysis. All these compounds gave a low intensity molecular ion in the MS spectrum, with important fragment ions at M^+-42, 105 and 43. The regiochemistry of furanones **2a–d** was attributed on the basis of the ^1H NMR spectrum analysis, which showed coupling between the C(3)–H and C(4)–H hydrogen atoms in **2a** and allylic coupling between the C(3)–H hydrogen and the C(4)-alkyl group. The regiochemistry of **2e** was attributed on the basis of n.O.e. experiments. Irradiation on the trimethylsilyl group signal caused a 5% enhancement of the vinylic proton signal.

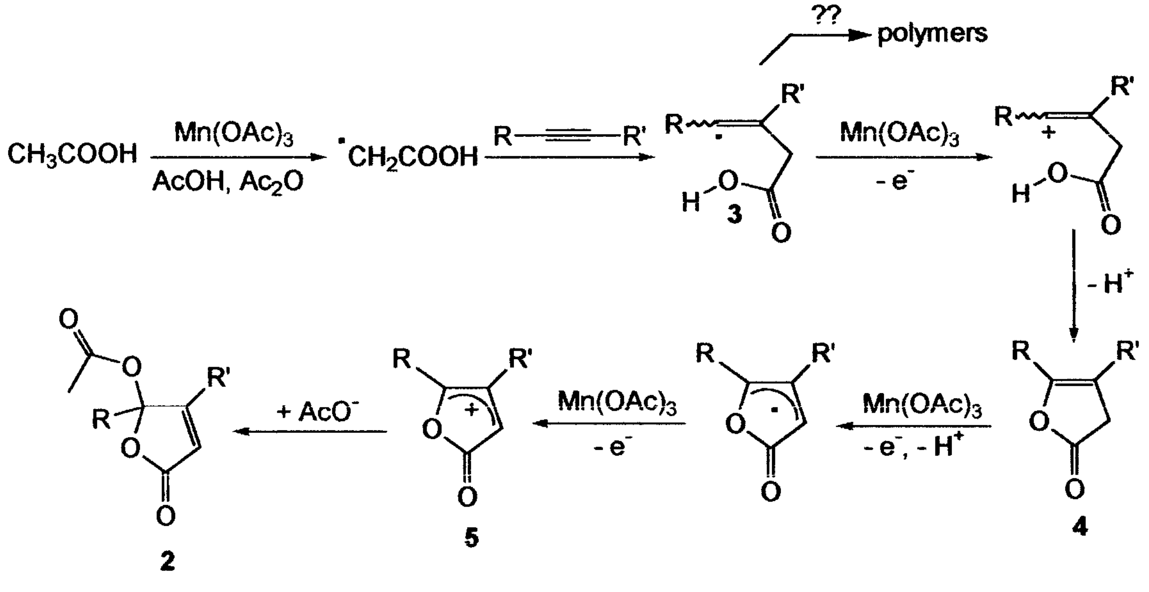
In contrast to **1a–e**, (trimethylsilyl)hexyne **1f** gave a complex mixture of products, from which furanone **2f** was separated by column chromatography in 25% yield, together with large amounts of polymeric compounds, which showed peaks at *m*/*z*>600 in the mass spectrum and unresolved bands in the aliphatic region in the ^1H NMR spectrum.

On the other hand, alkylacetylenes **1g**,**h** gave only unidentified, polymeric products which showed unresolved peaks in the aliphatic region in the ^1H NMR spectrum and peaks at *m*/*z*>600 in the MS spectrum. GC-MS analysis of the reaction mixtures did not indicate the formation of furanones **4g**,**h** or **2g**,**h**.

We think that the formation of polymeric materials in the case of alkynes **1f–h** might be attributed to a side reaction involving addition of radicals **3f–h** to the starting alkyne triple bond, which should occur in competition with the oxidative cyclization onto the oxygen atom.

The complete failure of **1g**,**h** to afford the desired furanones **2g**,**h** should result from the incapability of the vinyl radical intermediates **3g**,**h** of undergoing the oxidative cyclization onto the oxygen atom under the reaction conditions employed.

The different behaviour exhibited by vinyl radicals **3g**,**h**, as compared with radicals **3a–e**, might result from the fact that



Scheme 2.

radicals **3g**,**h**, belonging to the class of the sp^2-hybrizided, bent α-alkyl-substituted vinyl radicals, have the unpaired electron in a sp^2 orbital,[14] whereas radicals **3a**–**e**, belonging to the class of the sp-hybridized, linear α-aryl-substituted vinyl radicals, have the unpaired electron in a p orbital.[14,15] Thus, α-phenyl-substituted vinyl radicals **3a**–**e** would be expected to be more easily oxidised due to the lower ionisation potential of the p orbital with respect to the sp^2 one.

Conclusions

In summary, we have shown that the Mn(III)-promoted oxidative functionalization of acetylenes can lead to the corresponding 5-acetoxyfuranones **2** trough initial carboxymethyl radical addition to the alkyne triple bond, followed by oxidative cyclization of the ensuing vinyl radical **3**. The resulting furanones **4** give furanones **2** by further oxidation and eventual capture of allyl cations **5** by the acetoxy counterion. The key step of the entire process seems to be the oxidative cyclization of intermediate vinyl radicals **3**, which is governed by the nature of the α-substituent.

α-Phenylvinyl radicals **3a**–**e** generally gave the corresponding furanones **2a**–**e** in good yields, (trimethylsilyl)alkylacetylene **1f** gave the furanone **2f** in 25% yield only, whereas no furanone **2g**,**h** was detected with alkylacetylenes **1g**,**h**.

The short reaction time, the easy work up and the high yields make this reaction a useful method to synthesise functionalizated 5-acetoxy-5-aryl-2(5*H*)-furanones.

Experimental

^{1}H NMR spectra were recorded with a Varian Gemini 200 instrument using Me_4Si as an internal standard. ^{13}C NMR were recorded with a Varian Gemini 300 instrument. Mass spectra were recorded with a VG 7070E instrument using electron impact ionisation. IR spectra were recorded in $CHCl_3$ solution with a Perkin–Elmer FTIR 1600 instrument. GC-MS analyses were performed with a Carlo Erba QMD 1000 instrument. Elemental analyses were performed with a Carlo Erba 1106 instrument. Anhydrous Mn(III) triacetate was obtained by heating at 100°C under nitrogen atmosphere the commercially available dihydrate salt for more than 24 h. Alkynes **1a**–**h** are commercially available.

Reaction of alkynes 1a–i with Mn(III) triacetate. General procedure

Anhydrous Mn(III) triacetate (8 mmol, 2 g) was added to a solution of the appropriate alkyne **1a**–**i** (2 mmol) in a 1:1 acetic acid/acetic anhydride mixture (10 mL). The resulting mixture was refluxed for ca. 20 min, until the brown colour faded and a white precipitate of manganese(II) diacetate was separated. The reaction mixture was cooled and quenched with water (50 mL) and diethyl ether (50 mL). The organic layer was separated, washed 5 times with water and the organic solution concentrated under vacuum. The residue was analysed by ^{1}H NMR and then chromatographed on a silica gel column.

From 1a. Elution with petroleum ether (bp 40–70)/ethyl acetate 70:30 gave *5-acetoxy-5-phenyl-2(5H)-furanone* **2a** as a pale yellow oil (340 mg, 1.55 mmol, 78%) [δ_H (200 MHz, $CDCl_3$) 2.15 (3H, s), 6.3 (1H, d, J=5.3 Hz), 7.3–7.5 (5H, m), 7.75 (1H, d, J=5.3 Hz; collapsing to singlet upon irradiation at δ 6.3); δ_C (75.5 MHz, $CDCl_3$) 22.05 (CH_3), 106.8(C), 122.64(CH), 125.6(CH), 129.15 (CH), 130.4 (CH), 133.8 (C), 153.8 (CH),168.44 (C), 170.03 (C); *m/z* (rel. int.) 218 (M^+, 1), 176 (100), 159 (55), 131 (35), 105 (65), 77 (50), 43 (70); ν_{max} 1780 (CO, broad). Found: C, 66.24; H, 4.63. $C_{12}H_{10}O_4$ requires C, 66.05; H, 4.62; O, 29.33%].

From 1b. Elution with petroleum ether (bp 40–70)/ethyl acetate 70:30 gave *3-methyl-5-acetoxy-5-phenyl-2(5H)-furanone* **2b** as a pale yellow oil (400 mg, 1.72 mmol, 86%) [δ_H (200 MHz, $CDCl_3$) 1.9 (3H, d, J=1.8 Hz; collapsing to singlet upon irradiation at δ 5.9), 2.15 (3H, s), 5.9 (1H, q, J=1.8 Hz), 7.3–7.5 (5H, m); δ_C (75.5 MHz, $CDCl_3$) 13.1 (CH_3), 22.2 (CH_3), 106.8 (C), 117.7 (CH), 125.4 (CH), 129.1 (CH), 130.0 (CH), 135.1 (C), 167.2 (C), 168.2 (C), 170.5 (C); *m/z* (rel. int.) 232 (M^+, 5), 190 (50), 173 (30), 158 (25), 127 (50), 105 (100), 85 (55), 77 (55), 43 (95); ν_{max} 1780 (CO, broad). Found: C, 67.40; H, 5.20. $C_{13}H_{12}O_4$ requires C, 67.23; H, 5.21; O, 27.56%]. Further elution with ethyl acetate gave intractable tarry materials.

From 1c. Elution with petroleum ether (bp 40–70)/ethyl acetate 70:30 gave *3-propyl-5-acetoxy-5-phenyl-2(5H)-furanone* **2c** as a pale yellow oil (430 mg, 1.65 mmol, 82%) [δ_H (200 MHz, $CDCl_3$) 1.9 (3H, t, J=7 Hz); 1.4–1.65 (2H, m), 2.0 (1H, A part of an ABXY system, J_{AB}=18, J_{AX}=8.5, J_{AY}=6 Hz; lines broadened by coupling at δ 5.9), 2.18 (3H, s), 2.2 (1H, B part of an ABXY system, J_{AB}=18, J_{BX}=9.5, J_{AY}=6 Hz; lines broadened by coupling at δ 5.9), 5.9 (1H, t, J=1.5 Hz), 7.3–7.5 (5H, m); δ_C (75.5 MHz, $CDCl_3$) 13.44 (CH_3), 19.58 (CH_2), 21.52 (CH_3), 28.46 (CH_2), 106.28 (C), 115.70 (CH), 124.78 (CH), 128.63 (CH), 129.44 (CH), 134.86 (C), 167.61 (C), 170.24 (C), 171.03 (C); *m/z* (rel. int.) 260 (M^+, 5), 260 (M^+, 5), 218 (40), 201 (25), 173 (20), 155 (35), 113 (100), 105 (80), 77 (40), 43 (60); ν_{max} 1780 (CO, broad). Found: C, 69.40; H, 6.40. $C_{15}H_{16}O_4$ requires C, 69.21; H, 6.20; O, 24.59.]. Further elution with ethyl acetate gave intractable tarry materials.

From 1d. Elution with petroleum ether (bp 40–70)/ethyl acetate 80:20 gave *5-acetoxy-3,5-diphenyl-2(5H)-furanone* **2d** (230 mg, 0.8 mmol, 40%); ^{1}H NMR and MS spectra were as reported in the literature;[13] δ_C (75.5 MHz, $CDCl_3$) 21.6 (CH_3), 106.3 (C), 117.1 (CH), 126.0 (CH), 128.6 (CH), 129.4 (CH), 129.6 (CH), 130.5 (CH), 132.0 (CH), 136.3 (C), 163.7 (C), 168.1 (C), 169.8 (C). Further elution with ethyl acetate gave intractable tarry materials.

From 1e. Elution with petroleum ether (bp 40–70)/ethyl acetate 70:30, *3-(trimethylsilyl)-5-acetoxy-5-phenyl-2(5H)-furanone* **2e** as a pale yellow oil (485 mg, 1.67 mmol, 84%) [δ_H (200 MHz, $CDCl_3$) −0.05 (9H, s), 2.18 (3H, s), 6.3 (1H, s), 7.3–7.5 (5H, m); δ_C (75.5 MHz, $CDCl_3$) −1.4 (CH_3), 22.4 (CH_3), 109.7 (C), 125.8 (CH), 129.3 (CH), 130.1 (CH), 130.35 (CH), 135.8 (C), 168.45 (C), 168.45 (C), 171.2 (C), 172.8 (C); *m*/*z* (rel. int.) 290 (M^+, 1), 248 (10), 174 (25), 159 (100), 129 (10), 105 (15); ν_{max} 1780 (CO, broad). Found: C, 62.22; H, 6.23. $C_{15}H_{18}O_4Si$ requires C, 62.04; H, 6.25; O, 22.04; Si, 9.67.]. Further elution with ethyl acetate gave intractable tarry materials.

From 1f. The residue (360 mg) was constituted by a mixture of several products, as evidenced by the ^1H NMR spectrum. Column chromatography on silica gel column separated, by gradual elution with petroleum ether (bp 40–70)/ethyl acetate: (1) a ca. 1:1 mixture (70 mg) of **2f** and an unidentified product. The ^1H NMR spectrum, in addition to peaks ascribable to **2f**, showed peaks at δ 0.18 (s), 0.82 (t, J=7 Hz) and 2.08 (s); the GC-MS spectrum, in addition to **2f**, showed a chromatographic peak with *m*/*z* 239 (1), 212 (30), 169 (20), 73 (100), and 43 (70); (2) *3-butyl5-acetoxy-5-(trimethylsilyl)-2(5H)-furanone* **2f** as a pale yellow oil (110 mg, 0.4 mmol, 20%) [δ_H (200 MHz, $CDCl_3$) 0.20 (9H, s), 0.85 (3H, t, J=7 Hz), 1.1–1.4 (4H, m), 1.55–1.75 (1H, m), 2.0 (3H, s), 2.05–2.2 (1H, m), 6.22 (1H, s); δ_C (75.5 MHz, $CDCl_3$) −1.72 (CH_3), 13.90 (CH_3), 21.7 (CH_3), 22.4 (CH_2), 24.3 (CH_2), 37.1 (CH_2), 11.6 (C), 131.9 (CH), 167.4 (C), 168.2 (C), 170.3 (C); *m*/*z* (rel. int.) 270 (M^+, 3), 228 (25), 185 (50), 75 (70), 73 (100), 43 (90); ν_{max} 1780 (CO, broad). Found: C, 57.90; H, 8.23. $C_{13}H_{22}O_4Si$ requires C, 57.75; H, 8.20; O, 23.67; Si, 10.39%]; and (3) a mixture of unidentifiable, polymeric products (180 mg). MS spectrum of this fraction showed high weight peaks (*m*/*z*>600). ^1H NMR spectrum showed unresolved bands in the aliphatic region and no vinylic protons.

From 1g and 1h. The reaction mixture consisted of a thick oil (380 mg). MS spectrum showed high weight peaks (*m*/*z*>600). ^1H NMR spectrum showed unresolved bands in the aliphatic region and no vinylic protons.

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