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# Synthesis of vinyl 1,2-diketones ☆

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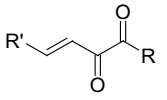
**Abstract**—A new route is outlined for preparation of vinyl 1,2-diketones via a three-step sequence. First, allylic alcohols are photooxidized by $^1O_2$ to hydroperoxides, which are reduced to vinyl 1,2-diols. These vinyl 1,2-diols are oxidized to vinyl 1,2-diketones with oxoammonium salts, which are prepared in situ from organic nitroxyl radicals. The new route is short, avoids the use of protecting groups, and is generally applicable to obtain aliphatic or aromatic vinyl 1,2-diketones.


As part of a program focusing on the synthesis of polyfunctional $C_4$ and $C_5$ ketoalcohols, we wanted to obtain vinyl 1,2-diketones as intermediate compounds. The vinyl group in these molecules can easily be further oxyfunctionalized, for example, by epoxidation or by dihydroxylation. Moreover, 1,2-diketones are widely employed in the preparation of heterocycles.[1] However, there are so far surprisingly few reports on the synthesis of vinyl 1,2-diketones ($R' = H$) or related compounds.




The only reported preparation of a vinyl 1,2-diketone is that of methyl vinyl 1,2-diketone ($R' = H$; $R = CH_3$), which was obtained by a pyrolytic retro-Diels–Alder reaction of 1-(bicyclo[2.2.1]hept-5-ene-2-yl)-1,2-propanedione at 600 °C in high vacuum.[2] Other routes have been reported for preparation of alkenyl 1,2-diketones ($R' = alkyl$).[3–5] A fairly general method is the condensation of 2,3-butanedione with aldehydes.[3] However, this method only provides satisfactory results with activated aldehydes such as enals. Starting from benzotriazole derivatives, some alkenyl 1,2-diketones have been obtained in a few steps,[4] but this method has not been demonstrated for vinyl 1,2-diketones. Finally, a substituted styryl 1,2-diketone was prepared by Wadsworth–Emmons reaction of an aromatic aldehyde with a (2-keto-3,3-dimethoxybutyl)phosphonate.[5] Summarizing, there is no general route to vinyl 1,2-diketones, which starts from simple precursors, and is generally useful for preparative purposes.

We here report an alternative, widely applicable route to vinyl 1,2-diketones with various substituents. A first key step is the photooxidation of allylic alcohols, which brings the double bond at the desired terminal position. In the last step, vinyl 1,2-diols are oxidized to vinyl 1,2-diketones using oxoammonium salts.

The newly proposed route starts from simple precursors, and comprises three steps as outlined in Scheme 1. First, crotonaldehyde reacts with bromomagnesium or lithium nucleophiles to obtain the variously substituted unsaturated alcohols **1**. Under visible light irradiation and in the presence of tetraphenylporphyrin and $O_2$, these unsaturated alcohols are oxidized by $^1O_2$ to the unsaturated hydroxy hydroperoxides.[6,7] Generally, the more apolar allylic alcohols, for example, **1c**, require longer reaction times to reach acceptable conversion levels. This could well be due to quenching of the $^1O_2$ by the C–H bonds in the long alkyl chains.

The hydroperoxides, which were formed in the photooxygenation were reduced in situ to the vinyl 1,2-diols **2**. A stoichiometric amount of triphenylphosphine

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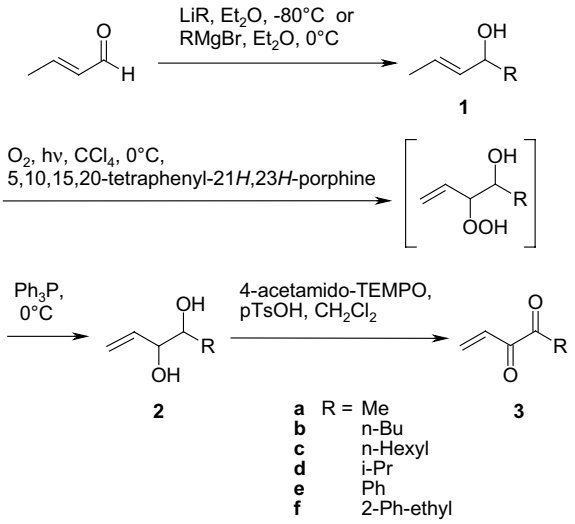



**Scheme 1.** Synthesis route for vinyl 1,2-diketones.

proved appropriate for this reduction, which was run overnight. After chromatography, the vinyl 1,2-diols are obtained in high purity.[7] NMR analysis of the reduced products shows indeed that the attack by the perepoxide intermediate of the $^1O_2$ reaction proceeds with high selectivity on the terminal methyl group, resulting in the migration of the double bond to the desired terminal position.[6]

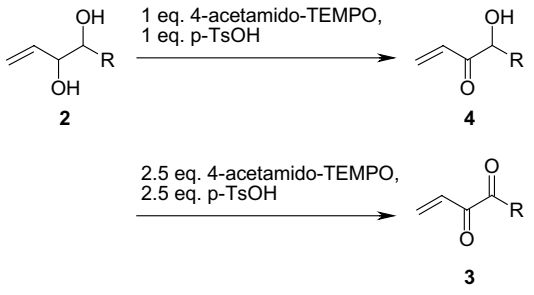
In the oxidation of the 1,2-diols **2** to the 1,2-diketones **3**, the first oxidation may be easy, but the second alcohol group will be more difficult to oxidize because of the adjacent electron-withdrawing ketone group. Several procedures were considered for this reaction. A $CrO_3$ oxidation has been reported for a related reaction, but the reaction was not fully selective, and chromic acid is an environmentally unfriendly reagent.[8] Swern reagents are also less suitable for such demanding oxidations, since they require the maintenance of anhydrous conditions and very low temperatures for extended periods of time.[9] In our hands, the oxidation of 4-pentene-2,3-diol using DMSO and oxalyl chloride following Swern's procedure yielded a complex mixture of several compounds. In the search for a more general and straightforward method, the relatively mild oxidation of alcohols with organic oxoammonium salts was investigated next.[10,11] In a preferred procedure for this reaction, the free radical 4-acetamido-2,2,6,6-tetramethyl-1-piperidinyloxy (4-acetamido-TEMPO) is disproportionated in the presence of a strong acid to form the hydroxylamine and the oxidizing oxoammonium salt in situ.

Oxidation of cyclic saturated diols or even unsaturated diols by oxoammonium salts has been reported by Banwell et al.[12] but other workers have reported that the presence of an oxygen atom in the β-position of the alcohol group strongly retards alcohol oxidation.[13] Nevertheless, in our hands, the oxoammonium method proved successful for the formation of vinyl 1,2-diketones. In a typical reaction, solid *p*-toluenesulfonic acid monohydrate was added to the cooled solution (0 °C) of the diol in dichloromethane. Then the 4-acetamido-TEMPO in dichloromethane was added slowly over a period of 15–30 min.[14]

The reaction takes place in two steps. The first oxidation can be performed without or with only a slight excess of the oxidation mixture (Scheme 2); it oxidizes the allylic alcohol rather than the homoallylic alcohol, and thus leads to the acyloins **4** in almost quantitative yields.[15] To form the diketones **3**, the reaction should be performed with 2.5 equiv of 4-acetamido-TEMPO and *p*-toluenesulfonic acid monohydrate for a prolonged time, usually 5–7 days. The two successive oxidations can be done in one pot; or alternatively, the intermediate **4** can be isolated and then subjected to a second reaction. In another, more lengthy approach, the intermediate **4** may be formed directly from the hydroperoxide, via acetylation with $Ac_2O$, base-catalyzed Kornblum-de la Mare rearrangement to the unsaturated ketone and deacetylation to form the acyloin **4**.[16]

On TLC, the eventual products **3** can be distinguished from the starting materials **1** and from the intermediates **4** by their more lipophilic character and by their bright yellow color. In the clear solution the color of the diketone is hidden by the orange color of the excess 4-acetamido-TEMPO, but when the excess of this reagent is destroyed, for example, by the addition of methanol, the residual yellow color originating from the diketone can be used as a measure for the progress of the reaction. The diketones can be quite easily purified by chromatography on a silica gel column with diethyl ether as the eluent. The desired compounds elute much before all other compounds of the mixture and are exceptionally easy to follow by their color.

The oxidation of 1,2-diols **2a**–**f** was monitored by $^1H$ and $^{13}C$ NMR analysis. This indicated that the mono and diketones were the only products formed; there was no evidence, for example, oxidative splitting of 1,2-diketones. Weighed yields of the analytically pure vinyl 1,2- diketones, obtained after column chromatography, are given in Table 1. The rather low yield for **3a**, methyl vinyl 1,2-diketone, is due to the volatility of this compound. Not only aliphatic vinyl 1,2-diketones, such as **3a**, **3b**, **3c**, and **3d**, are readily obtained; the method is equally useful for an aromatic diketone such as **3f**. Finally, the diol oxidation even leads to a high yield of




**Scheme 2.** Oxidation of vinyl 1,2-diols with oxoammonium salts.

**Table 1.** Oxidation of vinyl 1,2-diols to vinyl 1,2-diketones

| Compound | R= | Isolated yield (%) |
|---|---|---|
| **3a** | $-CH_3$ | 16 |
| **3b** | $-(CH_2)_3CH_3$ | 51 |
| **3c** | $-(CH_2)_5CH_3$ | 50 |
| **3d** | $-CH(CH_3)_2$ | 28 |
| **3e** | –Ph | 75 |
| **3f** | $-(CH_2)_2Ph$ | 52 |

vinyl phenyl 1,2-diketone **3e**, in which the phenyl group is directly conjugated with the vinyl 1,2-diketone moiety. These data show that, even if reaction times are long, the newly proposed route provides access to virtually all aliphatic or aromatic vinyl 1,2-diketones.

Summarizing, the new route to vinyl 1,2-diketones is short; it starts from simple and cheap molecules, and there is no need to use protecting or activating groups. The singlet oxygen reaction used to obtain the diols is only one of several possible ways to obtain the appropriate starting material **2** for the oxidation. The present route to vinyl 1,2-diketones will enable further transformation of these synthons, for example, via selective oxidation, or by incorporation in heterocycles.

## Supplementary information available

NMR data for vinyl 1,2-diols and acyloins.

## Acknowledgements

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7. For the photooxidation, 20 mmol olefin was dissolved in 20 mL $CCl_4$ at 0 °C, together with 10 mg 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine. A pure oxygen atmosphere was maintained, and the flask was irradiated by a 400 W lamp for 3–7 days. After reduction with $PPh_3$, the allylic alcohols were isolated by work-up on a $SiO_2$ chromatographic column. Isolated yields after chromatography are between 11% and 60%.
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14. For the synthesis of vinyl 1,2-diketones, 0.5 mmol of the diols **2a–f** were dissolved in 3 mL dichloromethane and cooled to 0 °C. Then 475 mg (2.5 mmol) of *p*-toluenesulfonic acid were added and the flask was closed with a rubber septum. Subsequently, the solution of 533 mg (2.5 mmol) 4-acetamido-TEMPO in 5 mL dichloromethane was added via a needle over 15–30 min. The reaction mixture was allowed to warm-up to room temperature overnight and stirred for 4–7 days until TLC control showed completion. The solvent was evaporated and the residue chromatographed on a silica gel column ($1 \times 20$ cm) using diethyl ether as eluent. Methyl vinyl 1,2-diketone, 4-penten-2,3-dione (**3a**). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.01 (dd, 1H, $J = 10.6$, 17.6 Hz), 6.53 (dd, 1H, $J = 1.5$, 17.6 Hz), 6.04 (dd, 1H, $J = 1.5$, 10.6 Hz), 2.40 (s, 3H); $^{13}$C NMR ($CDCl_3$) 198.7, 187.6, 134.1, 129.1, 24.7; MS (EI) $m/z$ 98 ($M^+$, 8), 55 (34), 43 (100). Butyl vinyl 1,2-diketone, 1-octene-3,4-dione (**3b**). $^1$H NMR ($CDCl_3$): $\delta$ 6.99 (dd, 1H, $J = 10.2$, 17.6 Hz), 6.52 (dd, 1H, $J = 1.5$, 17.6 Hz), 6.04 (dd, 1H, $J = 1.5$, 10.2 Hz), 2.80 (t, 2H, $J = 7.3$ Hz), 1.60 (quintet, 2H, $J = 7.3$ Hz), 1.36 (sextet, 2H, $J = 7.3$ Hz), 0.93 (t, 3H, $J = 7.3$ Hz); $^{13}$C NMR ($CDCl_3$): $\delta$ 201.2, 188.3, 133.8, 129.6, 36.8, 25.4, 22.6, 14.1; MS (EI) $m/z$, 140 ($M^+$, 2), 111 (3), 85 (35), 57 (60), 55 (100). Hexyl vinyl 1,2-diketone, 1-decene-3,4-dione (**3c**). $^1$H NMR ($CDCl_3$): $\delta$ 6.99 (dd, 1H, $J = 10.6$, 17.6 Hz), 6.52 (dd, 1H, $J = 1.5$, 17.6 Hz), 6.03 (dd, 1H, $J = 1.5$, 10.6 Hz), 2.80 (t, 2H, $J = 7.3$ Hz), 1.61 (quintet, 2H, $J = 7.3$ Hz), 1.35–1.26 (m, 6H), 0.88 (t, 3H, $J = 7.3$ Hz); $^{13}$C NMR ($CDCl_3$): $\delta$ 201.4, 188.4, 133.9, 129.7, 37.2, 31.9, 29.2, 23.3, 22.8, 14.4; MS (EI) $m/z$ 168 ($M^+$, 1), 139 (1), 125 (2), 113 (82), 111 (2), 85 (28), 57 (19), 55 (100). Isopropyl vinyl 1,2-diketone, 5-methyl-1-hexene-3,4-dione (**3d**). $^1$H NMR ($CDCl_3$): $\delta$ 6.93 (dd, 1H, $J = 11.0$, 17.6 Hz), 6.47 (dd, 1H, $J = 1.5$, 17.6 Hz), 6.05 (dd, 1H, $J = 1.5$, 11.0 Hz), 2.09–2.19 (m, 1H), 1.12 (d, 6H, $J = 7.3$ Hz); $^{13}$C NMR ($CDCl_3$): $\delta$ 201.3, 189.4, 133.5, 130.5, 34.8, 17.4; MS (EI) $m/z$ 126 ($M^+$, 5), 71 (34), 55 (100). Phenyl vinyl 1,2-diketone, 1-phenyl-3-butene-1,2-dione (**3e**). $^1$H NMR ($CDCl_3$): $\delta$ 7.97 (d, 2H, $J = 7.3$ Hz), 7.66 (t, 1H, $J = 7.3$ Hz), 7.51 (t, 2H, $J = 7.3$ Hz), 6.75 (dd, 1H, $J = 11.0$, 17.6 Hz), 6.41 (d, 1H, $J = 17.6$ Hz), 6.24 (d, 1H, $J = 11.0$ Hz); $^{13}$C NMR ($CDCl_3$): $\delta$ 193.7, 193.2, 135.2 (2C), 133.2, 132.9, 130.4, 129.3; MS (EI) $m/z$ 160 ($M^+$, 13), 105 (95), 77 (100), 55 (55). (2-Phenyl)ethyl vinyl 1,2-diketone, 1-phenyl-5-hexene-3,4-dione (**3f**). $^1$H NMR ($CDCl_3$): $\delta$ 7.28–7.20 (m, 5 H), 6.98 (dd, 1H, $J = 10.6$, 17.6 Hz), 6.50 (dd, 1H, $J = 1.5$, 17.6 Hz), 6.02 (dd, 1H, $J = 1.5$, 10.6 Hz), 3.16 (t, 2H, $J = 7.5$ Hz), 2.95 (t, 2H, $J = 7.5$ Hz); $^{13}$C NMR ($CDCl_3$): $\delta$ 200.0, 187.9, 140.7, 134.1, 129.4, 128.9, 128.7, 126.7, 38.7, 29.3; MS (EI) $m/z$ 188 ($M^+$, 5), 91 (15), 77 (30), 55 (100).
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