

Synthesis and Some Cycloaddition Reactions of 2-(Triisopropylsilyloxy)acrolein

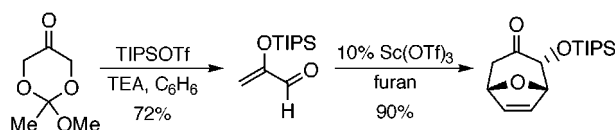
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Received June 30, 2000

ABSTRACT



2-(Triisopropylsilyloxy)acrolein is easily prepared by the reaction of triisopropylsilyl triflate and 2-methoxy-2-methyl-[1,3]dioxan-5-one in the presence of triethylamine. This dienophile reacts with selected dienes in the presence of catalytic amounts of scandium triflate to afford products that are formally 4 + 3 cycloadducts. An exception is seen in the case of butadiene, where only a 4 + 2 cycloadduct is observed.

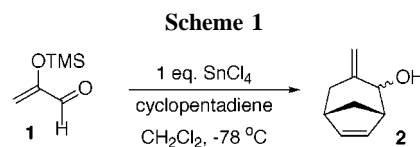
The preparation of seven-membered rings via a 4 + 3 cycloaddition reaction of an allylic cation with a diene is of current interest since it results in a rapid increase in molecular complexity from relatively simple starting materials.¹ Some recent advances in this area deal with the use of heteroatom-stabilized allylic cations as dienophiles in the reaction.² In particular, vinyl oxocarbenium ions are being studied with increasing frequency.³

As part of our program involving the development of vinyloxocarbenium ions in 4 + 3 cycloaddition reactions,⁴ particularly with respect to the development of asymmetric 4 + 3 cycloaddition reactions, we took an interest in exploring oxygen-substituted acroleins as dienophiles.

The study of such species in the context of Diels–Alder reactions is reasonably well-established.^{5–7} A recent example comes from the Funk group, who developed an efficient

synthesis of 2-(acyloxy)acroleins and demonstrated their use in Diels–Alder reactions with a number of dienophiles.⁶

The use of 2-(silyloxy)acroleins and related compounds in the 4 + 3 cycloaddition reaction has also been examined, but not extensively and with limited success to date.⁷ For example, Sasaki and co-workers demonstrated that treatment of aldehyde **1** with 1 equiv of SnCl₄ in the presence of a slight excess of cyclopentadiene afforded the cycloadduct **2** in 72% yield as a 2.7:1 mixture of endo and exo isomers, respectively (Scheme 1).^{7a} To the best of our knowledge,



this is the best example of this type of reaction reported to date.

(5) For some examples and leading references, see: (a) Ochoa, M. R.; Arias, M. S.; Aguilar, R.; Delgado, F.; Tamariz, J. *Tetrahedron* **1999**, *55*, 14535. (b) Dudones, J. D.; Sampson, P. *J. Org. Chem.* **1997**, *62*, 7508. (c) Creary, X.; Inocencio, P. A.; Underiner, T. L.; Kostromin, R. *J. Org. Chem.* **1985**, *50*, 1932. (d) Ireland, R. E.; Obrecht, D. M. *Helv. Chim. Acta* **1986**, *69*, 1273. (e) Ardecky, R. J.; Kerdesky, F. A. J.; Cava, M. P. *J. Org. Chem.* **1981**, *46*, 1483. (f) Brodsky, L.; Agosta, W. C. *J. Org. Chem.* **1974**, *39*, 2928.

(1) For recent reviews of the 4 + 3 cycloaddition reaction, see: (a) Harmata, M. *Tetrahedron* **1997**, *53*, 6235. (b) Harmata, M. In *Advances in Cycloaddition*; Lautens, M., Ed.; JAI: Greenwich, CT, 1997; Vol. 4, pp 41–86. (c) Rigby, J. H.; Pigge, F. C. *Org. React.* **1997**, *51*, 351. (d) Cha, J.; Oh, J. *Curr. Org. Chem.* **1998**, *2*, 217.

(2) Harmata, M. In *Recent Research Developments in Organic Chemistry*; Transworld Research Network: Trivandrum, 1997; Vol. 1, pp 523–35.

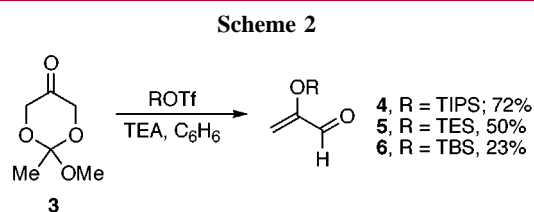
(3) For some recent examples, see: (a) Stark, C. B. W.; Pierau, S.; Wartchow, R.; Hoffmann, H. M. R. *Chem. Eur. J.* **2000**, *6*, 684. (b) Pierau, S.; Hoffmann, H. M. R. *Synlett* **1999**, 213. (c) Lee, J. C.; Jin, S.-J.; Cha, J. K. *J. Org. Chem.* **1998**, *63*, 2804.

(4) (a) Harmata, M.; Jones, D. E. *J. Org. Chem.* **1997**, *62*, 1578. (b) Harmata, M.; Jones, D. E.; Kahraman, M.; Sharma, U.; Barnes, C. L. *Tetrahedron Lett.* **1999**, *40*, 1831.

These results stimulated our interest in captodative alkenes such as **1** which we believe still have untapped potential in 4 + 3 cycloaddition chemistry. In the hope of taking advantage of recent progress in the development of new Lewis acid catalysts which have emerged over the past decade, we began a study of the synthesis and chemistry of alkenes related to **1**.⁸ This report deals with the preparation of the triisopropylsilyl congener (**4**) of **1** and some preliminary cycloaddition results.

Our synthesis of the target compound **4** was inspired by a method reported by Funk.⁶ In his approach, the enol(ate) of 2,2-dimethyl-5-dioxinone is functionalized at oxygen and the resulted alkene thermolyzed to afford the target aldehyde via a retro-Diels–Alder reaction. While this elegant approach would no doubt have proven viable, we sought to use a starting material that was more readily available. A report by Giese and co-workers suggested that dioxinone **3**, easily prepared from commercially available dihydroxyacetone and trimethyl orthoacetate, would be suitable.⁹ Thus, we chose to investigate the generation of **4**, starting with this compound.

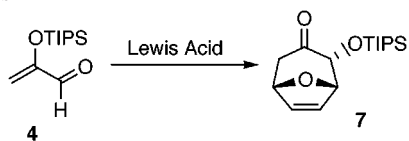
To our delight, we found that simply stirring a benzene solution of dioxinone **3** in the presence of TIPSOTf and triethylamine for 12 h afforded the desired aldehyde in 72% yield. Aldehydes **5** and **6** could be prepared in the same fashion, albeit in lower yields under the same reaction conditions (Scheme 2). The use of trimethylsilyl triflate



afforded no isolable product.¹⁰ While further optimization studies and mechanistic investigations are required, this method represents a particularly convenient way of producing aldehydes of this type relatively quickly.

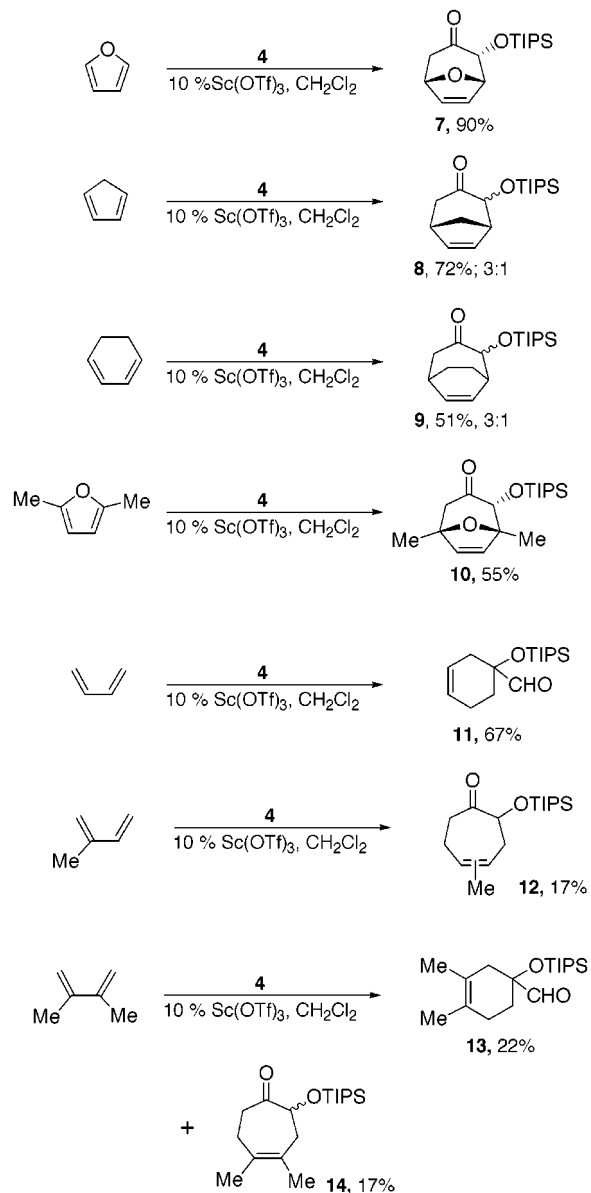
With **4** in hand, we began investigating its ability to engage in various Lewis acid mediated cycloaddition processes. Our initial studies used furan as the diene and a small number of

Table 1. Reaction of **4** with Furan in the Presence of Titanium Lewis Acids



Lewis acid	conditions	yield (%)
TiCl ₄	0.1 M, CH ₂ Cl ₂ , -78 °C	88
Ti(OiPr) ₄	0.1 M, CH ₂ Cl ₂ , -78 °C	NR
TiCl ₂ (OiPr) ₂	0.1 M, CH ₂ Cl ₂ , -78 °C	NR

Table 2. Cycloadducts from the Scandium Triflate Catalyzed Reaction of **4** with Various Dienes



titanium Lewis acids. Results are summarized in Table 1. Treatment of a mixture of **4** and furan with 1.1 equiv of titanium tetrachloride afforded the cycloadduct **7** as a single stereoisomer in 88% yield. The stereochemical assignment is based on precedent and comparison of NMR data with similar compounds of known stereochemistry.⁴ Neither titanium tetraisopropoxide nor dichlorotitanium diisopropoxide afforded any cycloadduct under the same conditions. Since the latter Lewis acid lacked activity, we were concerned that related Lewis acids, such as those based on TADDOL, would not be effective and therefore sought other reagents that would effect cycloaddition in catalytic amounts and under relatively mild conditions.¹¹

We chose to explore scandium triflate as the catalyst.¹² Though not without limitations, this catalyst turned out to

work out quite well in affording cycloadducts between **4** and various dienes.¹³ The results are summarized in Table 2.

The general reaction procedure consisted of treating a 0.2 M solution of **4** in dichloromethane with 10 mol % scandium triflate in the presence of 2.5 equiv of diene at 0 °C while warming the reaction to room temperature over the course of 2 h. With furan this produced the cycloadduct **7** as a single stereoisomer in 90% yield. With both cyclopentadiene and cyclohexadiene the yields and stereoselectivities were lower, perhaps indicative of a stepwise mechanism.¹⁴ 2,5-Dimethylfuran afforded a reasonable yield of the cycloadduct **10** as a single isomer.

Several acyclic dienes were examined as well. The reaction worked well with butadiene, but led to only the 4 + 2 cycloaddition product **11**. A mixture of 4 + 3 and 4 + 2 cycloaddition adducts was observed with 2,3-dimethylbutadiene, both in relatively low yields. Isoprene gave only a 4 + 3 cycloadduct as a mixture of regioisomers, but in low

(6) Funk, R. L.; Yos, K. J., III. *J. Org. Chem.* **1996**, *61*, 2598.

(7) (a) Sasaki, T.; Ishibashi, Y.; Ohno, M. *Tetrahedron Lett.* **1982**, *23*, 1693. (b) Blackburn, C.; Childs, R. F.; Kennedy, R. A. *Can. J. Chem.* **1983**, *61*, 1981.

(8) (a) Santelli, M.; Pons, J.-M. *Lewis Acids and Selectivity in Organic Synthesis*; CRC: Boca Raton, 1996. (b) *Lewis Acid Reagents. A Practical Approach*; Yaammoto, H., Ed.; Oxford University: Oxford, 1999.

(9) Müller, S. N.; Batra, R.; Senn, M.; Giese, B.; Kisel, M.; Shadyro, O. *J. Am. Chem. Soc.* **1997**, *119*, 2795.

(10) However, treatment of ketone **3** with TMSCl, triethylamine, and DMAP in refluxing dichloromethane gave the corresponding TMS enol ether.

(11) For a review of TADDOL Lewis acids and their applications, see: Gawronski, J.; Gawronska, K. *Tartaric and Malic Acids in Synthesis*; Wiley: New York, 1999; Chapter 12.

(12) Kobayashi, S. *In Lanthanides: Chemistry and Use in Synthesis*; Kobayashi, S., Ed.; Springer, 1999; pp 64–118.

(13) Dienes which did not afford good yields of cycloadducts upon reaction with **4** in the presence of scandium triflate: *N*-carbomethoxyprole, 2-methoxyfuran, 2-methylfuran, and 1,3-cycloheptadiene.

(14) (a) Cramer, C. J.; Barrows, S. E. *J. Org. Chem.* **1998**, *63*, 5523. (b) Cramer, C. J.; Barrows, S. E. *J. Phys. Org. Chem.* **2000**, *13*, 176.

yield. At present, it appears that only certain cyclic dienes are the useful substrates if one wishes to access 4 + 3 cycloadducts in good to excellent yields.

The mechanism of the reaction of **4** with dienes is not absolutely clear. The reactions involving 4 + 2 cycloadditions or 4 + 3 cycloadditions with high levels of simple diastereoselectivity might be regarded as concerted processes. On the other hand, the occurrence of stereoisomers as in the case of cyclopentadiene or the production of mixtures as with 2,3-dimethylbutadiene suggests the possibility of an intermediate which can afford both 4 + 2 and 4 + 3 cycloadducts or 4 + 3 cycloadducts with eroded diastereoselectivity. Further work is necessary to distinguish all of the possibilities.

In summary, we have developed a concise route to 2-(silyloxy)acroleins and have demonstrated the successful 4 + 3 and 4 + 2 cycloaddition reaction of one such compound under mild conditions using catalytic amounts of a Lewis acid. Broadening the scope of the reaction, finding an appropriate chiral Lewis acid catalyst, and applying the process in synthesis constitute our next goals in this area.

Acknowledgment. This work was supported by the Petroleum Research Fund, administered by the American Chemical Society. We thank the National Science Foundation for partial support of the NMR (PCM-8115599) facility at the University of Missouri—Columbia and for partial funding for the purchase of a 500 MHz spectrometer (CHE-89-08304).

Supporting Information Available: General procedures for the synthesis of **4** and its cycloaddition reaction with dienes and copies of proton and carbon spectra of **4–14**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL006281X