Samarium(II) Iodide-Promoted Reactions of 2,3-Epoxycycloalkanone Hydrazones

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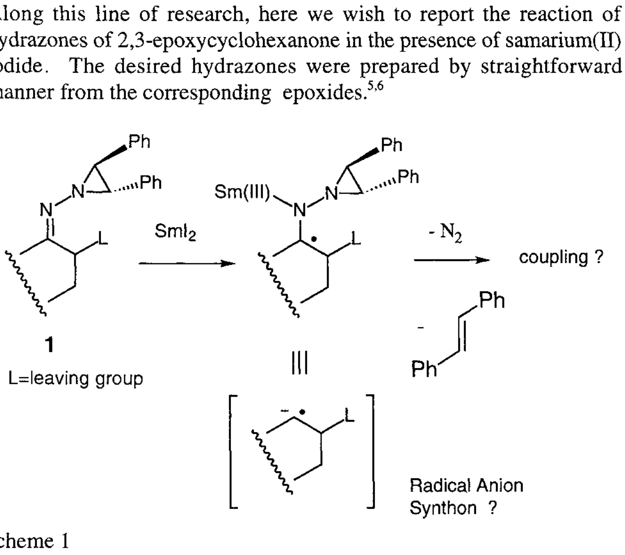
Abstract: The reaction of hydrazones of 2,3-epoxycycloalkanone promoted by samarium(II) iodide has been investigated to study the behavior of the compounds containing C=N bonds in the presence of this powerful single-electron transfer reagent. For the hydrazones derived from 2,3-epoxycyclopentanone and 2,3-epoxycyclohexanone, 3-iodo-2-cycloalkenols were isolated while the corresponding 2-cycloalkenols were the products when the hydrazones from 2,3-epoxycycloheptanone and 2,3-epoxycyclooctanone were reacted.

After pioneering research by the Kagan group, samarium(II) iodide has become a powerful reagent in synthetic organic chemistry since this reagent promotes a variety of reactions.[1] Although a number of reports on reactions centered on C=O bonds have appeared, examples of samarium(II) iodide-promoted reactions centered on C=N bonds have been quite limited. Several cases of samarium(II) iodide reactions on C=N bonds have reported including the coupling of imines as well as reduction of imines.[2,3]

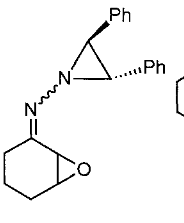
In connection with our interest on the reactions promoted by samarium(II) iodide, we have investigated the behavior of this reagent with C=N bonds. Although the tin radical addition to the hydrazone **1** has been reported,[4] the reaction of hydrazones with samarium(II) iodide has never been studied.

We anticipated that, when a hydrazone derivative was treated with samarium(II) iodide, transfer of an electron to the C=N bond would generate the intermediate that could be considered as a radical anion synthon from which, after releasing nitrogen and stilbene, some interesting reactions such as coupling would take place (Scheme 1). Along this line of research, here we wish to report the reaction of hydrazones of 2,3-epoxycyclohexanone in the presence of samarium(II) iodide. The desired hydrazones were prepared by straightforward manner from the corresponding epoxides.[5,6]

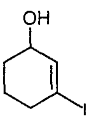


Scheme 1

First, the samarium(II) iodide-promoted reaction of the hydrazone **1a**, derived from 2,3-epoxycyclohexanone, was investigated. The entire reaction was performed with samarium(II) iodide in THF in the presence of tBuOH.[7] The product, which was later identified as an iodide **2**, was isolated. Spectroscopic properties of the product were very similar to those of the expected coupled product.



1a



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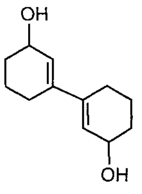

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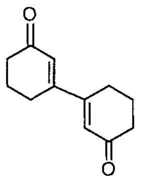

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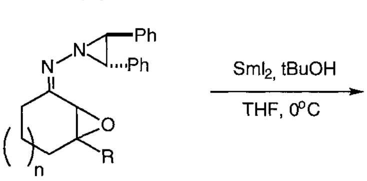
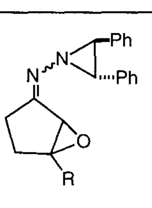
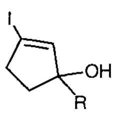
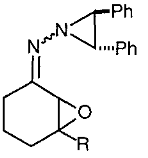
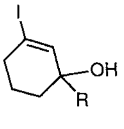
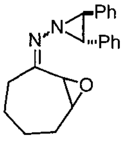
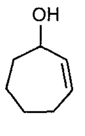
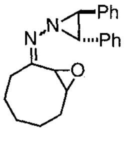
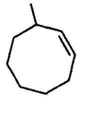
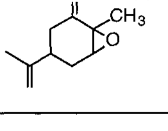
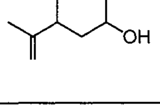
However, the ^1H NMR data of the ketone obtained after oxidation of the product **2** did not match with those of diketone **4**, the spectroscopic data of which were available in the literature.[8] By analysis of spectroscopic data and, more precisely, an X-ray crystallographic analysis of the *p*-nitrobenzoyl ester of the alcohol **2**, the structure of **2** was identified as 3-iodo-2-cyclohexenol (**2**).[9,10] We were surprised that the major compound **2** was not a dimer **3** but an iodinated alcohol **2**. Iodination in the presence of SmI_2 has been rare[11] and this makes an interesting example.

We investigated the reaction of 2,3-epoxycycloalkanone hydrazones with samarium(II) iodide and the results are summarized in Table 1. Both epoxycyclopentanone hydrazones (entries 1 and 2)

Table 1. Reactions of epoxyhydrazones with SmI_2

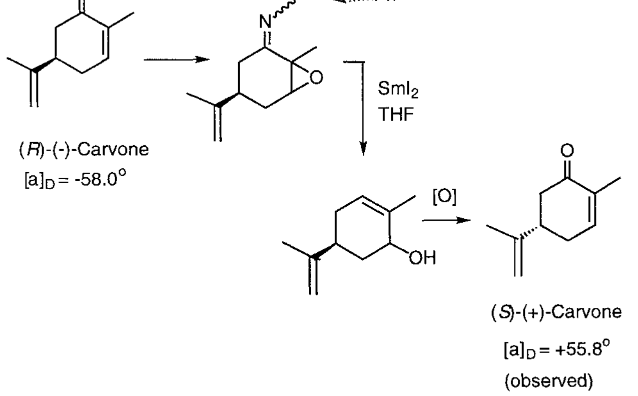


entry	n	R	Reactant	SmI_2 (equiv used)	Product	yield (%)
1	0	H		2.2		22
2	0	CH_3		4.3		18
3	1	H		2.2		35
4	1	CH_3		3.0		29
5	2	H		4.0		75
6	3	H		6.0		79
7	1	H		3.0		68

and epoxycyclohexanone hydrazones (entries 3 and 4) provide the corresponding 3-iodo-2-cycloalkenols. Low yields were presumably due to instability of the products. The compounds in the product column (Table 1) are the only products isolated in significant yields. In contrast, in the case of epoxycycloheptanone and cyclooctanone hydrazones (entries 5 and 6), the corresponding 2-cycloalkenols were isolated in reasonable yields. A more sterically demanding system, such as carvone hydrazone shown in entry 7, also provided a 2-cycloalkenol without retaining the iodine atom. The origin of the difference in products depending on the ring size is not clear at this moment.

To gain some further insight into the mechanism of the reaction, the following experiment was devised (Scheme 2). (*R*)-Carvone (α_D^{20} = +58.0°) was epoxidized and the corresponding hydrazone was prepared. After the reaction with samariun(II) iodide, the product, cycloalkenol was isolated (in 68% yield). Swern oxidation of the resulting alcohol to a ketone, regenerated carvone. Measurement of the optical rotation of the obtained carvone, revealed that α_D^{20} = +55.8° was obtained. From the reversal of the sign of the optical rotation from (*R*)-(-)-carvone, it is confirmed that 1,3-transposition of the oxygen functionality occurred as expected.

Several features of the reactions deserve comments. A complex mixture of products was obtained when HMPA was present in the reaction medium. Change in the order of addition and lowering the reaction temperature did not improve the reaction yields. Isomers of hydrazones from 2,3-epoxycyclohexanone were separated and treated with samarium(II) iodide. Since similar yields were obtained from both isomers, the stereochemistry of the C=N bond in hydrazones apparently does not affect the reaction rate.



Scheme 2

Acknowledgment. This investigation was supported in part by a grant from the Korea Science and Engineering Foundation (92-25-00-08).

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7. Typical procedure: To a solution of **1a** (83 mg, 0.27 mmol) and tBuOH(50 μL) in THF (10 mL) was added SmI_2(0.60 mmol) in THF at 0 °C. After stirring for 10 min at 0 °C, saturated NH_4Cl solution was added. Usual workup and silica-gel chromatography provided 3-iodo-2-cylclohexen-1-ol (**2**) (21 mg, 35%) as an oil.
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9. Crystal data for the *p*-nitrobenzoyl ester of **2**: $C_{13}H_{12}INO_4$, FW=373.14; monoclinic, space group P21/a; a=12.322(7), b=4.908(6), c=23.311(7) Å; β=97.96(4)°; *V*=1396(2) $Å^3$; Z=4; d(calcd) = 1.775 g/cm^3, Crystal size 0.26 x 0.35 x 0.43 mm^3. The final R value was 0.0454 for 1622 (I>3σ(I)) reflections.
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