Pergamon

Tetrahedron Letters, Vol. 37, No. 8, pp. 1177-1178, 1996

0040-4039/96 $15.00 + 0.00

0040-4039(95)02404-2

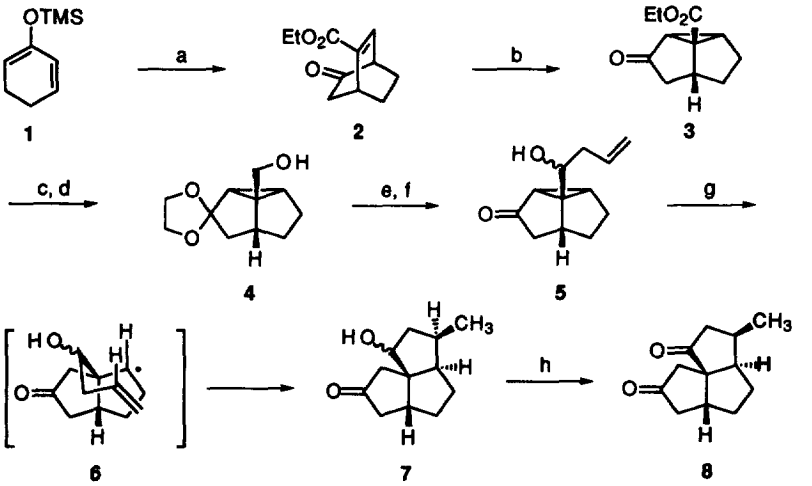
FRAGMENTATION-CYCLIZATION REACTIONS OF O-STANNYL KETYLS: THE SYNTHESIS OF AN ANGULAR TRIQUINANE SKELETON

Eric J. Enholm* and Zhaozhong J. Jia
Department of Chemistry, University of Florida
Gainesville, FL 32611, USA

Abstract: Fragmentation of a rigid tricyclo[3.3.0.0^{2,8}]octane-3-one ring system bearing an alkene tether resulted in the synthesis of an angular triquinane skeleton. This was achieved by a sequence involving a Diels-Alder cycloaddition, an oxa-di-π-methane rearrangement, and an O-stannyl ketyl ring scission (7 steps) in 36% overall yield.

The unique strained structure of the tricyclo[3.3.0.0^{2,8}]octane-3-one ring system allows it to function as an ideal skeletal precursor for the construction of fused polycyclopentanoid natural products.[1] We have recently begun a series of studies on the mechanistic and synthetic uses of this interesting tricyclic template with a particular focus on its O-stannyl ketyl-promoted cleavage.[2-4] This Letter contains the first application of this α-ketocyclopropane fragmentation where an intermediate radical is captured by a pendant alkene (**5** → **7**).[5] This general protocol provides for a new approach for the construction of an angular triquinane skeleton.[6-7]

To prepare precursor **5** for the key fragmentation, the Diels-Alder reaction of silyl ether **1** with ethyl propiolate gave bridged bicyclic product **2** (88%).[8,11] A triplet sensitized photochemical oxa-di-π-methane rearrangement readily constructed the desired strained tricyclo[3.3.0.0^{2,8}]octane-3-one ring system **3** in an excellent yield (88%).[11]



KEY: (a) HC≡CO_2Et, PhH, 75 °C, then H_3O^+; (b) hυ, Pyrex filter, acetone, 2d; (c) $HOCH_2CH_2OH$, PPTS, PhH, 80 °C, Dean-Stark; (d) Dibal (2.1 eq), CH_2Cl_2, -78 °C; (e) PDC, celite, CH_2Cl_2, RT; (f) allyl magnesiumbromide (2.0 eq), THF, -78 to 23°C, then H_3O^+; (g) nBu_3SnH, AIBN, PhH, 80 °C; (h) PCC, CH_2Cl_2, RT.

Protection of the ketone carbonyl in **3** (97%), followed by dibal reduction (90%) to **4** and PDC oxidation smoothly to give the desired aldehyde (67%).[11] The allyl unit was next added with allylmagnesium bromide

and the ketal protecting group was removed in a standard acidic workup (85%), producing 2 diastereomers of **5** (1.3 : 1) by GC analysis which were not separable by column chromatography.[11] Treatment with nBu_3SnH furnished the angular triquinane skeleton **7** in 93% yield.[11] High stereochemical control was realized in the 5-exo-trig radical cyclization where the endo:exo stereoselectivity for the methyl was found to be > 57 : 1. A Beckwith chair-like intermediate **6** supported the stereochemistry of the endo-methyl in **7**.[9] Diketone **8** was obtained by direct oxidation of **7** with PCC providing a single diastereomer of triquinane diketone **8** in 78% yield. The endo-methyl stereochemistry in **8** and its precursor **7** was readily established from Whitesell's earlier ^{13}C NMR studies of closely related fused-cyclopentanes.[10]

In summary, this work demonstrated an O-stannyl ketyl-promoted fragmentation of an α-ketocyclopropane can be efficiently coupled to the intramolecular radical trapping of a tethered alkene. The entire synthetic sequence here is very efficient, producing triquinane **7** in 36% overall yield from **1**.

Acknowledgement. We gratefully acknowledge support by the National Science Foundation (Grant CHE-9414240) for this work.

References:

(1) Demuth, M. in "Comprehensive Organic Synthesis," Trost, B. M.; Fleming, I., Eds., Pergamon Press: Oxford, 1992, *5*, Ch. 2.6.

(2) (a) Enholm, E. J.; Jia, Z. J. *Tetrahedron Lett.* **1995**, 6819; For related references, see: (b) Enholm, E. J.; Prasad, G. *Tetrahedron Lett.* **1989**, 4939; (c) Enholm, E. J.; Kinter, K. S. *J. Am. Chem. Soc.* **1991**, *113*, 7784; (d) Enholm, E. J.; Burroff, J. A. *Tetrahedron Lett.* **1992**, 1835; (e) Enholm, E. J.; Xie, Y.; Abboud, K. A. *J. Org. Chem.*. **1995**, *60*, 1112 (f) Rawal, V. H.; Krishnamurthy, V.; Fabre, A. *Tetrahedron Lett.* **1993**, *34*, 2899; (g) Beckwith, A. L. J.; Moad, G. *J. Chem. Soc. Perkin Trans. II* **1980**, 1473; (h) Enholm, E. J.; Kinter, K. S. *J. Org. Chem.* **1995**, *60*, 4850; (i) Rawal, V. H.; Dufour, C.; Iwasa, S. *Tetrahedron Lett.* **1993**, *34*, 2899; (j) Newcomb, M. *Tetrahedron*, **1993**, *49*, 1151; (k) Castellino, A. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1988**, *110*, 7512; (l) Harling, J. D.; Motherwell, W. B. *J. Chem. Soc. Chem. Comm.* **1988**, 1380; (m) Rawal, V. H.; Dufour, C.; *J. Am. Chem. Soc.* **1994**, *116*, 2613.

(3) For a reveiw of ketyl radical anions, see: Russell, G. A. in "Radical Ions", Kaiser, E. T.; Kevan, L. Eds., Wiley Interscience: New York, 1968, pp. 87-150.

(4) Examples of the Li-NH_3 opening: (a) Monti, S. A.; Bucheck, D. J.; Shepard, J. C. *J. Org. Chem.* **1969**, *34*, 3080; (b) Yates, P.; Stevens, K. E. *Tetrahedron* **1981**, *37*, 4401; (c) Dauben, W. G.; Deviny, E. J. *J. Org. Chem.* **1966**, *31*, 3794.

(5) Pereyre, M.; Quintard, J. -P.; Rahm, A. "Tin in Organic Synthesis", Butterworths: Boston, 1987.

(6) For reviews, see: (a) Hudlicky, T.; Rulin, F.; Lovelace, T. C.; Reed, J. W. "Studies in Natural Products Chemistry" Atta-ur-Rahman, Ed., Elsevier: Amsterdam, 1989, *3*, pp 3-72; (b) Paquette, L. A.; Doherty, A. M., "*Polyquinane Chemistry*", Springer-Verlag: Berlin, 1987.

(7) Other free radical approaches to the triquinanes: (a) Curran, D. P.; Rakiewicz, D. M. *J. Am. Chem. Soc.* **1985**, *107*, 1448; (b) Curran, D. P.; Chen, M. H. *Tetrahedron Lett.* **1985**, *26*, 4991; (c) Curran, D. P.; Kuo, S. -C. *J. Am. Chem. Soc.* **1986**, *108*, 1106; (d) Ferig, T. L.; Elliott, R. L.; Curran, D. P. *J. Am. Chem. Soc.* **1988**, *110*, 5064; (e) Jasperse, C. P.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 5601; (f) Curran, D. P.; Kuo, S. -C., *Tetrahedron* **1987**, *43*, 5653.

(8) Rubottom, G. M.; Krueger, D. S., *Tetrahedron Lett.* **1977**, 611.

(9) (a) Beckwith, A. L. J., *Tetrahedron*, **1981**, *37*, 3073; (b) Beckwith, A. L. J.; Schiesser, C. H., *Tetrahedron* **1985**, *41*, 3925.

(10) (a) Whitesell, J. K.; Matthews, R. S., *J. Org. Chem.* **1977**, *42*, 3878; see also: (b) Hudlicky, T.; Koszyk, F. J.; Kutchan, T. M.; Sheth, J. P. *J. Org. Chem.* **1980**, *45*, 5020.

(11) All new compounds exhibited ^1H and ^{13}C NMR, IR and combustion analysis consistent with the structure shown. A subsequent full paper will describe their preparation.

(*Received in USA* 5 *October* 1995; *revised* 8 *December* 1995; *accepted* 11 *December* 1995)