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[2+3] CYCLOPENTENE ANNULATION AND OTHER TRIMETHYLSILYL IODIDE-MEDIATED REARRANGEMENT PATHWAYS OF VINYLCYCLOPROPANES

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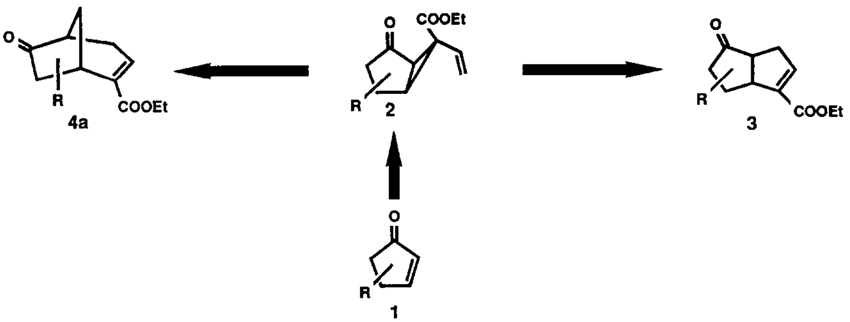
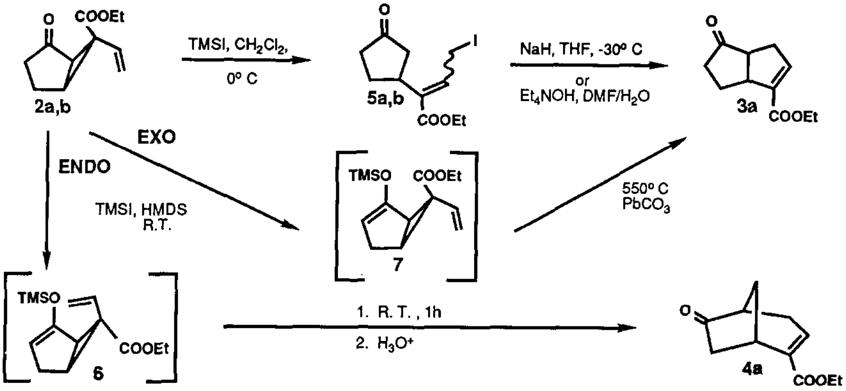
Abstract: Vinylcyclopropanes of type **2** were converted to either annulated cyclopentenes of type **3** or bicyclo [3.2.1] octenes of type **4** through carefully controlled rearrangement pathways. Factors affecting these rearrangements and their utility in synthesis are described.

The construction of annulated cyclopentene carboxylates of type **3** by pyrolyses of vinylcyclopropanes **2** has been established as an efficient method of carbocyclic syntheses, most notably in the preparation of various triquinane sesquiterpenes[2], where the cyclopentene carboxylate unit in **3** served as an element of stereochemical control for the peripheral substituent. The diradical fission of vinylcyclopropanes **2**, obtained via the intramolecular cyclopropanation of diazoketones,[3] was the primary method of acquisition of these annulated systems. We investigated a host of other, non-pyrolytic conditions to achieve the overall goal of cyclopentene annulation-among them acid catalyzed[4] and transition metal mediated[5] rearrangements. In this report we describe controlled rearrangements of vinylcyclopropanes to afford either cyclopentenes **3** or [3.2.1] octenes **4**.



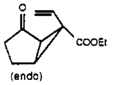
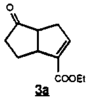
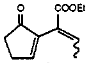
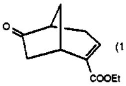
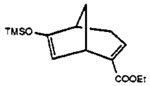
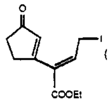
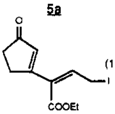
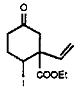
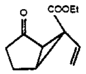
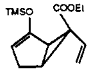
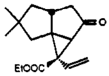
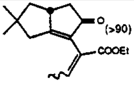
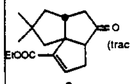
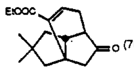
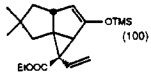
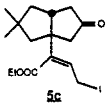
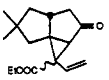
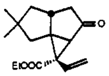
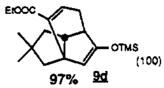
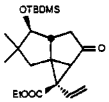
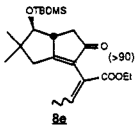
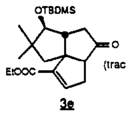
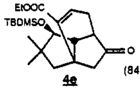
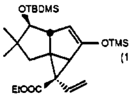
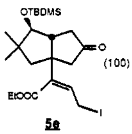
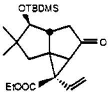
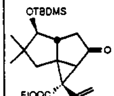
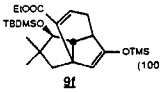
Recently, we reported on the high yielding synthesis of vinylcyclopropanes **2** from enones via the addition of lithium dienolate derived from ethyl 2-bomocrotonate.[6] This reaction provided vinylcyclopropanes as mixtures of <u>exo</u>- and <u>endo</u>-isomers, and preliminary experiments indicated that such isomer ratios could be controlled by changing the counter ion and/or the leaving group in the halocrotonate.[7] This new vinylcyclopropanation methodology coupled with the vinylcyclopropane-cyclopentene rearrangement thus constituted [2+3] Cyclopentene Annulation of enones.

In addition to pyrrolytic transformations of **2**, nucleophilic opening modes were investigated. Treatment of vinylcyclopropanes **2** with TMSI[8] at low temperature gave E/Z mixtures of allylic iodides **5**.[9] (See Table 1). The E-allylic iodides were then converted to cyclopentenes **3** using low temperature NaH or $Et_4N^+OH^-$ cyclizations, providing a mild complement to the thermolytic annulation method.



Exposure of endo-**2** to TMSI/HMDS at room temperature resulted in quantitative production of **4** on workup[10] whereas the exo-isomer gave, quantitatively, the corresponding TMS-enol ether **7**;[11] which was pyrolyzed to a mixture of **3** and **4**. This observation confirmed the supposition that the additional allylic stabilization of a diradical formed during pyrolysis of the enol-ether led to enhancement in production of **3** and completely prevented the formation of **8** previously observed on pyrolysis of cyclopropanes of type **2**. The exposure of endo-vinylcyclopropanes to TMSI/HMDS and ommitting work up yielded TMS enol-ethers of the bicyclo [3.2.1] octanones **9** quantitatively; these compounds could therefore be used in alkylative operations. These exciting discoveries bode well for rapid and selective preparation of either [3.3.0] or [3.2.1] bicyclic systems from the same intermediate. Table 1 summarizes these preliminary findings for several vinylcyclopropanes. The results of detailed studies on the mechanistic and controlling

TABLE 1 TRANSFORMATIONS OF VINYLCYCLOPROPANES

Starting Material	Pyrolysis	1. TMSI / HMDS 2. Pyrolysis 3. H^+	TMSI / HMDS	1. TMSI 2. H^+	1. TMSI 2. NaH or Et_4NOH
 (endo) 2a	 (47)[1] 3a  (42) 8a  (11) 4a 93%[2]		 (100) 9a 97%	 (21) 5a  (19) 5b  (42) 10 4a (18) 75%	3a with NaH 20% with Et_4NOH 40%
 2b (exo)	3a (98) 8a (2) 80%	3a (42) 4a (58) 90%	 7b 97%	5a (60) 5b (40) 85%	3a with NaH 20% with Et_4NOH 40%
 (exo) 2c	 (>90) 8c  (trace) 3c 91%	 (70) 4c 3c (30) 95%	 (100) 7c 97%	 (100) 5c 85%	 2c (67) 2d (33) 95%
 (endo) 2d	8c (>90) 3c (trace) 91%		 (100) 97% 9d	5c (100) 85%	2c (67) 2d (33) 95%
 (exo) 2e	 (>90) 8e  (trace) 3e 90%	 (84) 4e 3e (16) 90%	 (100) 7e 97%	 (100) 5e 85%	 2f (50) 2e (50) 90%
 (endo) 2f	8e (>90) 3e (trace) 90%		 (100) 9f 97%	5e (100) 85%	2f (50) 2e (50) 90%

Note: [1] ratios by NMR, [2] isolated total yields aspects of these reactions, as well as their application to the total synthesis of pentalenene, pentalenic acid, and quadrone[12], will be reported in due course.

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