SHORT PAPER

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Access to unsymmetrical 1,2-diketone intermediates *via* benzeneseleninic anhydride-promoted oxidation: application to indolone-N-oxide synthesis

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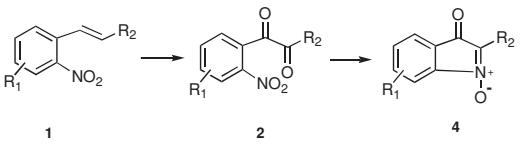
1,2-Dicarbonyl compounds employed as key-intermediates in indolone-N-oxide synthesis were prepared by direct oxidation of aryl, aryl- and aryl, alkyl-substituted alkenes assisted by benzeneseleninic anhydride.

Keywords: oxidation, 1,2-dicarbonyl systems, indolone-N-oxide, benzeneseleninic anhydride

1,2-Dicarbonyl compounds have found widespread applications in the synthesis of several heterocyclic compounds.[1] For instance, in our research project focused on the indolone-N-oxide derivatives synthesis of, dicarbonyl compound **2** has proved to be a useful intermediate[2,3] (Scheme 1).

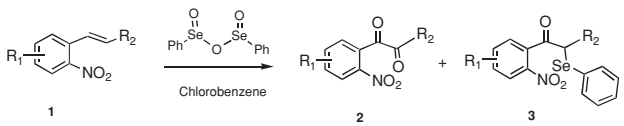


Scheme 1

Many good synthetic approaches for alkyl and aryl substituted 1,2-diketones involving (i) oxidation of benzoin, acyloin and vicinal diols, (ii) use of masked acyl anion synthons and (iii) others reactions, have been described.[4] However, these synthetic pathways involve a laborious preparation of the pivotal precursors. In contrast, there are relatively few examples documented for the preparation of 1,2-diketones by direct oxidation of the parent 1,2-disubstituted alkene[5] which can be easily prepared by a Wittig reaction.

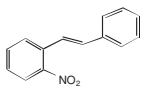
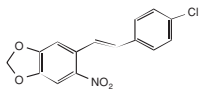
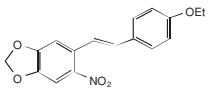
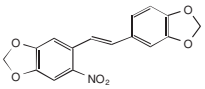
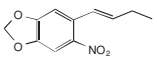
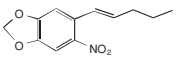
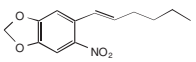
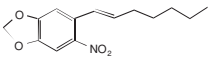
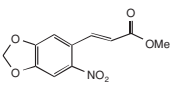
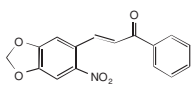
Our approach, which involved converting **1d** into **2d** (Table 1) using DMSO-based oxidative systems (HBr/DMSO and I_2/DMSO) did not provide satisfactory results. In contrast, **2a–e** were obtained from oxidation of **1a–e** by $KMnO_4$. Even though this procedure provides a good route for the preparation of dicarbonyl moieties, our results indicated that this reaction unavoidably led to the formation of a by-product (ketoacetate) which was sometimes difficult to eliminate by column chromatography thus lowering the yield. Recently, Rabideau *et al.*[6] reported that benzeneseleninic anhydride (BSA), a strong oxidising agent,[7] was able to convert stilbene into a dibenzil compound. Our interest in the synthesis of 1,2-dicarbonyl systems led us to investigate the general applicability of BSA towards the oxidation of a series of olefines which have been used as key intermediates for the synthesis of indolone-N-oxide. The scope and limitations of this reaction can be gauged from the wide range of substrates in Table 1. As precursors of diketone **2**, the parent alkenes **1** were synthesised by a Wittig reaction using a phase transfer catalysis agent (Bu_4NCl).

The transformation of stilbene derivatives **1a–d** into dicarbonyl compounds **2a–d** (Table 1) was cleanly and conveniently accomplished using BSA in dichlorobenzene at 120 °C (Scheme 2). These conditions converted both double bond isomers (*Z*/*E*). A long reaction time (ca 220 h) was



Scheme 2

Table 1 Benzene seleninic anhydride promoted-oxidation

Substrate		Reaction Time	Yield of **2**/%	Yield of **3**/%
1a		280 h	62%[a]	0%
1b		257 h	56%[a]	0%
1c		140 h	70%[a]	0%
1d		250 h	50%[a]	0%
1e		10 h	29%[b]	22%[b]
1f		17 h	40%[b]	19%[b]
1g		16 h	27%[b]	7%[b]
1h		18 h	20%[b]	10%[b]
1i		120 h	–	–
1j		120 h	–	–

The structures of the 1,2-diketone compounds were characterised by IR, NMR, MS, TLC and compared with data obtained from authentic samples.[2,3] [a] Isolated yields after silica gel column chromatography. [b] Isolated yields after silica gel column chromatography and preparative layer chromatography.

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

required to accomplish this conversion; however it offers the advantage of being completely selective affording diketones as a single product in good yields. The structures of all isolated reaction products were established by IR, NMR, MS and the spectral data were similar to those obtained for the products prepared by the $KMnO_4$ procedure.[2] In an attempt to extend this simple and straightforward methodology to the preparation of other dicarbonyl systems, we have also prepared aryl, alkyl-alkenes. BSA was also able to oxidise aryl, alkyl-alkenes **1e–h** into unsymmetrical disubstituted 1,2-diketones (Table 1). While oxidation of aryl, aryl-alkenes proceeds under harsher conditions giving only one product, aryl, alkyl-alkenes oxidations require shorter reaction times (ca 15 h) giving the desired diketone **2** accompanied by the α-phenylseleno ketone compound **3**. The latter was assigned the reported structure on the basis of its spectroscopic data. In particular the mass spectrum and the ^{1}H NMR spectrum which shows a double doublet at 3.8 ppm due to C*H*SePh. The diketones which were obtained showed spectral data identical to those of authentic samples obtained by another route ($KMnO_4$).[2,3] It is interesting to note that **3** even after reaction with an excess of BSA was not converted to a 1,2-diketone.

Oxidation reactions of alkenes attached to an electron withdrawing group (**1i–j**) were not possible in similar conditions. No significant reaction was detected even after 120 hours. Indeed this same behaviour was also observed when **1i** was treated with $KMnO_4$ in acetic anhydride. The non reactivity of **1i–j** can be mainly attributed to the strong electron withdrawing effect of the methoxy carbonyl and phenacyl groups reducing the electronic density of the double bond.

In conclusion, we have demonstrated that this process based on BSA-assisted diketone preparation provides an improved route to 2-aryl indolone-N-oxides. However, $KMnO_4$ remains the best oxidant agent for the synthesis of aryl, alkyl-diketones.

Experimental

A typical synthetic procedure for aryl, aryl 1,2-diketone: To a solution of alkene **1c** 64.6 mg (2.1 x 10^{-4} mol) in chlorobenzene (20 ml) was added BSA (224.6 mg, 4.1 x 10^{-4} mol). The final mixture was then heated at 120 °C with stirring for 140 h. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, eluent: cyclohexane then cyclohexane/ethyl acetate 95:5) to give the corresponding diketone.

1a: Yield 62 % Rf 0.33 (cyclohexane/ethyl acetate 70:30). FT-IR (KBr) cm^{-1}: 2919, 2853, 1809, 1694, 1674, 1597, 1526, 1450, 1345, 1318, 1258, 1203, 1183, 1040, 1019, 998, 860, 840, 806, 788, 769, 725, 688, 640. ^{1}H NMR ($CDCl_3$, 200 MHz) : δ 7.46–7.84 (m, 6H) ; 8.13-8.17 (m, 3H). MS (EI): *m*/*z* 255 (M+), 105, 77.

1b: Yield 56 % Rf 0.51 (cyclohexane/ethyl acetate 70:30). FT-IR (KBr) cm^{-1}: 3117, 3062, 2920, 2850, 1733, 1682, 1603, 1587, 1505, 1486, 1430, 1329, 1327, 1149, 1092, 1035, 929, 873, 816, 785, 761. ^{1}H NMR ($CDCl_3$, 200 MHz) : δ 6.25 (s, 2H) ; 7.10 (s, 1H) ; 7.51 (d, *J* = 8.5 Hz, 2H) ; 7.56 (s, 1H) ; 8.14 (d, *J* = 8.5 Hz, 2H). MS (EI): *m*/*z* 333 (M+), 303 (M+ - 30), 194, 178, 139, 120, 111, 75.

1c: Yield 70 % Rf 0.33 (cyclohexane/ethyl acetate 70:30). FT-IR (KBr) cm^{-1}: 1690, 1649, 1598, 1565, 1514, 1483, 1426, 1327, 1265, 1171, 1140, 1073, 1031, 922, 865, 784, 756. ^{1}H NMR ($CDCl_3$, 200 MHz) : δ 1.46 (t, *J* = 7.0 Hz, 3H), 4.14 (q, *J* = 7.0 Hz, 2H), 6.23 (s, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 7.08 (s, 1H), 7.58 (s, 1H), 8.16 (d, *J* = 9.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 14.9 (CH_3), 64.2 (CH_2), 104.2 (CH_2), 104.8 (CH), 109.9 (CH), 114.6 (CH × 2), 125.5 (C), 131.1 (C), 133.5 (CH × 2), 142.4 (C), 150.6 (C), 153.3 (C), 164.4 (C), 186.6 (C), 189.7 (C). MS (EI): *m*/*z* 313 (M+ - 30), 281, 194, 178, 166, 149, 121, 93, 65.

1d: Yield 50 % Rf 0.36 (cyclohexane/ethyl acetate 70:30). FT-IR (KBr) cm^{-1}: 3120, 3064, 2924, 2853, 1687, 1657, 1601, 1516, 1487, 1446, 1428, 1330, 1267, 1243, 1112, 1060, 1035, 923. ^{1}H NMR ($CDCl_3$, 200 MHz) : 6.12 (s, 2H) ; 6.27 (s, 2H) ; 6.98 (d, *J* = 8.3 Hz, 1H) ; 7.13 (s, 1H) ; 7.64 (s, 1H) ; 7.59 (d, *J* = 2.0 Hz, 1H) ; 7.93 (dd, *J* = 8.3 Hz, *J* = 2.0 Hz, 1H). MS (EI): 343 (M+), 314, 194, 179, 149, 121, 84.

A typical synthetic procedure for alkyl, aryl 1,2-diketone: To a solution of alkene **1f** 56.2 mg (2.4 × 10^{-4} mol) in chlorobenzene (20 ml) was added BSA (370 mg 7.2 × 10^{-4} mol). The final mixture was then heated to 120 °C with stirring for 17 h. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel eluent: cyclohexane then cyclohexane/ethyl acetate 95:5) and then by preparative layer chromatography (eluent: toluene) to give the corresponding 1,2-diketone.

1e: Yield 29 % Rf 0.41 (cyclohexane/ethyl acetate 70:30). FT-IR (KBr) cm^{-1}: 2978, 2916, 1706, 1607, 1524, 1509, 1483, 1426, 1368, 1332, 1275, 1114, 1036, 927, 886, 873, 811. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.13 (t, *J* = 7.2 Hz, 3H), 2.95 (q, *J* = 7.2 Hz, 2H), 6.17 (s, 2H), 6.87 (s, 1H), 7.54 (s, 1H). MS (CI/NH_3): *m*/*z* 286 (M+ + 35), 269 (M+ + 18), 251 (M+ + 1), 195.

1f: Yield 40 % Rf 0.48 (cyclohexane/ethyl acetate 70:30). FT-IR (KBr) cm^{-1}: 2965, 2931, 2876, 1702, 1624, 1609, 1523, 1507, 1486, 1430, 1370, 1333, 1275, 1035, 930, 877, 799, 759, 741, 659, 601. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.94 (t, *J* = 7.3 Hz, 3H), 1.64 (m, 2H), 2.91 (t, *J* = 7.3 Hz, 2H), 6.17 (s, 2H), 6.87 (s, 1H), 7.54 (s, 1H). MS (CI/CH_4): *m*/*z* 294 (M+ + 1).

1g: Yield 27 % Rf 0.46 (cyclohexane/ethyl acetate 70:30). FT-IR (KBr) cm^{-1}: 2960, 2930, 2874, 1709, 1524, 1505, 1485, 1430, 1331, 1277, 1035, 929, 876, 816, 756, 725. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.89 (t, 3H, *J* = 7.2 Hz) ; 1.20–1.70 (m, 4H) ; 2.92 (t, 2H, *J* = 7.2 Hz) ; 6.17 (s, 2H) ; 6.87 (s, 1H) ; 7.54 (s, 1H). MS (CI/NH_3): *m*/*z* 297 (M+ + 18).

1h: Yield 20 % Rf 0.51 (cyclohexane/ethyl acetate 70:30). FT-IR (KBr) cm^{-1}: 2956, 2918, 2850, 1691, 1522, 1506, 1483, 1426, 1334, 1272, 1035, 929, 874, 816, 741, 691, 668. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.86 (t, 3H, *J* = 7.0 Hz) ; 1.15-1.80 (m, 6H) ; 2.91 (t, 2H, *J* = 7.0 Hz) ; 6.17 (s, 2H) ; 6.86 (s, 1H) ; 7.54 (s, 1H). MS (CI/NH_3): *m*/*z* 328 (M+ + 35), 311 (M+ + 18), 294 (M+ + 1).

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