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# Chemoselective Selenium Dioxide Oxidation of 1,4-Adducts Derived from Substituted Arylidene Acetophenones

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**Abstract:** The chemoselective reactions of selenium dioxide with differently substituted adducts generated by 1,4-addition on benzylidene acetophenone are described. This reaction has been shown to be dependent on the nature of the substituent present, leading to different products by α-oxidation/α-oxidation followed by dehydrogenation/dehydrogenation, enolization, and cyclization.

**Keywords:** Chemoselectivity, 1,2-diketones, selenium dioxide oxidation

1,2-Diketones are synthetically important because they are well known as precursors for the synthesis of heterocyclic compounds such as pyrazine,[1] oxazoline,[2] quinoxaline,[3] imidazoles,[4] and heterocyclic N-oxides.[5,6] Obviously different methods of generating 1,2-diketones receive attention, and there are a number of synthetic routes available for the preparation of 1,2-diketones, the most important being the selenium dioxide oxidation of active methyl or methylene group α- to the carbonyl group.[7] 1,2-Diketones can also be prepared by the nitrosation of enols using sodium nitrite and hydrochloric acid,[8] self-coupling

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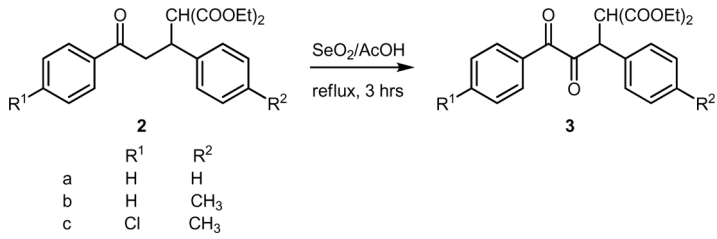



***Scheme 1.*** Selenium dioxide oxidation of diethyl 2-(3-oxo-1,3-diarylpropyl) malonate.

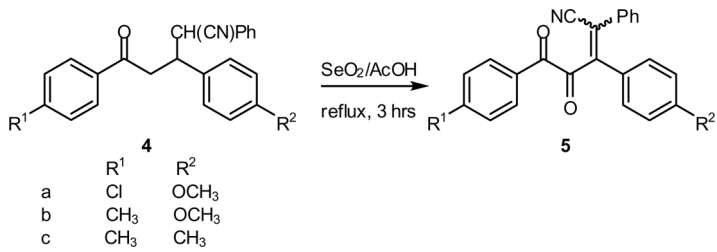


reactions of acyl group catalyzed by lanthanide salts such as samarium diiodide,[9,10] and oxidation of substituted alkenes[11] and alkynes.[12] Recently, α-diketones have been prepared using cobalt phthalocyanine tetrasulphonamide[13] and ruthenium complex[14] as catalysts. This article describes selenium dioxide–mediated oxidation of ketones generated by 1,4-addition on benzylidene acetophenone to give 1,2-diketones.

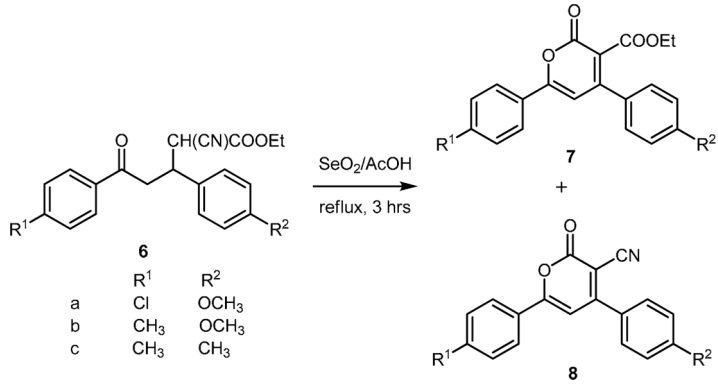
The starting materials, 1-propanone derivatives (**2, 4,** and **6**), were prepared by the Michael addition of corresponding nucleophiles to substituted benzylidene acetophenone **1**. Compounds **2** and **4** were prepared by the addition of diethyl malonate and benzyl cyanide respectively to substituted chalcones in the presence of sodium ethoxide in diethyl ether at room temperature.[15]

The selenium dioxide oxidation of compound **2** was effected in acetic acid in a 1:5 ratio of substrate–selenium dioxide by heating the reaction mixture on a water bath for 3 h (Scheme 1). The product **3** was isolated as a viscous liquid by silica-gel chromatography in 30% yield. The structure of **3** was analyzed by infrared (IR), mass, and $^{1}H$ and $^{13}C$ NMR spectroscopy.

It is interesting to note that when 3,5-diaryl-5-oxo-2-phenylpentanenitrile (**4**) has been subjected to selenium dioxide oxidation under the same conditions, product **5** was obtained in 30–35% yield (Scheme 2).




***Scheme 2.*** Selenium dioxide oxidation of 3,5-diaryl-5-oxo-2-phenylpentanenitrile.




***Scheme 3.*** Selenium dioxide oxidation of ethyl 3,5-diaryl-2-cyano-5-oxopentanoate.

The structural features of the product, **5**, were analyzed by IR and $^{1}H$ and $^{13}C$ NMR spectroscopy.

The oxidation of ethyl 3,5-diaryl-2-cyano-**5**-oxopentanoate (**6**) was then investigated under identical conditions (Scheme 3). The reaction led to the formation of two products, **7** and **8**, in an overall yield of 40%, with the former one being the major product. Compounds **7a** and **8b** were separated from the reaction mixture by column chromatography in pure form, but the other compounds **(7b, 8a, 7c,** and **8c)** could not be obtained in pure form.

## EXPERIMENTAL

Melting points are uncorrected. One- and two-dimensional NMR spectra were recorded on a Bruker 300-MHz instrument in $CDCl_3$ using tetramethylsilane (TMS) as internal standard. Chemical shifts are given in parts per million (δ-scale), and coupling constants are given in hertz. IR spectra were recorded on a Jasco Fourier transform (FT)–IR instrument (KBr pellet/$CHCl_3$ solution).

### General Procedure for the Reaction of Michael Adducts with Selenium Dioxide

A solution of 2.77 g (0.025 mol) of finely powdered selenium dioxide in 10 mL of glacial acetic acid was added by portions to a warm solution of 0.005 mol of Michael adduct **2, 4,** or **6** in 10 mL of glacial acetic acid, and the reaction mixture was heated on a water bath for 3 h. The

deposited selenium metal was filtered off, and the filtrate was poured onto crushed ice and extracted with chloroform. The product was purified by column chromatography using silica gel (60–120 mesh) with petroleum ether–ethyl acetate (98:2).

## Data

Diethyl 2-(2,3-dioxo-1,3-diphenylpropyl)malonate (**3a**)

Viscous liquid (30%): IR ($CHCl_3$) $cm^{-1}$: $\nu_{max}$ 2983, 2939, 2906, 2873, 1730, 1676, 1597, 1371, 1306. $^1H$ NMR (300 MHz, $CDCl_3$): δ 0.95 (t, $J = 7.2$ Hz, 3H), 1.25 (t, $J = 7.2$ Hz, 3H), 3.95 (q, $J = 7.2$ Hz, 2H), 4.22 (q, $J = 7.2$ Hz, 2H), 4.41 (d, $J = 12.0$ Hz, 1H), 5.34 (d, $J = 12.0$ Hz, 1H), 7.22–7.36 (m, 5H), 7.40 (m, 2H), 7.54 (t, $J = 7.5$ Hz, 1H), 7.87 (d, $J = 8.1$ Hz, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 14.1, 14.4, 52.6, 55.0, 61.9, 62.6, 128.9, 129.0, 129.5, 129.9, 130.7, 132.4, 132.8, 134.7, 167.6, 168.3, 190.2, 197.0 ppm.

Diethyl 2-[1-(4-methylphenyl)-2,3-dioxo-3-phenylpropyl]malonate (**3b**)

Viscous liquid (28%): IR ($CHCl_3$) $cm^{-1}$: $\nu_{max}$ 2983, 2939, 2906, 2873, 1730, 1676, 1597, 1371, 1306 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 1.00 (t, $J = 7.2$ Hz, 3H), 1.26 (t, $J = 7.2$ Hz, 3H), 2.26 (s, 3H), 3.97 (q, $J = 7.2$ Hz, 2H), 4.22 (q, $J = 7.2$ Hz, 2H), 4.36 (d, $J = 11.7$ Hz, 1H), 5.30 (d, $J = 11.7$ Hz, 1H), 7.09 (d, $J = 8.1$ Hz, 2H), 7.20 (d, $J = 8.1$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.55 (tt, $J = 7.5$, 1.8 Hz, 1H), 7.87 (dd, $J = 7.5$, 1.8 Hz, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 13.8, 14.0, 21.1, 51.9, 54.6, 61.5, 62.2, 128.5, 128.7, 129.3, 129.8, 130.3, 132.5, 134.2, 138.3, 167.2, 168.0, 189.9, 196.7 ppm.

Diethyl 2-[3-(4-chlorophenyl)-1-(4-methylphenyl)-2,3-dioxopropyl]malonate (**3c**)

Viscous liquid (27%): IR ($CHCl_3$) $cm^{-1}$: $\nu_{max}$ 2983, 2939, 2906, 2873, 1730, 1680, 1589, 1371, 1307 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 1.00 (t, $J = 7.2$ Hz, 3H), 1.26 (t, $J = 7.2$ Hz, 3H), 2.27 (s, 3H), 4.00 (q, $J = 7.2$ Hz, 2H), 4.22 (q, $J = 7.2$ Hz, 2H), 4.36 (d, $J = 12.0$ Hz, 1H), 5.27 (d, $J = 12.0$ Hz, 1H), 7.09 (d, $J = 8.1$ Hz, 2H), 7.20 (d, $J = 8.1$ Hz, 2H), 7.39 (d, $J = 8.4$ Hz, 2H), 7.84 (d, $J = 8.4$ Hz, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 13.8, 14.0, 21.1, 51.7, 54.6, 61.5, 62.2, 128.6, 128.9, 129.2, 129.9, 130.8, 131.7, 138.4, 140.9, 167.1, 168.0, 188.5, 196.3 ppm.

5-(4-Chlorophenyl)-3-(4-methoxyphenyl)-4,5-dioxo-2-phenyl-2-pentenenitrile (**5a**)

Colorless solid (30%), mp 150°C. Anal. calcd. for $C_{24}H_{16}ClNO_3$: C, 71.73; H, 4.01; N, 3.49. Found: C, 71.79; H, 4.10; N, 3.51. IR (KBr): $\nu_{max}$ 1604, 1670, 2208 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 3.87 (s, 3H), 7.00 (d, $J = 7.5$ Hz, 2H), 7.15–7.45 (m, 7H), 7.54 (d, $J = 8.7$ Hz, 2H), 7.75 (d, $J = 8.7$ Hz, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 55.4, 114.5, 117.6, 117.8, 126.7, 128.7, 129.4, 129.7, 129.9, 130.5, 130.6, 130.9, 131.3, 141.1, 152.6, 161.5, 187.7, 193.4 ppm.

3-(4-Methoxyphenyl)-5-(4-methylphenyl)-4,5-dioxo-2-phenyl-2-pentenenitrile (**5b**)

Colorless solid (34%), mp 156°C. Anal. calcd. for $C_{25}H_{19}NO_3$: C, 78.72; H, 5.02; N, 3.67. Found: C, 78.75; H, 5.09; N, 3.71. IR (KBr): $\nu_{max}$ 1602, 1658, 1677, 2212 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 2.41 (s, 3H), 3.92 (s, 3H), 6.97 (d, $J = 9.0$ Hz, 2H), 7.38 (d, $J = 8.4$ Hz, 2H), 7.43 (m, 5H), 7.52 (d, $J = 9.0$ Hz, 2H), 7.70 (d, $J = 8.4$ Hz, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 21.9, 55.4, 114.5, 117.6, 117.8, 126.8, 128.8, 129.1, 129.2, 129.5, 130.2, 130.3, 130.9, 132.9, 145.8, 153.0, 161.3, 188.5, 193.5 ppm.

3,5-Bis(4-methylphenyl)-4,5-dioxo-2-phenyl-2-pentenenitrile (**5c**)

Colorless solid (31%), mp 117°C. Anal. calcd. for $C_{25}H_{19}NO_2$: C, 82.17; H, 5.24; N, 3.83. Found: C, 82.20; H, 5.27; N, 3.86. IR (KBr): $\nu_{max}$ 1656, 1691, 2206 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H), 2.41 (s, 3H), 7.12–7.52 (m, 11H), 7.72 (d, $J = 8.4$ Hz, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 21.5, 21.9, 117.6, 118.7, 129.0, 129.1, 129.1, 129.2, 129.5, 129.8, 130.3, 130.4, 131.6, 132.8, 141.0, 149.9, 153.5, 188.6, 193.6 ppm.

Ethyl 6-(4-chlorophenyl)-4-(methoxyphenyl)-2-oxo-2*H*-pyran-3-carboxylate (**7a**)

Colorless solid (32%), mp 119°C. Anal. calcd. for $C_{21}H_{17}ClO_5$: C, 65.55; H, 4.45. Found: C, 65.59; H, 4.52. IR (KBr): $\nu_{max}$ 1604, 1625, 1708 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 1.13 (t, $J = 7.2$ Hz, 3H), 3.84 (s, 3H), 4.20 (q, $J = 7.2$ Hz, 2H), 6.71 (s, 1H), 6.96 (d, $J = 8.7$ Hz, 2H), 7.41 (d, $J = 8.7$ Hz, 2H), 7.42 (d, $J = 9.0$ Hz, 2H), 7.79 (d, $J = 9.0$ Hz, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 13.8, 55.4, 61.8, 103.6, 114.3, 115.9,

127.1, 128.0, 128.9, 129.2, 129.3, 137.6, 154.5, 158.9, 159.3, 161.3, 165.1 ppm.

4-(4-Methoxyphenyl)-6-(4-methylphenyl)-2-oxo-2*H*-pyran-3-carbonitrile (**8b**)

Colorless solid (37%), mp 199°C. Anal. calcd. for $C_{20}H_{15}NO_3$: C, 75.70; H, 4.76; N, 4.41. Found: C, 75.68; H, 4.77; N, 4.43. IR (KBr): $\nu_{max}$ 1602, 1617, 1743, 2217 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 2.44 (s, 3H), 3.90 (s, 3H), 6.89 (s, 1H), 7.07 (d, $J = 8.7$ Hz, 2H), 7.32 (d, $J = 8.4$ Hz, 2H), 7.76 (d, $J = 8.7$ Hz, 2H), 7.82 (d, $J = 8.4$ Hz, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 21.6, 55.4, 102.2, 114.6, 115.2, 126.3, 126.4, 127.2, 129.9 (two carbons merged here), 130.0, 143.6, 157.6, 162.7, 162.9, 163 ppm.

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