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Selective formation of non-conjugated olefins by samarium(II)-mediated elimination/isomerization of allylic benzoates

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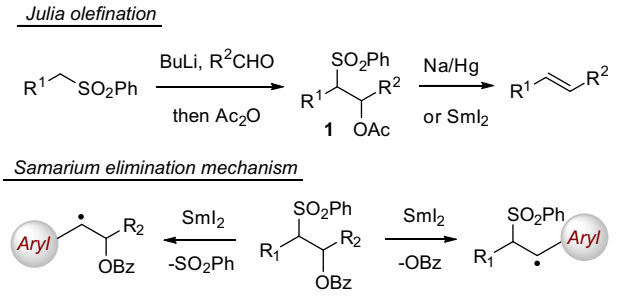
ABSTRACT

Aromatic allylic benzoates can be selectively transformed to the corresponding benzoate eliminated olefin by the action of samarium diiodide. Depending on the substrate and the elimination conditions, high selectivity for the non-conjugated alkene product can be achieved.

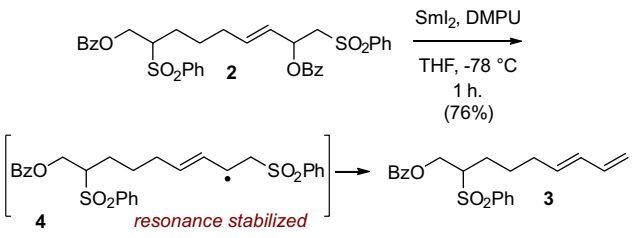
Recently our group has had an interest in non-traditional reactions of acyloxysulfones of type **1** (Scheme 1).[1] Typically once compounds of this type are formed, both the acyl and sulfonyl groups are immediately eliminated in order to complete the powerful Julia–Lythgoe olefination process.[2] Historically, this elimination was performed with sodium–mercury amalgam (Na/Hg) but has more recently been described using samarium diiodide (SmI_2).[3] We have shown that the mechanism by which samarium-mediated acyloxysulfone elimination occurs is highly dependent on the substrate structure.[4] Specifically, single-electron transfer (SET) can occur in to either the sulfone or benzoyl (Bz) groups and is likely reversible. Subsequent carbon radical formation is rate-determining and it is the relative stability of the resulting radical that then determines whether the sulfonyl or benzoyl group is lost first.

This rate-dependence on substrate structure can be exploited for chemoselective samarium-mediated eliminations of bis-acyloxysulfone substrates. For instance elimination of **2** gave diene **3** containing an intact acyloxysulfone, presumably proceeding through the resonance stabilized intermediate **4** (Scheme 2).

For a similar investigation bis-benzoyloxysulfone **5** was prepared by the addition of the lithium dianion generated from **6** to benzaldehyde followed by acylation with benzoyl chloride as outlined in Scheme 3.[5] It was anticipated that treatment of **5** with SmI_2 would result in chemoselective elimination of the benzylic benzoyl group and formation of carbon radical **7**. This intermediate would then decompose to generate allylic benzoate **8**. Unexpectedly, it was not **8** that was obtained but rather the fully eliminated non-conjugated alkene product **9**.[6] Herein we describe additional experiments aimed at understanding the mechanism of this appar-



Scheme 1. Samarium and the Julia–Lythgoe olefination.



Scheme 2. Chemoselective samarium-mediated acyloxysulfone elimination.

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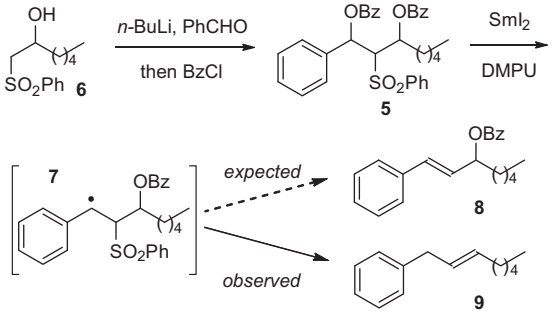


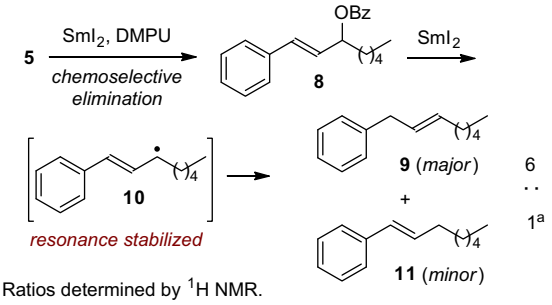
Scheme 3. Unexpected elimination of a bis-benzoyloxysulfone.

ent elimination/isomerization process with the goal of developing a useful method for the preparation of synthetically challenging non-conjugated olefinic systems.

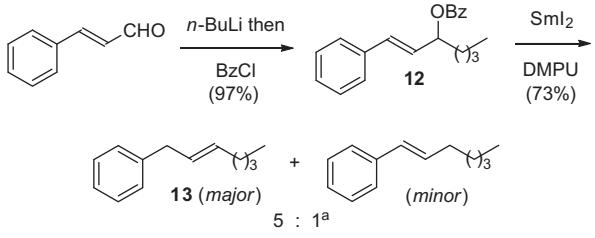
Upon closer inspection it is perhaps not surprising that **8** was not obtained from the reaction of **5**. Following chemoselective elimination generating **8**, further samarium-mediated elimination of the benzoyl group would now give a resonance stabilized radical intermediate **10** (Scheme 4). Selectivity for the formation of **9** from this intermediate as opposed to the corresponding conjugated isomer **11** was however not immediately clear.

To test the intermediacy of **8** in the production of **9** from **5**, analogue **12** was prepared by the addition of *n*-butyllithium (*n*-BuLi) to cinnamaldehyde followed by trapping with benzoyl-chloride (Scheme 5). Treatment of **12** to elimination conditions using SmI_2 and DMPU gave **13**[7] along with minor amounts of the conjugated isomer in essentially the same ratio as **9** to **11** obtained from compound **5** (Scheme 4). This is consistent with a reaction pathway for **5** proceeding by first chemoselective elimination to generate **8** and subsequent elimination/isomerization affording **9**.

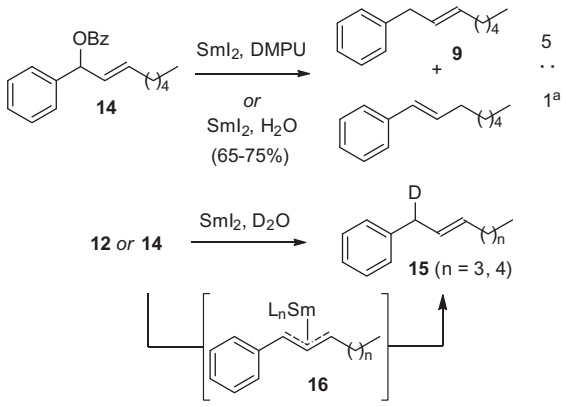
Placement of the benzoyl group at the benzylic position as in **14** or the reaction using SmI_2 and H_2O[8] gave comparable results in terms of both yield and ratio of non- to conjugated products (Scheme 6).[9] When the reaction was performed with **12** or **14** in D_2O the major product for each was the monodeuterated adduct



Scheme 4. Proposed formation of **9** from **8**.



Scheme 5. Samarium allylic benzoate elimination/isomerization.



Scheme 6. Samarium/water elimination and deuterium labeling.

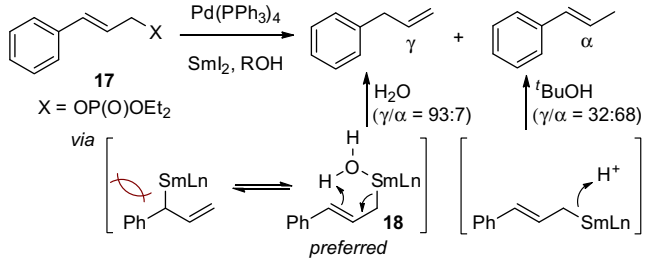
15, suggestive that both substrates converge to the same organosamarium intermediate of type **16**.[10]

Regarding the selectivity for formation of the non-conjugated olefin product, previous work from Yoshida et al. using a palladium tetrakis triphenylphosphine ($Pd(PPh_3)_4$)/SmI_2 system suggested that this is primarily due to steric reasons.[11] This group reported that the reduction of allylic phosphonate **17** with $Pd(Ph_3)_4$/SmI_2 and H_2O gave primarily the γ-isomer via internal delivery of a proton from a sterically preferred organosamarium–H_2O complex **18** (Scheme 7). Switching to *tert*-butanol (^{t}BuOH) as the proton source leads to the α-product as the major isomer proceeding through a presumably open protonation mechanism.

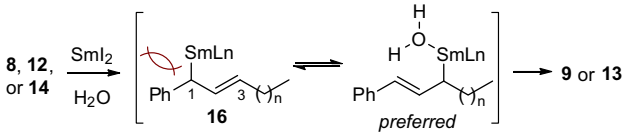
In analogy, the results in Schemes 4–6 can be explained as a steric preference for intermediate **16** to exist as the $\Delta^{1,2}$-structure (Scheme 8). Internal protonation with H_2O (upon quench when using DMPU under anhydrous conditions) would then give compounds **9** or **13**.

The use of ^{t}BuOH in place of H_2O with compound **12** resulted in an erosion of this selectivity consistent with the observations of Yoshida et al. (Scheme 9). The ratio of products could also be affected by manipulating the substrate structure. For instance reduction of the *tert*-butyl substrate **19** using SmI_2 with DMPU, H_2O or ^{t}BuOH gave little product selectivity perhaps due to minimal preference for either the $\Delta^{1,2}$- or $\Delta^{2,3}$-organosamarium intermediate. For each, the product was obtained as a mixture with what have been tentatively assigned as radical dimerization adducts conceivably formed as the rate of protonation is slowed for this sterically encumbered substrate.[12]

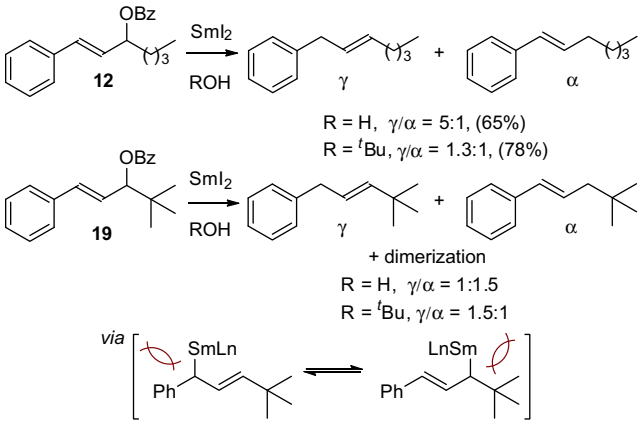
The present method thus appears to be in line with the results described by Yoshida et al. In order to directly compare the two reactions, compounds **20**[13] and **21**[14] were prepared and subjected to samarium elimination conditions[15] (Scheme 10). The reactions with SmI_2/H_2O gave a complex mixture of products. However with SmI_2/^{t}BuOH both **20** and **21** were converted primarily to allylbenzene with identical yield and selectivity, again consistent that each



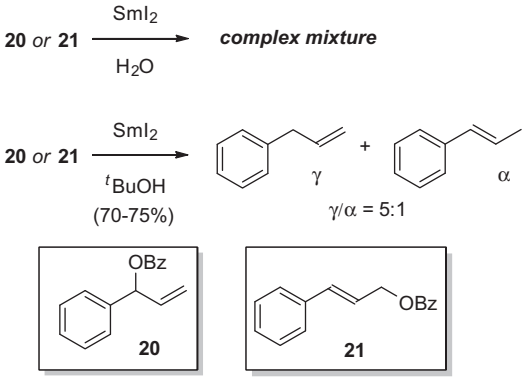
Scheme 7. Yoshida et al. palladium-catalyzed allylic samarium reduction.



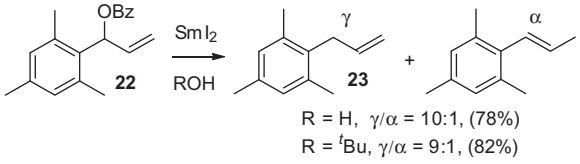
Scheme 8. Proposed origin of selectivity.



Scheme 9. Protonation and substrate impact on selectivity.



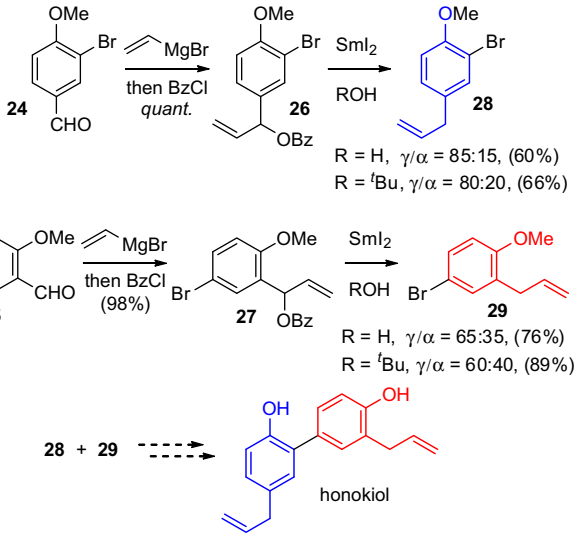
Scheme 10. Terminal non-conjugated alkene synthesis.



Scheme 11. Steric influence on terminal allylic benzoate reductions.

isomer converges to the same organosamarium intermediate. Interestingly, this is not the major isomer that would be predicted based on results from Yoshida et al. palladium-catalyzed system using ^{t}BuOH as the proton source (Ref. Scheme 7).

In order to further investigate this apparent reversal in selectivity, trimethylbenzyl substituted allylic benzoate **22**[16] was prepared and treated with SmI_2 in the presence of both H_2O and ^{t}BuOH (Scheme 11). Irrespective of the proton source, high levels of selectivity for the γ-isomer **23**[17] were obtained. Reactions of **22** also tended to be much cleaner and higher yielding when compared



Scheme 12. Preparation of honokiol substituted aromatics.

to the unsubstituted benzene derivative **20**. Efforts to explain these substrate and proton source effects are ongoing.

While mechanistic aspects of this reaction are still under investigation, the ease of substrate preparation, mild reaction conditions, along with good yields and selectivity particularly for polysubstituted aromatic terminal non-conjugated olefins make this an attractive synthetic method. As an example, addition of vinylmagnesium bromide to commercial aldehydes **24** and **25** followed by in situ acylation with benzoyl chloride gave **26** and **27**, respectively, in excellent yield (Scheme 12). Treatment of **26** with SmI_2 and ^{t}BuOH cleanly afforded compound **28** in 66% yield as an 80:20 mixture in favor of the non-conjugated isomer. Switching to H_2O as the proton source gave essentially the same result with slight enhancement for isomer **28**. Similarly **27** could be converted to **29** in excellent yield albeit with lower selectivity for the γ-isomer when compared to **28**. It is noteworthy that in each case the aryl bromide was untouched by these reducing conditions. Together compounds **28** and **29** represent both properly substituted aromatic rings in the medicinally important natural product honokiol.[18]

In conclusion, during the course of investigations on chemoselective acyloxysulfone eliminations we have discovered a novel samarium-mediated isomerization/elimination of aromatic allylic benzoates. The reaction gives predominantly the non-conjugated alkene product and the selectivity can be controlled by both proton source and substrate structure. These selectivities can in part be rationalized by steric considerations of a proposed organosamarium intermediate that is consistent with a model put forth for a related palladium-catalyzed samarium elimination process. However results for the production of terminal olefin products are not entirely congruent with this previous work suggesting that some aspect of the present method is unique which is currently under investigation. This protocol allowed for the concise synthesis of the two differentially substituted aromatic subunits of the natural product honokiol. Current efforts are aimed at better understanding the mechanism and the controlling factors leading to conjugated versus non-conjugated products.

Acknowledgements

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Supplementary data

Supplementary data (analytical data and experimental procedures for new compounds **12**, **14**, **19**, **22**, **26**–**29**) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.08.136.

References and notes

1. (a) O'Neil, G. W.; Moser, D. J.; Volz, E. O. *Tetrahedron Lett.* **2009**, *50*, 7355; (b) Carter, K. P.; Moser, D. J.; Storvick, J. M.; O'Neil, G. W. *Tetrahedron Lett.* **2011**, *52*, 4494; (c) Storvick, J. K.; Ankoudinova, E.; King, B. R.; Van Epps, H.; O'Neil, G. W. *Tetrahedron Lett.* **2011**, *52*, 5858.
2. (a) Julia, M.; Paris, J. M. *Tetrahedron Lett.* **1973**, *14*, 4833; (b) Kocienski, P. J.; Lythgoe, B.; Ruston, S. *J. Chem. Soc.* **1978**, 829.
3. (a) de Pouilly, P.; Chenede, A.; Mallet, J.-M.; Sinay, P. *Tetrahedron Lett.* **1992**, *33*, 8065; (b) Hojo, M.; Harada, H.; Yoshizawa, J.; Hosomi, A. *J. Org. Chem.* **1993**, *58*, 6541; (c) Kunzer, H.; Stahnke, M.; Sauer, G.; Wiechert, R. *Tetrahedron Lett.* **1991**, *32*, 1949; (d) Ihara, M.; Suzuki, S.; Taniguchi, T.; Tokunaga, Y.; Fukumoto, K. *Synlett* **1994**, 859.
4. Volz, E. O.; O'Neil, G. W. *J. Org. Chem.* **2011**, *76*, 8428.
5. (a) Takinaga, R.; Hosoya, K.; Kaji, A. *Chem. Lett.* **1987**, 829; (b) Takinaga, R.; Hosoya, K.; Kaji, A. *J. Chem. Soc. Perkin Trans. 1* **1988**, 2397; (c) Grimaud, L.; Rotulo, D.; Ros-Perez, R.; Guitry-Azam, L.; Prunet, J. *Tetrahedron Lett.* **2002**, *43*, 7477.
6. Peña-López, M.; Ayán-Varela, M.; Sarandeses, L. A.; Sestelo, J. P. *Chem.-Eur. J.* **2010**, *16*, 9905.
7. Biradar, D. B.; Gau, H.-M. *Org. Biomol. Chem.* **2012**, *10*, 4243.
8. Szostak, M.; Spain, M.; Parmar, D.; Procter, D. J. *Chem. Commun.* **2012**, 330.
9. For an example of benzylic benzoyl reductive cleavage using SmI_2 see: Anker, T.; Hilmersson, G. *Tetrahedron* **2009**, *65*, 10856.
10. For another report of an η^3-allyl samarium complex see: Collin, J.; Bied, C.; Kagan, H. B. *Tetrahedron* **1991**, *32*, 629.
11. Yoshida, A.; Hanamoto, T.; Inanaga, J.; Mikami, K. *Tetrahedron Lett.* **1998**, *39*, 1777.
12. For reports of samarium(II) induced carbon radical dimerization see: (a) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1992**, *57*, 3132; (b) Xu, Q.; Cheng, X.; Zhai, H. *Org. Lett.* **2009**, *11*, 4136.
13. Stanley, L. M.; Bai, C.; Ueda, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 8918.
14. Niwa, T.; Nakada, M. *J. Am. Chem. Soc.* **2012**, *134*, 13538.
15. *General procedure for samarium elimination/isomerization with H_2O or ^tBuOH:* To a freshly prepared solution of SmI_2 (0.1 M in degassed THF, 6 equiv) at −78 °C was added degassed H_2O (3 equiv) and the mixture was warmed to 0 °C for 10 min. The solution was cooled to −78 °C before adding the substrate (1 equiv) and the mixture was then warmed to room temperature for 1 h. The reaction was quenched with aq NH_4Cl and extracted with ethyl acetate. The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. The resulting residue was purified by flash chromatography on florisil®.
16. Serra-Muns, A.; Guérinot, A.; Reymond, S.; Cossy, J. *Chem. Commun.* **2010**, 4178. For an alternative synthesis of **22** see Supplementary data.
17. Matsubara, R.; Gutierrez, A. C.; Jamison, T. F. *J. Am. Chem. Soc.* **2011**, *133*, 19020.
18. Kong, Z. L.; Tzeng, S. C.; Liu, Y. C. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 163. and references cited therein.