ORGANIC LETTERS

1999
Vol. 1, No. 3
375−377

A New Tandem Route to Angular Tetraquinanes. Synthesis of the Waihoensene Ring System

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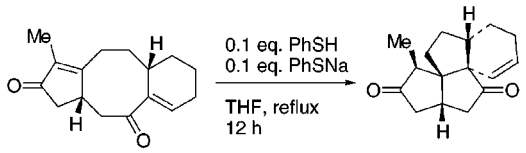
Received April 8, 1999

ABSTRACT

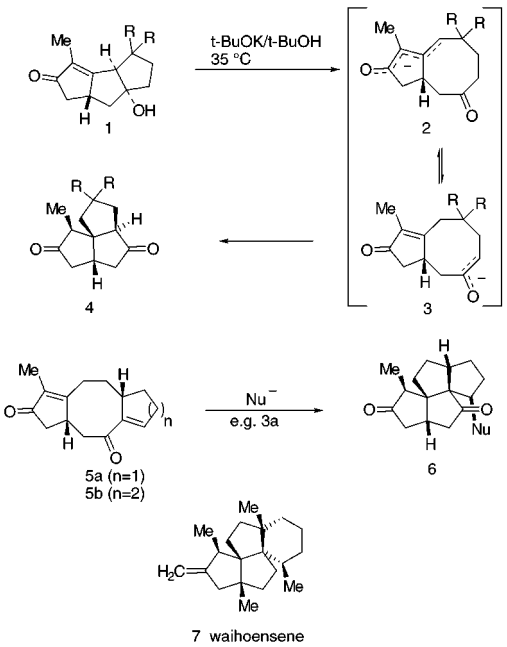


This paper describes a new tandem reaction sequence leading to angularly fused polyquinanes from squaric acid-derived bicyclo[6.3.0]-undecadienediones. Such compounds undergo a dual Michael addition. The enolate form in the first intermolecular addition undergoes the second intramolecuar transannular addition to give the angular polyquinanes. A particularly interesting example is a catalytic transformation of *cis*-13-methylyricyclo[10.3.0.0^{4,9}]pentadeca-4(5),12(13)-diene-3,14-dione to (3*R,3a*S**,5a*R**,9a*R**,11a*R**)-3-methyl-1,2,3,5,5a,6,7,10,11,11a-decahydro-4*H*-pentaleno[6a,1-*c*]indene-2,10-dione, a compound having the tetracyclic ring system found in the natural product waihoensene. The mechanism and synthetic scope of these reactions are discussed.**

Reported here is a new tandem reaction sequence leading to angularly fused polyquinanes from squaric acid-derived bicyclo[6.3.0]undecadienediones. The method rests, in part, on a previous report that linear triquinanes such as **1** efficiently rearrange to their angular isomers **4** upon treatment with t-BuOK/t-BuOH.[1,2] This transformation is envisaged to proceed via a retro-aldol ring cleavage to give equilibrating enolates **2** and **3**. Transannular Michael addition of **3** then provides the angular triquinanes **4** (Scheme 1). We now report a related study in which compounds such as **5a** undergo a tandem dual Michael sequence to give angularly fused tetraquinanes **6**. A particularly interesting example is a catalytic transformation of **5b** to **13**, a compound having the tetracyclic ring system found in the natural product waihoensene (**7**).[3]

The starting bicyclo[6.3.0]undecadienediones **5a**,**b** were readily prepared as outlined in Scheme 2. Specifically, treatment of bicyclo[3.2.0]heptenone **8**[4] with a slight excess of 1-lithio-6-methoxycyclohexene at −78 °C gives adduct **9** which immediately undergoes an oxy-Cope ring expansion

Scheme 1

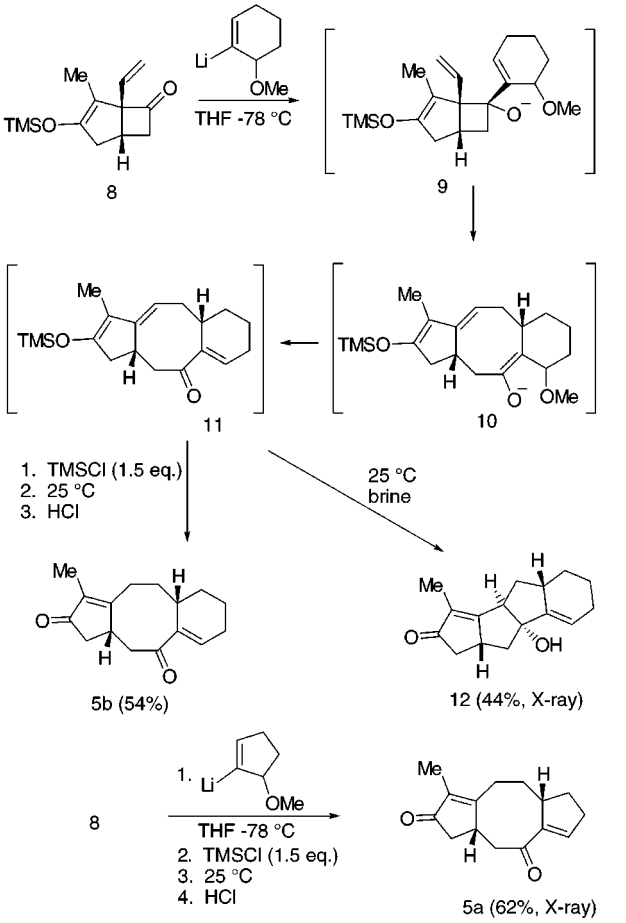


to **10** followed by elimination of methoxide to provide **11**.[5] This product was not isolated but subjected directly to

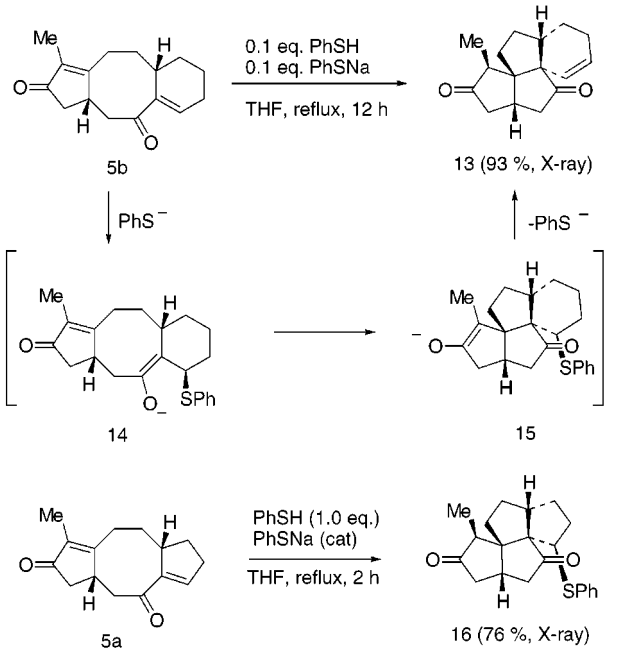
(1) MacDougall, J. M.; Moore, H. W. *J. Org. Chem.* **1997**, *62*, 4554.
(2) MacDougall, J. M.; Santora, V. J.; Verma, S. K.; Trunbull, P.; Hernandez, C. R.; Moore, H. W. *J. Org. Chem.* **1998**, *63*, 6905.
(3) Clarke, D. B.; Hinkley, S. F. R.; Weavers, R. T. *Tetrahedron Lett.* **1997**, *38*, 4297.
(4) Xu, S. L.; Moore, H. W. *J. Org. Chem.* **1989**, *54*, 6018.

10.1021/ol990023m CCC: $18.00
Published on Web 07/15/1999

Scheme 2



Scheme 3



hydrolytic workup, the specific conditions of which dictate the overall outcome of the reaction. That is, treatment of crude silylenol ether **11** with aqueous brine (basic conditions)[6] results in hydrolysis of the silylenol ether and concomitant intramolecular aldol cyclization to give the linear tetraquinane **12** (44%).[7] In contrast, acidic workup conditions gave **5b** (54%). In a like manner, treatment of **8** with 1-lithio-5-methoxycyclopentene followed by the acidic workup conditions gave **5a** in 62% isolated yield.

*A remarkable transformation was observed when a THF solution of **5b** and a catalytic amount of thiophenol and sodium thiophenolate was refluxed for 12 h. This resulted in a nearly quantitative rearrangement of **5b** to the angularly fused tetraquinane **13** (93%)* (Scheme 3). This unusual transformation is envisaged to involve a 3-fold tandem sequence of reactions, i.e., initial Michael addition of the thiolate to **5b** from the β-face to give **14** which then undergoes a transannular ring closure to provide **15**. This enolate in **15** then induces an intramolecular E_2 *trans*-diaxial elimination to give the observed product **13** and regenerate the thiophenolate catalyst. This last step is perhaps the most surprising of the sequence and is presumably possible because of the close proximity of the enolate in **15** to the β-proton that is *trans* disposed to the thiophenol leaving group (molecular models).

In contrast, when the homologue **5a** was subjected to the same conditions, little reaction was observed. However, when a stoichometic amount of thiophenol was employed along with a catalytic amount of sodium thiophenolate the angularly fused tetraquinane **16** was obtained in 76% isolated yield. That the reaction terminates at this stage is not unexpected since inspection of molecular models reveals that the enolate ion in the precursor to **16** is not proximally disposed to facilitate the E_2 elimination step.

Other reactions of **5a**,**b** were studied in attempts to induce the tandem sequence using carbon-based nucleophiles. For example, when **5b** was treated with trimethylallylsilane in the presence of $TiCl_4$ (Sakurai reaction), no ring closure was observed but rather the allylated product **17** was obtained in 87% yield (Scheme 4).[8] This addition is noteworthy in that the allyl group enters from the α-face of the starting material, a surprising result since the X-ray structure of **5b** shows this to be the more congested face (see ORTEP of **5b**). Apparently, for the intermediate Lewis acid adduct precursor to **17,** at least one additional accessible conformation exists in which congestion of the β-face becomes dominate.

A particularly interesting reaction was observed when **5a** was treated with trimethylsilyl cyanide in the presence of triethylaluminum, conditions reported to favor 1,4-addition of TMSCN to enones.[9] This gave the tetraquinane enol ether **19** in 60% isolated yield. A mechanism envisaged to account

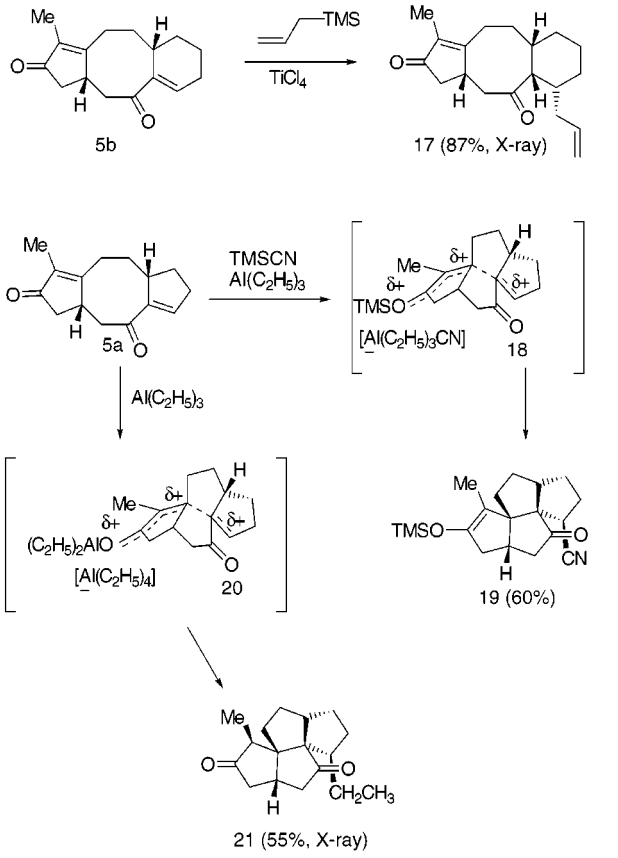
(5) For examples see: Paquette, L. A. *Eur. J. Org. Chem.* **1998**, 1709. Paquette, L. A. *Tetrahedron* **1997**, *53*, 13971.

(6) Since a slight excess of the lithium reagent was used, workup under the aqueous conditions provides a basic reaction media.

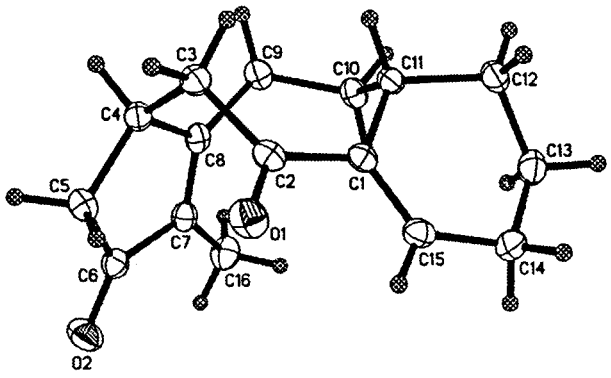
(7) This is in analogy to related oxy-Cope/transannular ring closures to polyquinanes staring with bicyclo[3.2.0]heptenones. See, for example: Santora, V. J.; Moore, H. W. *J. Am. Chem. Soc.* **1995**, *117*, 8486.

(8) Langkopf, E.; Schinzer, D. *Chem. Rev.* **1995**, *95*, 1375.

Scheme 4



for this unusual transformation involves initial 1,2-addition of TMSCN to the cyclopentenone carbonyl group followed by anchimeric assisted Lewis acid [Al(C_2H_5)$_3$] catalyzed ionization to the nonclassical carbocation **18**, an intermediate having only the β-face available for trapping of the nucleophile. Thus, transfer of the cyano group from the aluminate anion provides **19**.



ORTEP of Compound **5b**

In a related reaction, **5a** was treated with triethylaluminum in the absence of TMSCN.[10] Here again, tetraquinane formation was realized in that **21** was obtained as the only isolable product in 55% yield. A nonoclassical carbocation **20** is proposed which leads to **21** upon ethyl transfer to the β-face.

The structures of compounds **5a**, **12**, **13**, **16**, **17**, and **21** were unambiguously established by single-crystal X-ray crystallography. The structure of **19** is based on its spectral properties. Particularly revealing is the observation that the methyl group absorption in its ^{1}H NMR spectrum appears as a triplet at δ, 1.65, $J = 2.1$ Hz. This triplet, showing only coupling to an allylic methylene group, allows assignment of the regiochemistry of the silylenol ether moiety. The indicated stereochemistry is tentatively assigned and is based on the assumption that it would be the same as in **21**, the product in a related reaction.

In conclusion we note the following significant points concerning this study: (1) an unusual and efficient catalytic rearrangement of **5b** to the **13** is reported, thus providing the polycyclic ring system found in the natural product waihoensene; (2) in related reactions the tetraquinanes **19** and **21** stem from **5a**; (3) these transformations add to the growing number of complex polycyclic ring systems (including linear and angular polyquinanes, bicyclo[6.3.0]undecenones, bicyclo[5.2.1]decenones, and bicyclo[4.2.1]nonenones) arising from squarate-derived bicyclo[3.2.0]heptenones.[1,2,5,11]

Acknowledgment. The authors thank the National Institutes of Health (GM-36312) for financial support. We are also grateful to Dr. Joseph Ziller and Professor Everly B. Fleischer for X-ray crystallographic analyses.

Supporting Information Available: Procedures and characterization data, X-ray data for compound **5a**, **12**, **13**, **16**, **17**, and **21** and copies of ^{1}H NMR and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) Utimoto, K.; Wakabayashi, Y.; Horiie, T.; Inoue, M.; Shishiyama, Y.; Obayashi, M.; Nozaki, H *Tetrahedron* **1983**, *39*, 973

(10) Schlosser, M., Ed. *Organometallics in Synthesis: a Mannual*; Wiley: Chichester, West Sussex, England, New York, 1994.

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