Oxidation of 1,2,5-Thiadiazolidine 1,1-Dioxides: Synthesis of Diaryl 1,2-Diketones

Sunil V. Pansare* and Mahesh G. Malusare

Division of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune 411008, India

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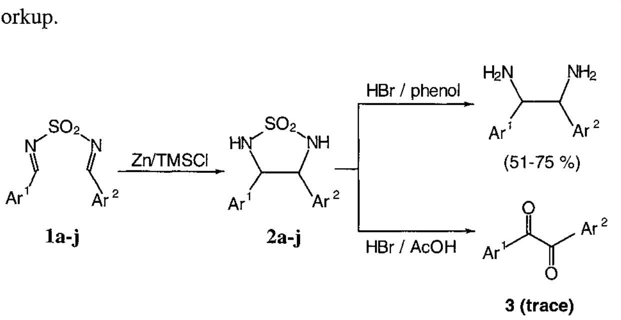
Abstract: Treatment of 3,4-diaryl 1,2,5-thiadiazolidine 1,1-dioxides with selenium dioxide followed by hydrolysis of the crude oxidation product furnishes the corresponding diaryl 1,2-diketones. Symmetrical and unsymmetrical diketones are readily prepared by this method.

The 1,2-diketone functionality has found several applications in synthesis[1] and in biological systems.[2] The synthesis of symmetrical and unsymmetrical 1,2-diketones has therefore been actively investigated in recent years. Most of the current approaches rely on sequential functionalization of oxalyl diamides,[3] oxidation of alkenes and alkynes,[4] elaboration of acylanion equivalents[5] and oxidation of phosphoranes,[6] 1,2-diols,[7] ketones[8] and α-hydroxy ketones.[9] Herein we describe preliminary results on a new approach to symmetrical and unsymmetrical 1,2-diaryl ketones that involves oxidation of 1,2,5-thiadiazolidine 1,1-dioxides.

Sulfamide bisimines **1** are readily converted to 1,2,5-thiadiazolidine 1,1-dioxides **2** by treatment with Zn/TMSCl[10] (Scheme 1). These thiadiazolidines can be converted to vicinal diamines by acid mediated (HBr/phenol) cleavage of the heterocyclic ring.[10] During these studies, especially when HBr/AcOH was used for sulfamide cleavage, we observed the formation of trace amounts of α-diketones. Considering that acid mediated cleavage of sulfonamides involves a redox process,[11] it seemed plausible that the diketones were obtained by oxidation of the thiadiazolidine to a thiadiazole which underwent hydrolysis[12] during workup.



Scheme 1

Attempts to optimize the oxidation reaction by treatment with HBr, HI or bromine under a variety of conditions were unsuccessful and we therefore focused on other oxidising agents.

Orienting experiments were performed with **2a** (mixture of *cis* and *trans* isomers) and sodium hypochlorite[13] as the oxidant. Although the yields of the diketone **3a** (15-20%) were higher than with HBr, the product was always contaminated with benzaldehyde and *p*-tolualdehyde and purification was difficult. The aldehydes are probably obtained from the bisimine **1a** which may be formed by mono *N*-chlorination of **2a** followed by a fragmentative elimination of HCl (Figure 1).

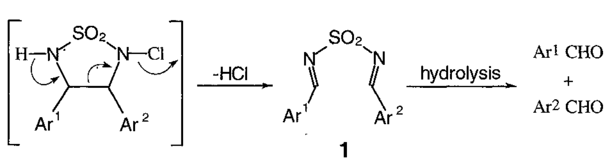
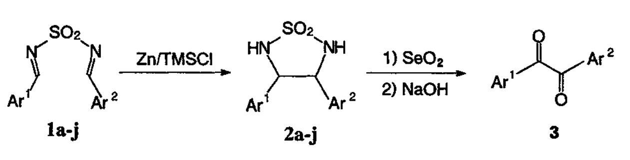


Figure 1

Modification of the procedure by treatment with sodium hypobromite or *tert*-butyl hypochlorite[14] did not suppress aldehyde formation. Although **2a** could not be oxidized with lead tetraacetate[15] or with DDQ,[16] oxidation with selenium dioxide[17] was successful. The reaction proceeded in solvents such as acetic acid, dioxane or benzene but the solvent of choice was DMF. The crude oxidation product obtained by treatment of **2a** with SeO_2 was hydrolysed with aq. NaOH to furnish the diketone **3a**[18] in 65% yield (Scheme 1). The conversion constitutes a new approach to aryl α-diketones involving a reductive coupling/ oxidation sequence that is based on the aryl aldehydes as starting materials. The reaction is applicable to a variety of substrates with alkyl and alkoxy substitution in the aromatic ring and more importantly, provides an access to the unsymmetrical diketones by a cross-coupling of aryl aldehyde imines followed by oxidation. The results are summarized in Table 1. The conversion of **2** to **3** also emphasizes the utility of 1,2,5-thiadiazolidine 1,1-dioxides as synthetic intermediates for vicinally functionalized molecules.

Tablel. Conversion of 3,4-diaryl 1,2,5-thiadiazolidine 1,1-dioxides 2 to diaryl 1,2-diketones 3



Compound	Ar^1, Ar^2	Yield %, 2^a	Yield %, 3^b
1a	Ph, 4MePh	85	65
1b	Ph, 4MeOPh	55	52
1c	Ph, 2naphthyl	75	52
1d	Ph, piperonyl	66	45
1e	Ph, 2MePh	63	-
1f	Ph, Ph	72	58
1g	Ph, 4ClPh	71	-
1h	4MePh, 4MePh	70	64
1i	Ph, 2furyl	38	-
1j	4MeOPh, 4MeOPh	90	48

a: *cis/trans* mixture. b: Isolated, unoptimised yields

The SeO_2 oxidation of **2** probably generates the corresponding thiadiazole 1,1-dioxide which was isolated (21% yield) in the oxidation of **2h**. However, due to the instability of the thiadiazole 1,1-dioxides on silica gel and the presence of other products which render crystallization impractical, the crude oxidation product was used further without purification. Oxidation of **2i** led to a complex mixture, presumably due to side reactions involving the furan ring. The reasons for the lack of diketone formation from **2e** and **2g** are not apparent at present.

In conclusion, we have developed a new approach to diaryl α-diketones from the readily available aryl aldehydes. The method is applicable to the synthesis of unsymmetrical 1,2-diaryl 1,2-ethanediones.

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18. Satisfactory ^{1}H NMR, IR and mass spectral data were obtained for all diketones. All new diketones also exhibited satisfactory microanalytical data.

    General procedure for preparation of 1,2-diketones 3: To a solution of **2** in anhydrous DMF was added SeO_2. The resulting mixture was heated at 78-80 °C under argon for 10-12 h and the reaction was monitored by TLC. The reaction mixture was cooled, diluted with EtOAc and filtered through celite. The filtrate was washed with saturated aq. $NaHCO_3$, aq. thiourea and water. The residue obtained after concentration was used further without purification. The crude oxidation product was dissolved in THF and 2N NaOH was added. The mixture was stirred at room temperature for 4-6 h and the diketone was isolated by extraction with EtOAc and chromatography on basic alumina. Thus, reaction of **2d** (160 mg, 0.5 mmol) with SeO_2 (222 mg, 2.0 mmol) in anhydrous DMF (5 ml) at 78-80 °C for 12 h furnished 162 mg of a red gum which was dissolved in THF (1 ml), 2N NaOH (2 ml) added and the mixture was stirred at room temperature for 4 h. The crude product (97 mg) was purified (basic alumina, 95/5 petroleum ether/EtOAc) to give analytically pure **3d** (58 mg, 45%). Data for **3d**: mp. 117-119 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.95 (m, 2 H, Ar*H*), 7.7-7.6 (m, 1 H, Ar*H*), 7.6-7.5 (m, 4 H, Ar*H*), 6.9 (d, $J = 8.5$, 1 H, Ar*H*), 6.1 (s, 2 H, CH_2O). IR (CCl_4): 3066, 1663, 1599, 1503, 1488, 1446, 1364, 1179, 1145, 1112, 1102, 1074, 1036, 999, 935, 924, 882, 850, 821, 810 cm^{-1}. ^{13}C NMR: (75.5 MHz, $CDCl_3$): δ 194.4 (Ar*C*O), 192.7 (Ar*C*O), 153.4 (*CO ipso*), 148.6 (*CO ipso*), 134.7, 133.2 (*C ipso*, Ph), 129.8, 128.9, 127.8, 108.4 (Ar*C*), 102.2 (CH_2O). MS (EI, 70 eV): m/z 65 (50), 77 (60), 91 (9), 105 (30), 121 (26), 149 (100), 254 (M^+ (2)). TLC: R*f* 0.29 (SiO_2, pet. ether/EtOAc, 95/5). Anal. Calcd. for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96. Found: C, 70.67; H, 4.00.