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UNEXPECTED FRAGMENTATIONS LEADING TO QUINANES AND HYDRINDANES MEDIATED BY A SILYL RADICAL

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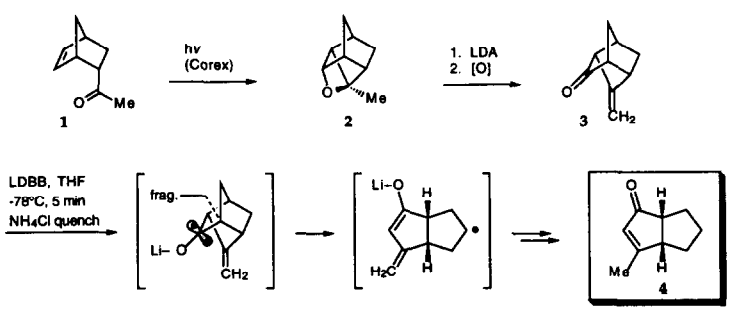
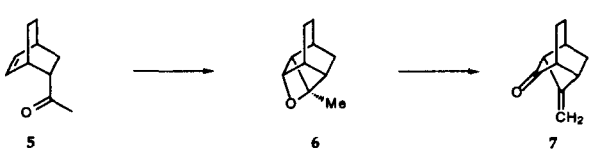
Abstract: Useful bicyclic ring systems are obtained by *tris*-trimethylsilylsilyl radical ($TMS_3Si\bullet$) mediated fragmentation of strained alkene precursors.

We recently reported a general strategy to di- and triquinane structures that takes advantage of a reductive fragmentation of readily available, strained precursors (Scheme 1).[2] Thus the Diels-Alder adduct of cyclopentadiene and methyl vinyl ketone was irradiated through Corex to give the Paterno-Büchi product **2**,[3] which was converted to ketoalkene **3** in high yield. Reductive fragmentation of **3** gave diquinane **4** as the major product, arising from scission of the "back bond". In an effort to expand the scope of this strategy, we have examined other substrates and fragmentation protocols. We describe here the remarkably different fragmentation pathways taken by two closely related strained precursors.

Scheme 1



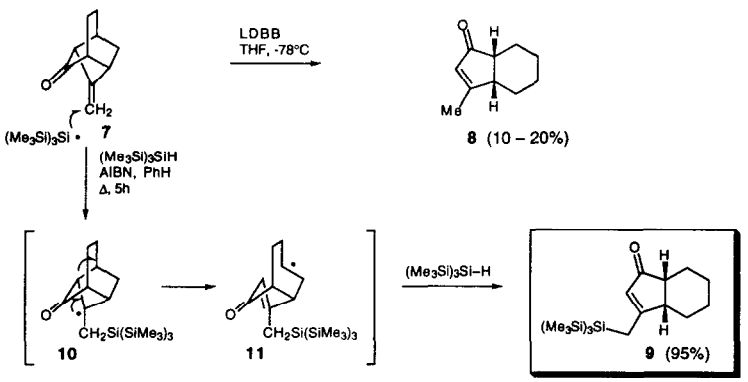
In extending the above strategy, it was recognized that fragmentation of the next larger homolog of **3** would give a functionalized *cis*-hydrindane, a subunit that may be of use for the synthesis of numerous natural products, particularly steroids. Irradiation of a benzene solution of 5-acetylbicyclo[2.2.2]octene, prepared by silica gel mediated Diels-Alder reaction between 1,3-cyclohexadiene and methyl vinyl ketone (0–10 °C, 2-3 days; 89% yield, >30:1 *endo:exo*),[4] with Corex filtered light (450 W Hanovia medium pressure Hg lamp, 2-3 d) gave the Paterno-Büchi product **6** in 85% yield (Eq. 1).[5] Acid catalyzed opening of the oxetane gave the known hydroxyalkene (74%),[5] which on oxidation using PDC in the presence of Celite afforded ketoalkene **7** (84%).



(1)

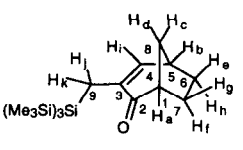
Unfortunately, under our standard reductive fragmentation conditions (LDBB, THF)[2] ketoalkene **7** gave the desired hydrindenone **8** in only 10-20% yield (Scheme 2). Other reagents that were expected to promote the fragmentation include trialkyltin[6] or trialkylsilyl[7] radicals, both of which are known to add to carbonyl groups to give ketyl-type radicals. Indeed, the reaction of ketoalkene **7** with $(Me_3Si)_3SiH$ (1.5 equiv) and AIBN (cat.) in refluxing benzene resulted in a clean fragmentation and gave in 95% yield silyl-substituted hydrindanone **9**, although not from the expected pathway. The silyl radical evidently adds first to the C-C double bond, rather than to the carbonyl oxygen, to give tertiary radical **10**. This intermediate is expected to be highly strained and can relieve that strain by cleaving an adjacent C-C bond. As with the ketyl radical fragmentation reported earlier (Scheme 1),[2] radical **10** also rearranges by cleavage of the (presumably more strained) "back bond" to give radical **11**, which after hydrogen abstraction yields the observed product. The preferential addition of the silyl radical to the alkene over the carbonyl group is consistent with literature reports.[7,8]

Scheme 2



Given the high yielding formation of **9** from **7**, one would expect an analogous transformation for the norbornane derived ketoalkene **3** to the silyl-substituted diquinane **12** (Scheme 3). When keto alkene **3** was treated with $(Me_3Si)_3SiH$ and AIBN in refluxing benzene, a single major product was formed in 89% yield. The product was not, however, the expected diquinane **12**. Extensive NMR studies showed the major product to be the silyl containing bicyclo[3.2.1]octenone **13**. The assigned structure is consistent with data reported for related compounds.[9] Decoupling, C-H, and long-range C-H correlation enabled the assignment of the different protons and carbons of **13** (Figure 1).

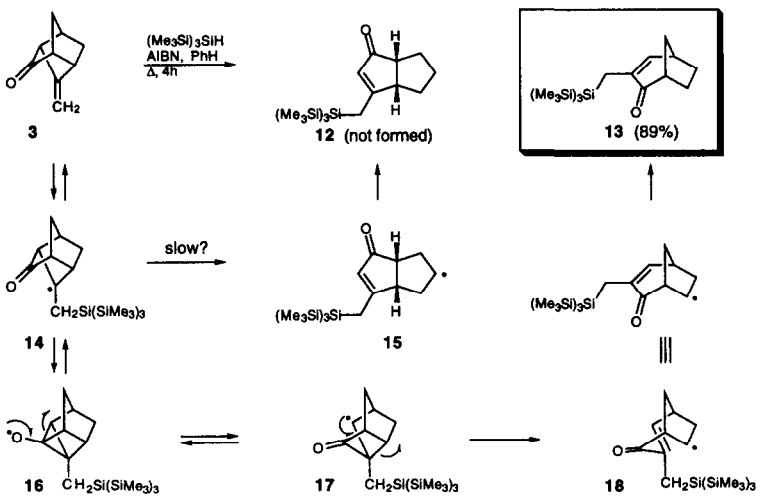
Figure 1



13

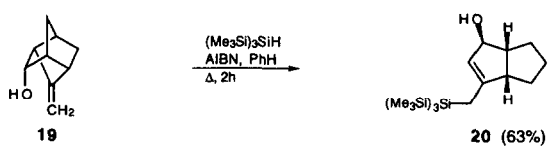
Proton	δ (ppm)	Carbon	δ (ppm)
H_a	2.95	1	50.20
H_b	2.80	2	202.19
H_c	1.50	3	137.99
H_d	1.95	4	148.35
H_e	1.89	5	37.49
H_f	1.58	6	29.32
H_g	2.05	7	24.51
H_h	1.4	8	39.91
H_i	6.8	9	8.21
H_j, H_k	1.65, 1.98		

Scheme 3



A plausible mechanism for the formation of this unexpected product is shown in Scheme 3. Unlike in the preceding case, tertiary radical intermediate **14** evidently does not fragment to diquinane radical **15** but, instead, adds to the carbonyl group to generate alkoxy cyclopropyl radical **16**,[10,11] which rearranges by cleavage of the other cyclopropane C-C bond to produce radical **17**. This radical is also adjacent to a strained ring, a cyclobutanone, and triggers its fragmentation to give intermediate **18**,[11,12] which on abstraction of a hydrogen gives the observed bicyclic product. What is remarkable about these two examples is the complete change in the fragmentation pathway caused by shortening of one of the bridging chains by one methylene unit.

The mechanism proposed for the fragmentation leading to **13** implies either that the rearrangement of radical **14** to diquinane **15** is slow compared with its addition to the carbonyl group or that it is not favored at all. To test this hypothesis, we examined the fragmentation of a precursor lacking the carbonyl group, alcohol **19** (Eq. 2). When alcohol **19** was subjected to the standard silane mediated fragmentation conditions, the expected silyl containing diquinane product **20** was formed cleanly in 63% yield, along with recovered starting material (27%). This result is consistent with the fragmentation of radical **14** being slower than its addition to the carbonyl. In the absence of the latter option, the "normal" fragmentation is followed to give a diquinane.



(2)

These studies further illustrate the usefulness of our Paterno-Büchi/reductive fragmentation strategy for the synthesis of carbocyclic compounds. Moreover, the present results show that relatively minor perturbations in the structure of the starting material can result in dramatically different fragmentation products. Studies aimed at providing an explanation for these unexpected results are in progress.

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