COMMUNICATION

Observations on the samarium diiodide-promoted C–C fragmentation/ring expansion chemistry of some aliphatic 1,4-diketones

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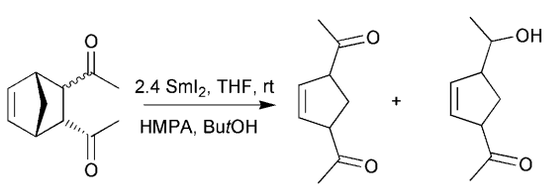
Received (in Cambridge, UK) 9th October 2000, Accepted 7th December 2000
First published as an Advance Article on the web 10th January 2001

Various multicyclic and bridged 1,4-diketones were subjected to the reductive conditions of the SmI_2–HMPA system, often affording surprising results and reactivity upon fragmentation of the 2,3 C–C bond to provide the corresponding ring enlarged product.

Although some SmI_2-promoted C–C fragmentation reactions have been reported, these have been restricted to ring-strained systems.[1] Our previous endeavours in the field of SmI_2-mediated reactions[2] have led us to investigate some fragmentation reactions, and we have recently described the first SmI_2-mediated C–C fragmentation reactions of open chain aromatic 1,4-diketones.[3] As an extension of that work, we investigated similar reactions making use of non-aromatic substrates. Herein, we detail the often unpredicted reactivity of some multicyclic/bridged 1,4-dicarbonyl substrates, and the influence of reaction conditions and remote functionality on the outcome of these reactions. In this respect, we noticed that some photochemical electron transfer,[4] as well as SmI_2-mediated,[5] transformations have been carried out on similar substrates, the latter produced results different from our own (see conclusion).

Subsequent to our work on aromatic 1,4-diketone substrates,[3] we turned our attention to more strained systems, in an attempt to gauge the generality of this reductive transformation, making use of the work of Ghosh[6] as a benchmark. We could readily repeat those results (Scheme 1), but found that

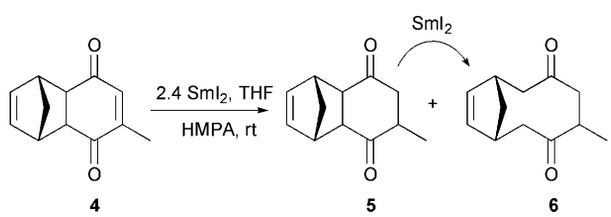


1a: *endo,endo* **1b:** *endo,exo* **2** **3**

Scheme 1

some starting material remained after completion of the reaction (as identified by disappearance of the unmistakable colour of the SmI_2–HMPA complex), along with the expected product of fragmentation **2**. In addition to these compounds, a small amount of the keto-alcohol **3** was isolated,[7] the production of which would also have consumed SmI_2; this would account for the unreacted starting material. During the synthesis of the *endo,endo* substrate **1a**,[8] we also isolated some of the *endo,exo* analogue **1b**.[9] We subjected this substrate to reaction with SmI_2–HMPA at room temperature, and found that the fragmented product **2** could be isolated in a yield of 18%, along with an intractable mass. Heating to reflux, cooling to 0 °C, or the addition of a proton source did not have any positive effect on the outcome of the reaction. It can be reasonably argued that, given the otherwise identical molecule, the ability or not of the SmI_2–HMPA complex to chelate the 1,4-dicarbonyl moiety in the one case (*endo,endo*) and not in the other (*endo,exo*) is the primary factor that determines the success of the fragmentation reaction. This was to be the first indication of the influence of structure on the reactivity of 1,4-dicarbonyl systems.

In keeping with the theme of norbornene † derivatives, several other 1,4-diketone Diels–Alder adducts were prepared according to the literature,[8c] and subjected to reaction with SmI_2–HMPA in THF (addition of the substrate to the SmI_2 solution at room temperature).[3] Diolefin **4** afforded the analogous mono-olefin **5** (41%) and the fragmented macrocyclic product **6** (25%), upon reaction with 2.4 equivalents of SmI_2 (Scheme 2).

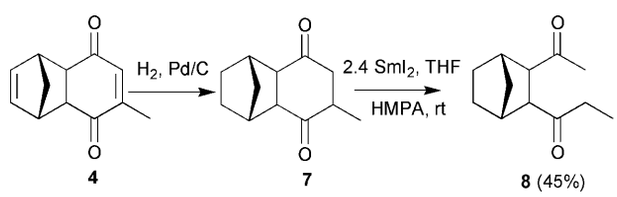


4 **5** **6**

Scheme 2

Making use of an excess (4.8 equivalents) of SmI_2, the selectivity of the reaction could be reversed, affording the products **5** and **6** in yields of 17% and 41%, respectively. These results indicate that the rate of the reduction of the conjugated double bond is faster than the rate of fragmentation, and that diketone **5** is an intermediate in the transformation of **4** into **6**. The latter theory was confirmed by re-subjecting compound **5** to reaction with SmI_2–HMPA in THF, which afforded the anticipated fragmented material **6**.

The diolefin **4** was readily saturated under the action of H_2 in the presence of Pd/C, to afford the saturated product **7** in good yield (Scheme 3). Surprisingly, this substrate afforded the product of the fragmentation of the '*external*' bond (**8**, Scheme 3) in



4 **7** **8** (45%)

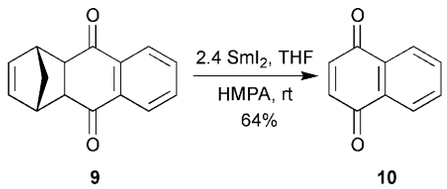
Scheme 3

reactions in which **7** was added to a solution of SmI_2–HMPA in THF: no macrocyclic product of fragmentation of the '*internal*' C–C bond was detected from these reactions. This result, together with the previous reaction of the mono-reduced compound **5**, indicated that the presence or absence of the 'norbornene double bond' is determinative of which C–C bond fragments. The change in selectivity is possibly due to subtle

DOI: 10.1039/b008110h

energy differences in the '*external*' *versus* the '*internal*' bond, these differences are due either to additional ring strain, or to conformational considerations, induced by the double bond.

When added in a dropwise fashion to SmI_2–HMPA in THF, the adduct **9** yielded an altogether different product from any other norbornene derivative that we had studied. While the aromatic macrocyclic product of fragmentation was expected, the reaction provided the quinone product **10** of a retro Diels–Alder reaction (Scheme 4). The product was proved to be that

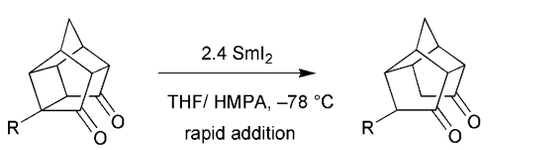


9 **10**

Scheme 4

of a reaction with SmI_2 rather than with *in situ* generated Sm(III) salt (which is known to be a Lewis acid)[10] by a separate reaction of substrate **9** with an *ex situ* generated SmI_2OBn salt. The reaction can reasonably be anticipated to have proceeded *via* the disamarium(III) salt of hydronaphthoquinone; this intermediate would have undergone facile auto-oxidation to naphthoquinone upon contact with air. This observation might represent an alternative means of protecting a naphthoquinone moiety in synthesis.

In response to the interesting results obtained from the norbornene derivatives, we wished to investigate the reactivity of diketone cage compounds,[11] which were readily prepared from the corresponding Diels–Alder adducts by a [2+2] photo-induced cycloaddition. When the cage compounds **11** were treated with SmI_2–HMPA in THF at either the reflux temperature of the reaction mixture or at any temperature above –50 °C, an intractable mixture of products was formed. However, cooling of the reaction mixture to –78 °C allowed the isolation of the fragmented products **12** (Scheme 5) after the SmI_2–



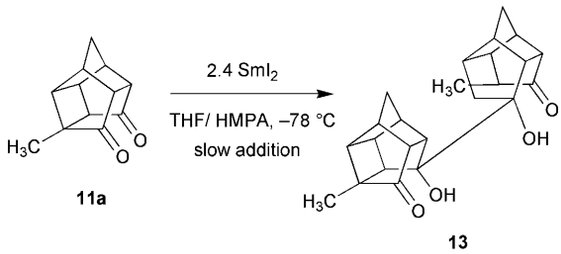
11a: R = CH_3
11b: R = H

12a: R = CH_3 (48%)
12b: R = H (53%)

Scheme 5

HMPA solution had been added in a rapid dropwise fashion. Not unexpectedly, it was the more strained 2,3 C–C bond that fragmented. The fact that the reaction had to be carried out at such a low temperature demonstrated the remarkable degree of ring strain, and hence the ease with which the C–C bond is fragmented, in cage compounds. Similar fragmentation reactions have been carried out on cage compounds under reductive[12] and under photochemical electron transfer[4] conditions, with inconsistent results.

In a repeat reaction making use of cage compound **11a**, the THF solution of SmI_2–HMPA was added to the substrate by very slow dropwise addition. It was of interest to us to note that, along with the C–C fragmented product **12a** (15%), the reaction yielded a dimeric material **13** (17%, Scheme 6), in which one of the cage units had undergone a sequential



11a **13**

Scheme 6

fragmentation–pinacol coupling reaction to an intact cage unit (based on our tentative structural assignment).[7] The slow addition of the SmI_2–HMPA solution presumably afforded the ketyl radicals (that had formed upon initial single electron transfer to the ketone) sufficient time to combine in a pinacol-type reaction, rather than undergo further reduction by excess SmI_2 to afford the fragmented monomeric material (**12a**) previously isolated.

In summary, we have shown that certain strained compounds undergo C–C fragmentation reactions, in an often unpredicted manner. This methodology has allowed ready access to some interesting macrocyclic and other structures, and has yielded an unexpected retro Diels–Alder reaction. In contrast to previous work in which HMPA was not employed as cosolvent for SmI_2-promoted reactions of similar substrates,[5] and in which products of *oxidation* were obtained, our experiments consistently afforded the products of reductive fragmentation. Once again, the dramatic influence of HMPA on the outcome of some SmI_2-mediated reactions has been demonstrated.[3]

Acknowledgement

We thank the Rand Afrikaans University for support of this work.

Notes and references

† The IUPAC name for norbornene is bicyclo[2.2.1]hept-2-ene.

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