ORGANIC LETTERS

2005
Vol. 7, No. 3
463−465

Decarboxylative Claisen Rearrangement Reactions of Allylic Tosylmalonate Esters

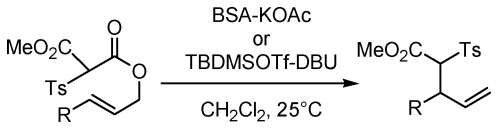
Donald Craig* and Fabienne Grellepois

Department of Chemistry, Imperial College London, South Kensington Campus, London SW7 2AZ, UK

d.craig@imperial.ac.uk

Received November 24, 2004

ABSTRACT

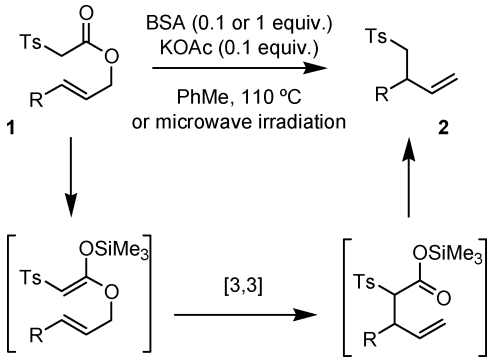


Two different combinations of silylating agent and base are used for one-pot [3,3]-sigmatropic rearrangement–decarboxylation reactions of tosylmalonic mono(allylic) esters under mild conditions, providing the products of formal regiospecific allylation of methyl tosylacetate at the more substituted allylic terminus.

The Claisen rearrangement continues to be the focus of considerable synthetic chemistry research effort.[1] Since its introduction in 1972,[2] the Ireland silyl ketene acetal variant in particular has been widely used in complex target-oriented synthesis.[3] This modified process benefits from the ease of preparation of the ketene acetal substrates and the relatively mild conditions for the sigmatropic rearrangement. In addition, it enables overall C-allylation of carboxylic acids using allylic alcohols as the surrogate electrophiles, with *regiospecific* allylic double-bond transposition.

We recently reported[4] a novel variant of the Ireland−Claisen rearrangement reaction in which α-tosyl silyl ketene acetals formed in situ from allylic tosylacetates **1** in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and potassium acetate undergo [3,3]-sigmatropic rearrangement followed by acetate-induced desilylation−decarboxylation in situ to provide homoallylic sulfones **2** (Scheme 1).[5,6] During the course of this study, we became interested in examining

Scheme 1. Synthesis of Homoallylic Sulfones by the Decarboxylative Claisen Rearrangement Reaction



the effect on reactivity of introducing additional electron-withdrawing groups on the α-position of substrates **1**.[7] Specifically, we wished to look at the decarboxylative Claisen rearrangement (dCr) reactions[8] of methyl allyl esters

(1) For recent reviews on Claisen and related rearrangements, see: Martin Castro, A. M. *Chem. Rev.* **2004**, *104*, 2939−3002.

(2) (a) Ireland, R. E.; Mueller, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 589−5898.

(3) For review on the Ireland−Claisen rearrangement: (a) Pereira, S.; Srebnik, M. *Aldrichimica Acta* **1993**, *26* (1), 17−29. (b) Chai, Y.; Hong, S.; Lindsay, H. A.; McFarland, C.; McIntosh, M. *Tetrahadron* **2002**, *58*, 2905−2928.

(4) Bourgeois, D.; Craig, D.; King, N. P.; Mountford, D. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 618−621.

(5) For the first report of a stepwise Ireland−Claisen rearrangement followed by decarboxylation in a separate step, see: Davidson, A. H.; Eggleton, N.; Wallace, I. H. *J. Chem. Soc., Chem. Commun.* **1991**, 378−380.

(6) For a related Carroll-type reaction, see: Hatcher, M. A.; Posner, G. H. *Tetrahedron Lett.* **2002**, *43*, 5009−5012.

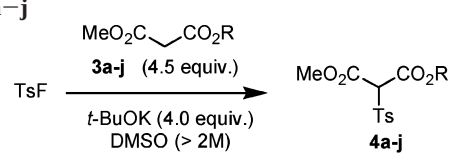
10.1021/ol047577w CCC: $30.25
Published on Web 01/11/2005

of tosylmalonic acid,[9] which would in principle provide a concerted, regiospecific alternative to the stepwise, regioselective metal-catalyzed allylic alkylation reactions of methyl tosylacetate under basic conditions.[10] Herein we compare the effectiveness of several alternatives to the BSA−KOAc reagent system for the decarboxylative Claisen rearrangement reaction of methyl allyl tosylmalonates and show that [3,3]-sigmatropic rearrangement is a viable strategy for the formal regiospecific allylation of methyl 2-tosylacetate.

The tosyl-substituted allylic malonate esters **4a**−**j** required for this study were prepared by alkylation of tosyl fluoride[11] with an excess of the potassium salt of the corresponding allylic malonate esters **3a**−**j**[12] in DMSO (Table 1).[13,14]

Expecting that the presence of the additional methyl ester group would lower the temperature required for the dCr reactions to proceed, the tosyl-substituted cinnamyl malonate ester **4a** was submitted initially to the conditions previously described[4] (1 equiv of BSA and 0.1 equiv of KOAc), at room temperature (Table 2, entry 1). The carboxymethyl-substituted homoallylic sulfone **5a** was formed in high yield (81%). No reaction was observed when 0.1 equiv of BSA was employed. Substitution of KOAc with Et_3N (0.1 equiv) also gave **5a** (entry 2). This behavior was in marked contrast to that of monoesters **1**, which had undergone rearrangement but not decarboxylation on exposure to BSA−Et_3N.[4] This prompted a study of the reaction of **4a** with several silylating agent−base combinations. With chlorosilanes in place of BSA, zero or low levels of conversion into **5a** were observed (entries 3 and 4). However, treatment of **4a** with silyl triflates[15] (2.1 equiv) and Et_3N or DBU (2.1 equiv) gave good yields of **5a**, much more rapidly than the BSA−KOAc system (entries 6−8).

Table 1. Preparation of Tosyl-Substituted Allylic Malonate Esters **4a**−**j**



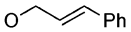
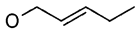
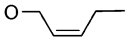
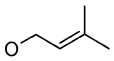
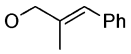
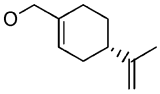
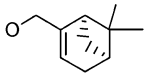
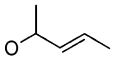
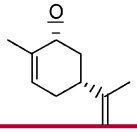
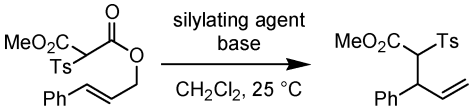
substrate **3a-j**	OR	compound **4a-j**	yield of tosyl malonate **4a-j**
3a		**4a**	70%
3b		**4b**	67%
3c		**4c**	65%
3d		**4d**	75%
3e		**4e**	90%
3f		**4f**	56%
3g		**4g**	81%
3h		**4h**	78%
3i		**4i**	79%
3j		**4j**	74%

Table 2. Decarboxylative Claisen Rearrangement of **4a** at Room Temperature



entry	silylating agent (equiv)	base (equiv)	time	yield[a]
1	BSA (1)	KOAc (0.1)	4 h	81%
2	BSA (1)	Et_3N (0.1)	15 h	59%
3	TMSCl (2.1)	DBU (2.1)	22 h	9%
4	TBDMSCl (2.1)	DBU (2.1)	24 h	0%
5	TBDMSOTf (1.2)	DBU (1.2)	18 h	43%
6	TBDMSOTf (2.1)	DBU (2.1)	15 min	83%
7	TBDMSOTf (2.1)	Et_3N (2.1)	30 min	73%
8	TMSOTf (2.1)	DBU (2.1)	1 h 30 min	80%

[a] Isolated yield.

Next, a more thorough comparison of the two dCr reagent systems was carried out. Substrates **4a**−**j** were subjected to

(7) For Ireland−Claisen rearrangements of silyl ketene acetals derived from simple methyl allyl malonates involving desilylation and decarboxylation in a separate step, see: Fehr, C.; Galindo, J. *Angew. Chem., Int. Ed* **2000**, *39*, 569−573.

(8) For recent examples of regio- and enantioselective metal-catalyzed decarboxylative allylation reactions, see: Burger, E. C.; Tunge, J. A. *Org. Lett.* **2004**, *6*, 2603−2605, 4113−4115.

(9) For *high-temperature* thermal decarboxylative Claisen rearrangement of β-ketoester-derived silyl enol ethers involving silatropic rearrangement, see: Coates, R. M.; Sandefur, L. O.; Smillie, R. D. *J. Am. Chem. Soc.* **1975**, *97*, 1619−1621. We thank a referee for bringing this article to our attention.

(10) For metal-catalyzed allylic alkylation reactions of methyl 2-tosylacetate, see: (a) Godleski, S. A.; Villhauer, E. B. *J. Org. Chem.* **1984**, *49*, 2246−2252. (b) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033−2046. (c) Masumaya, Y.; Hirai, H.; Kurusu, Y.; Segawa, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1525−1526. (d) Masumaya, Y.; Mitsunaga, Y.; Kurusu, Y.; Segawa, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3431−3432.

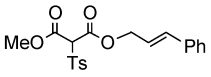
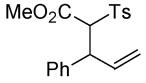
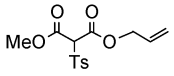
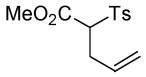
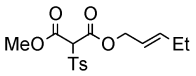
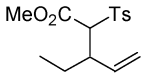
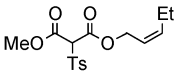
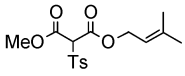
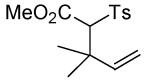
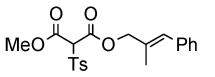
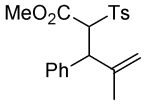
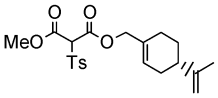
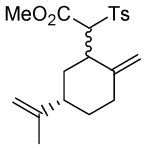
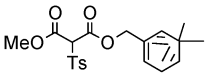
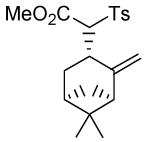
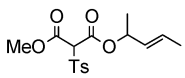
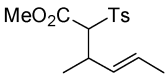
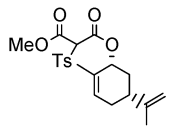
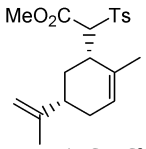
(11) (a) Hirsh, E.; Hünig, S.; Reissig, H.-U. *Chem. Ber.* **1982**, *115*, 399−401. (b) Kende, A. S.; Mendoza, J. S. *J. Org. Chem.* **1990**, *55*, 1125−1126. (c) Sandanayaka, V. P.; Zask, A.; Venkatesan, A. M.; Baker, J. *Tetrahedron Lett.* **2001**, *42*, 4605−4607.

(12) Allylic malonate esters **3a**−**j** were prepared by a two-step sequence: malonic acid monomethyl ester was prepared by treatment of Meldrum's acid with methanol (Brooks, D. W.; Castro de Lee, N.; Peevey, R. *Tetrahedron Lett.* **1984**, *25*, 4623−4626); subsequent condensation with the allylic alcohol in the presence of DCC and DMAP provided **3a**−**j** (see Supporting Information).

(13) A dramatic drop in yield was observed using less than 4 equiv of the potassium salt of allylic malonate esters **3a**−**j** or using less concentrated reaction mixtures. The excess allylic malonate ester **1a**−**j** may easily be recovered after purification by chromatography (see Supporting Information).

(14) No reaction was observed using LDA in THF at −78 °C. Comparable yields were obtained using NaH at 50 °C instead of *t*-BuOK at room temperature.

Table 3. Decarboxylative Claisen Rearrangement Reaction of Tosyl-Substituted Allylic Malonate Ester **4a**−**j**

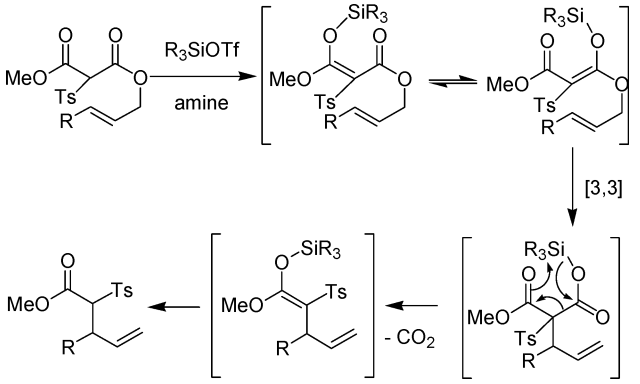
	substrate	product (mixture of diastereoisomers)		method[a] yield[b]
4a		**5a** (53:47)		A: 81% B: 83%
4b		**5b** (53:47)		A: 62% B: 73%
4c		**5c** (53:47)		A: 74% B: 61%
4d		**5c** (53:47)		A: 0%[c] B: 18%
4e		**5e** (53:47)		A: 80% B: 71%
4f		**5f** (70:30)		A: 59% B: 55%
4g		**5g** (70:30)[d]	 anti:syn 97:3	A: 45% B: 0%[e]
4h		**5h** (53:47)		A: 72% B: 76%
4i		**5i** (53:47)		A: 88% B: 83%
4j		**5j** (61:39)		A: 19% B: 57%

[a] Method A: BSA (1.0 equiv), KOAc (0.1 equiv), CH_2Cl_2, rt, 4−15 h. Method B: TBDMSOTf (2.1 equiv), DBU (2.1 equiv), CH_2Cl_2, rt, 15−30 min. [b] Isolated yield. [c] No reaction was observed at room temperature, but **5c** was isolated in 4% yield after reaction in CH_2Cl_2 under reflux for 18 h. [d] "Anti" product. [e] Extensive decomposition was observed.

the BSA−KOAc (respectively 1 and 0.1 equiv; method A) and TBDMSOTf−DBU (each 2.1 equiv; method B) conditions. In most cases, **5** was formed in similar yields under the two contrasting sets of conditions. Also, several of the substrates (**4g**,**h**,**j**) underwent rearrangement−decarboxylation with a high degree of stereoselectivity.[16] Table 3 summarizes the results.

As only rearranged *and* decarboxylated products **5** were isolated from these transformations (even when using BSA in conjunction with nonnucleophilic Et_3N), it seems likely that the silyl esters formed initially in the [3,3]-sigmatropic rearrangement process lose CO_2 by a mechanism other than desilylation−decarboxylation.[4] We speculate that silatropic rearrangement[17] of the silyl esters gives a new silyl ketene acetal, which undergoes hydrolysis during isolation/purification (Scheme 2). This explanation is consistent with the need for 1 equiv of silylating agent, since it is effectively consumed by formation of the silyl ketene acetal derivatives of the isolated products **5**.

Scheme 2. Proposed Mechanism for the Decarboxylative Claisen Rearrangement Reaction Mediated by the Trialkylsilyl Triflate/Amine Combination



In summary, these studies show that the dCr reaction provides an effective, *regiospecific* alternative for metal-catalyzed allylation of methyl tosylacetate. Present studies are directed toward probing the relative rates of monorearrangement of unsymmetrical bis(allylic) tosylmalonates. The results of these investigations will be reported in due course.

Acknowledgment. This research was supported by the European Community Human Potential program (Marie Curie Individual Fellowship) under Contract HPMT-CT-2002-02015.

Supporting Information Available: Experimental procedures, full characterization of compounds **4a**−**j** and **5a**−**c**,**e**−**j**, and copies of ^{1}H NMR and ^{13}C NMR spectra of **3a**−**j**, **4a**−**j**, **5a**−**c**,**e**−**j**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL047577W

(15) Kobayashi, M.; Masumoto, K.; Nakai, A.; Nakai, T. *Tetrahedron Lett.* **1996**, *37*, 3005−3008.

(16) Structures of **5g**,**h**,**j** were assigned by comparison of their NMR spectra with those of related compounds. For **5g**,**h** see: ref 3. For **5j**, see: Ireland, R. E.; Maienfisch, P. *J. Org. Chem.* **1988**, *53*, 640−651.

(17) Slutsky, J.; Kwart, H. *J. Am. Chem. Soc.* **1973**, *95*, 8678−8685.