A New Method for the Synthesis of Spiro γ-Butyrolactone *via* Samarium(II) Iodide-induced Cyclization

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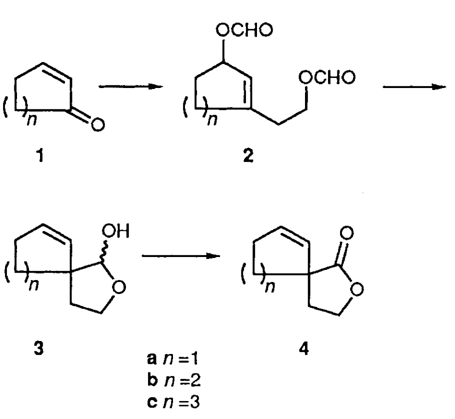
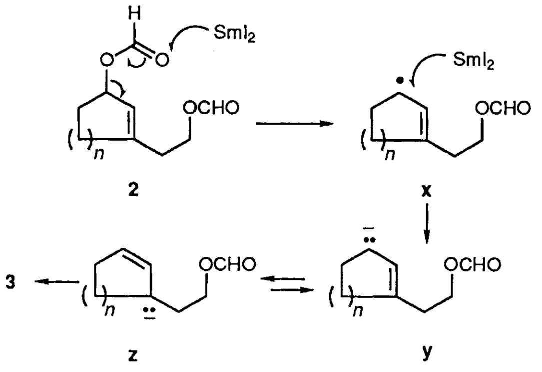
Reactions of 1-(2-formyloxyethyl)-3-formyloxycycloalkenes **2** with samarium(II) iodide give hemiacetals **3** which are subsequently converted to spiro γ-butyrolactones **4**.

Much interest is presently being directed to reactions using samarium(II) iodide (SmI_2) in organic synthesis.[1] During a study on SmI_2-induced reactions, new intramolecular reductive carbon–carbon bond formation was noted in reactions of 1-(2-formyloxyethyl)-3-formyloxycycloalkenes **2** with SmI_2 giving the spiro hemiacetals **3**. Diformates **2** could be easily prepared from the corresponding conjugated cycloalkenones **1** and the hemiacetal **3** converted to spiro γ-butyrolactones **4**, thus showing this method to be an effective means for the synthesis of spiro γ-butyrolactones **4** from **1**.

Diformates **2** were synthesized from enones **1** in four steps:† (*i*) 1,2-addition of the lithium enolate of *tert*-butyl acetate to enones; (*ii*) reduction with lithium aluminium hydride; (*iii*) formylation of the primary hydroxy groups; and (*iv*) sequential 1,3-rearrangement–formylation of the allylic alcohols with formic acid (Scheme 1). Treatment of diformates **2** with SmI_2 from samarium metal and 1,2-diiodoethane[2] in a 2:1 mixture of tetrahydrofuran (THF)–hexamethylphosphorictriamide (HMPA) at room temperature gave hemiacetal **3** as a diastereoisomeric mixture.‡ In the absence of HMPA, this reaction caused considerable decrease in the yield of **3** (5 to



Scheme 1



Scheme 2

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† *Reagents and conditions*: for preparation of **2b**: (*i*) $MeCO_2Bu^t$ (2 equiv.), lithium diisopropylamide (LDA) (2 equiv.), THF, −78 to 0 °C, 95%; (*ii*) $LiAlH_4$ (3 equiv.), THF, 0 °C to room temp., 94%; (*iii*) AcOCHO (1.2 equiv.), pyridine (1.6 equiv.), CH_2Cl_2, 0 °C to room temp.; (*iv*) HCO_2H–1,4-dioxane (2:1), 84% (two steps).

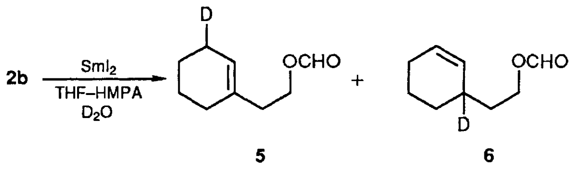
‡ *Typical procedure*: to a solution of SmI_2 (1.5 mmol) in THF (6 ml)–HMPA (3 ml) was added a solution of **2b** (99 mg, 0.50 mmol) in THF (1 ml) at room temperature under an argon atmosphere. The mixture was stirred for 10 min at this temperature, quenched with aqueous ammonium chloride, and extracted with diethyl ether. The ethereal solution was dried. Following removal of the solvent under reduced pressure, the crude product was purified by silica gel column chromatography to give **3b** (56 mg) in 73% yield.

Table 1

Diformate[a]	Cyclization product[a,b] Yield (%)[c]	Oxidation product[a,d] Yield (%)[c]
2a (n = 1)	**3a** (55%)	**4a** (81%)
2b (n = 2)	**3b** (73%)	**4b** (82%)
2c (n = 3)	**3c** (75%)	**4c** (83%)

[a] All compounds were fully characterized by ^{1}H NMR (400 MHz), IR and high resolution mass spectroscopy and/or combustion analysis.¶ [b] **3a**, **3b** and **3c** are diastereoisomeric mixtures of 7 : 3, 7 : 3 and 1 : 1, respectively. [c] Yields refer to chromatographically homogeneous material. [d] Oxidation was conducted using 2 equiv. of PDC in methylene chloride at room temperature.

10% yield).§ This reaction can be performed irrespective of ring size (five-, six- or seven-membered cycloalkenes) as evident from Table 1. Hemiacetals **3** could be easily converted to the corresponding spiro γ-butyrolactones **4** by pyridinium dichromate (PDC) oxidation.



Scheme 3

A plausible reaction pathway for the present SmI$_2$-induced intramolecular cyclization is shown in Scheme 2. Allylic anions **z** from intermediates **x** and **y** are trapped intramolecularly by formyl carbonyls to give **3**. The presence of the allylic anions was supported by the formation of deuteriated products **5** and **6** (4 : 1, 64% yield) when the reaction of **2b** with SmI$_2$ was carried out in THF–HMPA–D$_2$O (20 : 10 : 1).[4]

The present method makes possible not only the synthesis of spiro γ-butyrolactones **4** from **1**, but also conversion of the carbonyl carbon of α,β-unsaturated ketones **1** to the quaternary carbon. Studies on the use of these reactions for the synthesis of natural products are presently being conducted.

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¶ *Selected spectroscopic data* for **2a**: ^{1}H NMR (270 MHz, CDCl$_3$) δ 1.10–2.70 (6H, m), 4.32 (2H, t, J 6.8 Hz), 5.59 (1H, d, J 2.0 Hz), 5.78 (1H, br s), 8.02 (1H, s), 8.04 (1H, s); IR (neat) ν/cm^{-1} 1720. **2b**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.50–2.15 (6H, m), 2.36 (2H, t, J 6.8 Hz), 4.27 (2H, t, J 6.8 Hz), 5.38 (1H, br s), 5.56 (1H, br s), 8.04 (1H, s), 8.06 (1H, s); IR (neat) ν/cm^{-1} 1720. For **2c**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.30–2.42 (8H, m), 2.35 (1H, t, J 6.9 Hz), 4.23 (2H, t, J 6.9 Hz), 5.50 (2H, br s), 8.04 (2H, s); IR (neat) ν/cm^{-1} 1720. For **4a**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.85–2.0 (2H, m), 2.15–2.7 (4H, m), 4.24–4.38 (2H, m), 5.61 (1H, dt, J 5.9 and 2.0 Hz), 6.02 (1H, dt, J 5.9 and 2.4 Hz); IR (neat) ν/cm^{-1} 1761. For **4b**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.51–1.76 (2H, m), 1.88–2.34 (6H, m), 4.22–4.39 (2H, m), 5.51 (1H, dt, J 9.9 and 2.0 Hz), 5.98 (1H, dt, J 9.9 and 3.8 Hz); IR (neat) ν/cm^{-1} 1765. For **4c**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.53–2.40 (10H, m), 4.19–4.34 (2H, m), 5.57 (1H, d, J 11.7 Hz), 5.94 (1H, dt, J 11.7 and 5.8 Hz); IR (neat) ν/cm^{-1} 1768.

§ The reaction of **2b** or 1-(2-formyloxyethyl)-3-acetyloxycyclohexene with SmI$_2$ in the presence of palladium catalyst[3] in THF, gave a complicated mixture.

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