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Structure dependent rearrangement of the cyclopropylmethyl cation—isolation of a bicyclo[3.2.0]heptene

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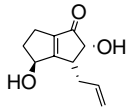
Abstract—Access to 7-allyl substituted norbornene derivatives for tandem olefin metathesis via cationic rearrangement of cyclopropylmethanol substituted norbornenes is shown to be structure dependent. In some cases products that arise from cationic rearrangement of a cyclopropylmethyl cation are furnished. Thionyl chloride is shown to be superior to silica for inducing the desired rearrangement.

The current interest in olefin metathesis as a method for organic synthesis has resulted in a number of notable achievements.[1] A subset of the larger field that is olefin metathesis is a class of reactions described as domino or tandem processes; these consist of a number of consecutive olefin metathesis operations to provide the final structure. Some notable examples can be found in the work of Blechert,[2] Winkler,[3] Aube,[4] Phillips,[5] Tadano[6] and others.[7]

The olefin metathesis of 7-substituted norbornenes has recently been evaluated and has resulted in a couple of successful synthetic applications, namely the synthesis of (+)-africanol by Schrock and Hoveyda[8] and the synthesis of the cyclopenta- and cyclohexa-[*c*]indene core of the natural products desogestrel and magellamine.[9] Both of these approaches exploited the ability to install an allyl or homoallyl chain at the 7-position of a 7-oxonorbornene via standard anionic chemistry.

Intrigued by the synthetic opportunity that is presented by a 7-allyl substituted norbornene, we chose to explore these compounds as possible substrates for further elaboration via tandem olefin metathesis directed towards the synthesis of xialenon A (**1**).[10]



xialenon A (**1**)

Methods for the synthesis of simple 7-substituted norbornenes are limited, most routes proceeding via the aforementioned 7-oxonorbornene. One method that does not follow this route was reported by Diaz,[11] who prepared 7-allylnorbornenes **3** via a cationic route from the corresponding spirocyclic precursors **2** (Fig. 1). Application of this methodology would efficiently lead to a series of 7-allyl norbornenes required for our tandem metathesis studies. We report here the unexpected results encountered when we applied Diaz's conditions to analogues of **2** and a new protocol for accomplishing the desired transformation.

Synthesis of compounds analogous to **3** begins with the preparation of the required spirobicyclic cyclopentadiene **4** using standard literature protocols.[12] Diels–Alder reaction of **4** with methyl acrylate, *tert*-butyl acrylate and acrylonitrile was performed by adding the diene to the dienophile and stirring overnight. Yields were quantitative and the selectivity, as expected, was for the *endo*-isomer (Scheme 1). Rearrangement was achieved via a

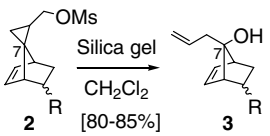


Figure 1. Diaz's synthesis of 7-allylnorbornenes.

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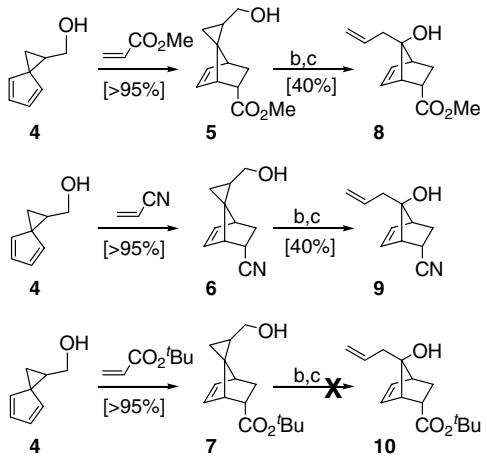
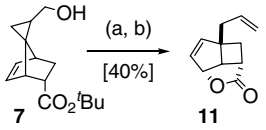


Scheme 1. Reagents and conditions: (a) dienophile (5 equiv), rt, 18 h; (b) MsCl, Et_3N, CH_2Cl_2; (c) silica gel, CH_2Cl_2.

two step one-pot method, involving conversion of the alcohol to the corresponding mesylate and then addition of silica gel. By this method, Diels–Alder adducts **5** and **6** were converted to the expected 7-allylnorbornenes **8** and **9** in 40% yield. The yields of these reactions were below those reported by Diaz et al. Furthermore, the reaction using the *tert*-butyl substituted Diels–Alder adduct **7** did not give the expected product **10**.

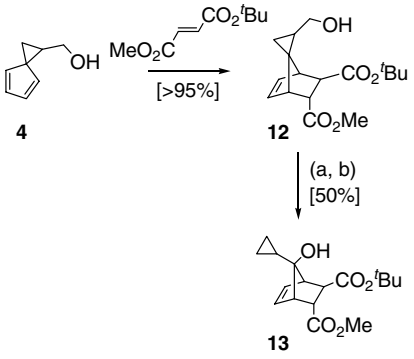
Characterization of the product from the rearrangement of **7** was achieved using NMR spectroscopic analysis and indicated that the molecule had undergone a structural rearrangement to give a substituted bicyclo[3.2.0]heptene **11** (Scheme 2).[13] The mechanism through which this product **11** was formed must presumably proceed via the formation of the expected anchimerically stabilized cation at the bridging carbon atom.[14] This can then undergo skeletal rearrangement with the production of a stabilized allyl cation. Cyclization of the ester onto the cation and loss of the *tert*-butyl cation results in the material isolated (Scheme 3).



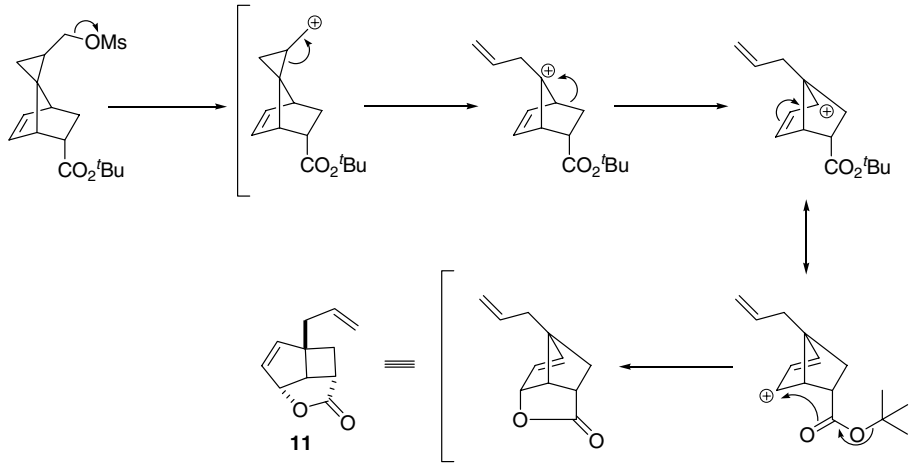
Scheme 2. Reagents and conditions: (a) MsCl, Et_3N, CH_2Cl_2; (b) silica gel, CH_2Cl_2.

Reaction of **4** with *tert*-butyl methyl fumarate gave the expected Diels–Alder adduct **12** (Scheme 4). Rearrangement of **12** using the conditions reported by Diaz et al. resulted in the isolation of the 7-cyclopropyl-substituted norbornene **13** in 50% yield. Products of a similar structure were reported by Diaz et al. as the major side products.

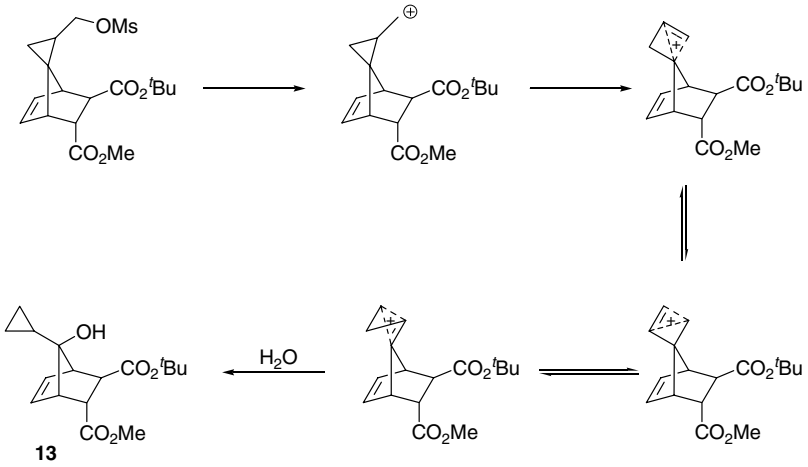
The isolation of **13** can be rationalized on the basis of an increase in the longevity of the initially formed cation. This is reasonable given that the skeletal rearrangement seen in the conversion of **7** to **11** will be effectively retarded by the presence of an ester on both C1 and C2. In the absence of an effective migratory pathway, the cyclopropylmethyl cation can form a non-classical bicyclobutonium ion as described by Roberts and Synder.[15] These non-classical cations can be drawn as a three-centre carbonium ion, which exist as a series of equilibrating species (Scheme 5). The product distribution from simple bicyclobutonium ions is biased towards



Scheme 4. Reagents and conditions: (a) MsCl, Et_3N, CH_2Cl_2; (b) silica gel, CH_2Cl_2.



Scheme 3. Proposed mechanism for the formation of the bicyclo[3.2.0]heptene derivative **11**.



Scheme 5. Proposed mechanism for the formation of cyclopropylnorbornene **13**.

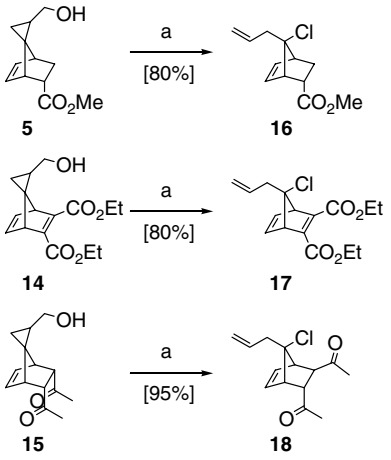
formation of cyclopropyl and cyclobutyl products, Roberts reported these as being formed in a 1:1 ratio.[16] To account for the difference in product distribution observed for the conversion of **12** into **13** the non-classical cation leading to **13** must be a thermodynamic minimum. The stability of this cation over other cations that exist can be rationalized when anchimeric stabilization from the norbornene C=C bond is considered. Thus, attack of adventitious water will result in the cyclopropyl-substituted norbornene **13**.

Having evaluated the silica induced cationic rearrangement of a number of Diels–Alder adducts it was concluded that this chemistry did not provide a general procedure for the synthesis of 7-allyl substituted norbornenes. A search of the literature revealed a communication by Menzek,[17] who described the ring opening of complex cyclopropylmethylalcohols with thionyl chloride.

In order to ascertain the usefulness of thionyl chloride as a reagent to accomplish the introduction of an allyl group at the 7-position of our target norbornenes, methyl ester **5** was treated with thionyl chloride. Ester **5** was rapidly and efficiently converted into the desired 7-allyl-7-chloro substituted norbornene **16**; no other readily identifiable products were isolated (Scheme 6).

The thionyl chloride conditions proved to be a general method for the production of the 7-allyl norbornenes, with further examples given in Scheme 6. The conversion of the norbornene derived from diethyl acetylenedicarboxylate **14** gave an 80% yield of the desired product **17**. A more sensitive substrate the *endo* diketone **15** gave the desired 7-allyl-7-chloro norbornene **18** in 95% yield. Notably, the relative stereochemistry of the acetyl substituents was found to have been isomerized from cis to trans.

In summary, the silica gel induced ring opening, reported by Diaz et al., in our hands, was found to result in a number of unexpected rearrangements; the most intriguing of these leading to the isolation of **11**. The bicyclo[3.2.0]heptane framework forms the core of a



Scheme 6. Reagents and conditions: (a) thionyl chloride, $CHCl_3$, rt, 1 h.

number of natural products and we are currently evaluating this rearrangement as an entry towards these compounds.[18] The application of Menzek's thionyl chloride methodology enabled access to the desired 7-allyl substituted norbornenes in good yield and further studies towards xialenon A are underway.

Acknowledgement

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