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Thermo-cage opening of 4-iodo-1-vinylcubane to a novel styrene derivative

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Abstract

Cubane (**1**) and its derivatives have been cited for exhibiting unusual properties, including explosive and antiviral activity. An additional characteristic of these compounds is their tendency to undergo cage opening under certain conditions. In our attempt to polymerize 4-iodo-1-vinylcubane (**4**), 4-vinyl-trans-β-iodostyrene (**10**) was formed quantitatively. By examining both the thermolytic and Lewis acid-assisted rates, a possible mechanism for the rearrangement of **4**→**10** has been proposed.

Since the initial synthesis of cubane (**1**) by Eaton and Cole[1] in 1964, numerous publications dealing with the special qualities of its derivatives have been reported. Octonitrocubane has been classified as the most powerful non-nuclear explosive.[2] In a quite different area, cubylamines have been reported to be antiviral.[3] Cubanes also have a tendency to behave as quasi-aromatic molecules, participating in reactions that are typically associated with benzene.[4–7] Cubane derivatives have been studied as to their tendency to undergo cage-opening under certain conditions; for example cubanol will spontaneously open to form vinylcyclobutenylketene.[8,9] Ring opening has also been observed with cubylamines[10,11] and cubanethiol.

Cubane has been reported to rearrange in the presence of certain metals (Fig. 1).[9,12] When cubane (**1**) was treated with silver(I) ions, it rearranged to form cuneane (**2**).[13] In the presence of rhodium(I), *syn*-tricyclooctadiene (**3**) was formed.[14] In our quest to synthesize a tethered, cubane-based polymer, a vinylcubane monomer was initial prepared. Although the polymerization of a tethered cubane was successfully accomplished via an alternate route,[15] the use of vinylcubane monomers under various polymerization techniques yielded no polymers. In many cases a 4-vinylstyrene derivative was produced. This directed us to explore this cage opening/rearrangement more closely, and the results are reported herein.

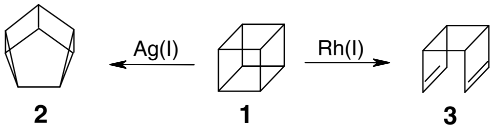

Fig. 1. Reactivity of cubane (**1**) with silver and rhodium.

In our work, we specifically chose 4-iodo-1-vinylcubane (**4**) as our monomer due to the additional functionality, which could facilitate further transformations in post-polymer functionalization reactions.[15] The synthesis of **4** was accomplished in a five-step pathway (Scheme 1). Commercially available dimethyl-1,4-cubane dicarboxylate (**5**) underwent partial base hydrolysis to form the 4-methoxycarbonyl cubane carboxylic acid (**6**). This was followed by a Moriarty reaction, then an additional base hydrolysis yielding the 4-iodocubanecarboxylic acid (**7**). Borane reduction[16] of **7** followed by Swern oxidation of **8**,[12,17] provided aldehyde, **9**. A Wittig reaction afforded 4-iodo-1-vinylcubane (**4**)[18] in an overall 66% yield from **5**.

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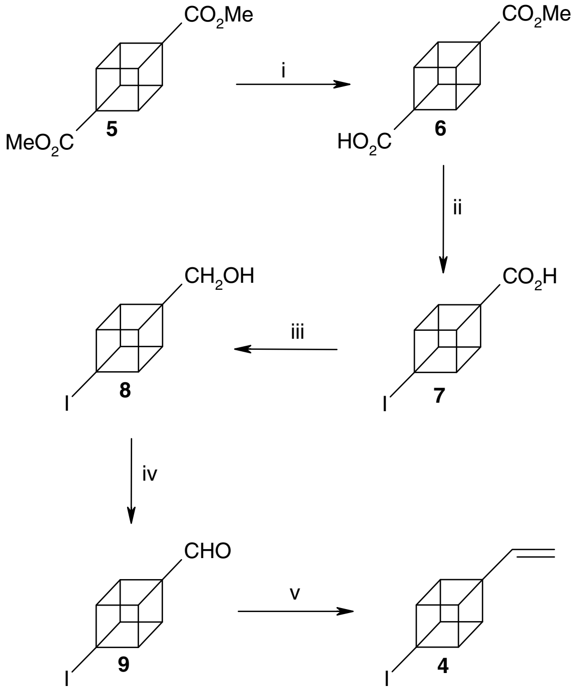
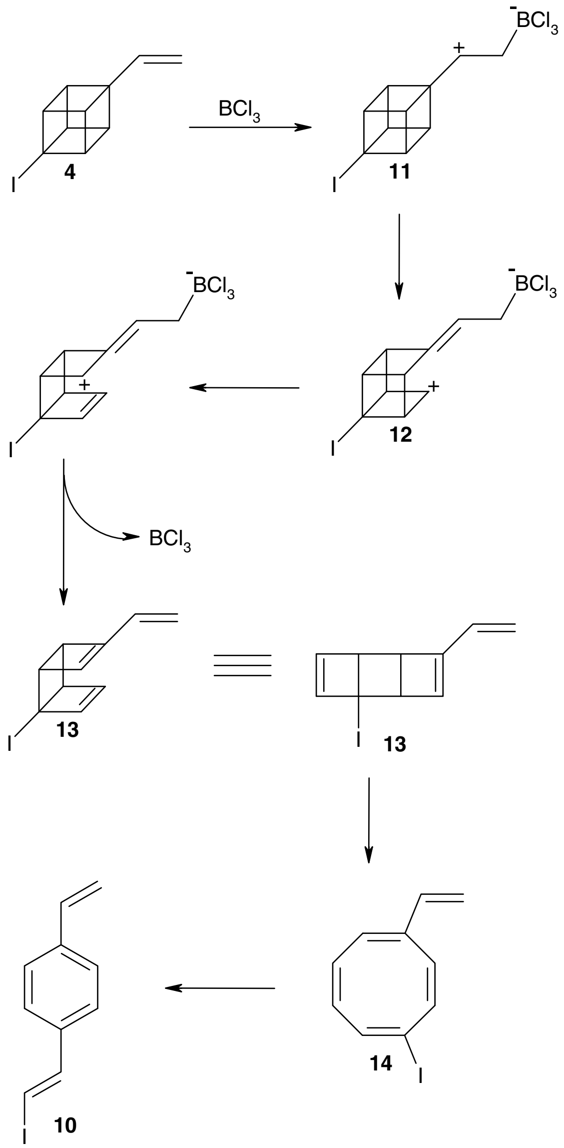


Scheme 1. Reagents and conditions: (i) (a) 1 equiv NaOH/MeOH/THF, (b) HCl, 92%; (ii) (a) IBDA, I_2, benzene, Δ, 6 h, (b) NaOH/MeOH, (c) HCl, 92%; (iii) (a) $BH_3{\cdot}SMe_2$/THF, 0 °C, (b) HCl, 95%; (iv) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, 93%; (v) Ph_3PCH_3Br, n-BuLi, THF, 88%.



Scheme 2. Proposed mechanism of the conversion of 4-iodo-1-vinylcubane (**4**) to the rearrangement product, 4-vinyl-trans-β-iodo-styrene (**10**).

Attempted polymerization of **4** via cationic, anionic, and free-radical techniques were all unsuccessful.[12] However, with cationic and free-radical procedures where elevated temperatures are employed, an aromatic product was detected, which was ultimately determined to be 4-vinyl-*trans*-β-iodostyrene (**10**).[19] In these instances, complete conversion was observed after 2 and 3 days, respectively. When **4** was refluxed in toluene with or without the presence of a UV-light source, complete conversion was accomplished in 3 days. This indicated to us that the reaction was not a radical process. The decrease in reaction time with the addition of 10% of a Lewis acid ($AlBr_3$, $AlCl_3$, BCl_3, or BF_3) suggested that the reaction may be acid-catalyzed. A similar cubane conversion had been previously reported; however this required the addition of $[Ru(COD)Cl]_2$ for the initial opening to the cyclooctatetraene intermediate.[20]

In our case we postulate that the initial alkene attack on the Lewis acid did occur, as would be expected for polymerization (Scheme 2). However, the subsequent attack on the carbocation product **11** by an additional alkene, **4**, did not take place. Instead, the cage opened to form the less strained derivative, **12** which would further open to form the tricyclooctadiene derivative, **13** and ultimately cyclooctatetraene, **14**. Tricyclooctadienes have been reported to open to give the cyclooctatetraene derivatives in the presence of Rh(I).[14]

In addition, it has been reported that halogenated cyclooctatetraene derivatives rearrange upon heating (>80 °C) to give *trans*-β-halostyrene.[21] In order to determine whether the reaction was indeed being accelerated by the presence of a Lewis acid, different equivalences of BCl_3 were added and the reaction was monitored by GC. When **4** was heated in refluxing toluene, complete conversion to **10** was accomplished in 72 h. Samples were taken every 12 h and analyzed by GC. It was necessary to lower the injection temperature to 150 °C in order to observe the starting material, **4**. When employing a higher injection temperature, the intensity of the peak at 13.3 min increased.[22] It is reasonable to postulate that this signal corresponds to cyclooctatetraene, **14** (starting 4-iodo-1-vinylcubane (**4**) is detected at 12.4 min, Fig. 2).

Vinyl cubane **4**, had completely disappeared after 36 h; the final 36 h was needed to convert the remaining cyclo-

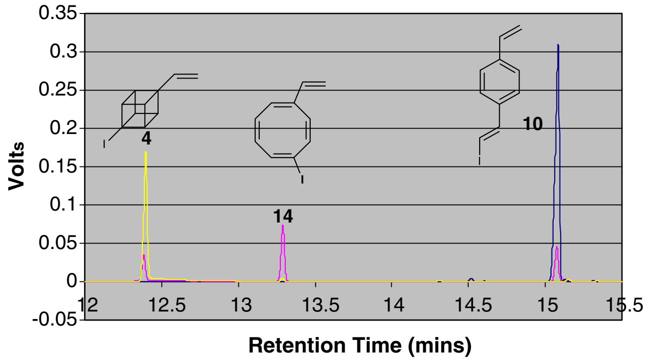


Fig. 2. Time profile rearrangement of 4-iodo-1-vinylcubane (**4**) to 4-vinyl-trans-β-iodostyrene (**10**) shown at time zero (yellow), 12 h (pink), and 72 h (blue) heating in toluene.

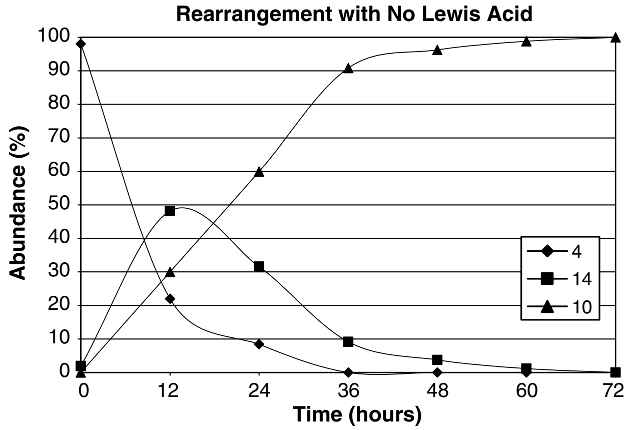


Fig. 3. Time profile rearrangement of 4-iodo-1-vinylcubane (**4**) to 4-vinyl-trans-β-iodostyrene (**10**).

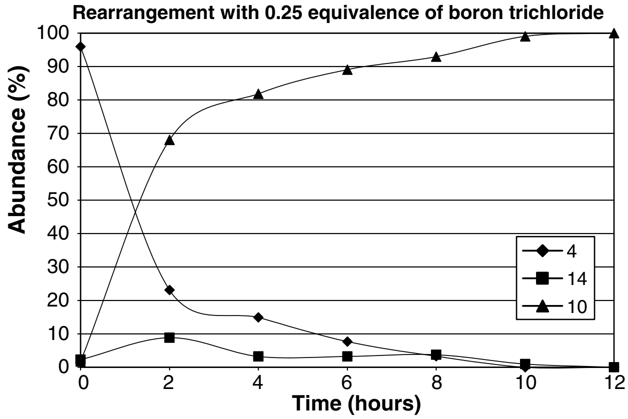


Fig. 4. Time profile rearrangement of 4-iodo-1-vinylcubane (**4**) to 4-vinyl-trans-β-iodostyrene (**10**) using 0.25 equiv BCl_3.

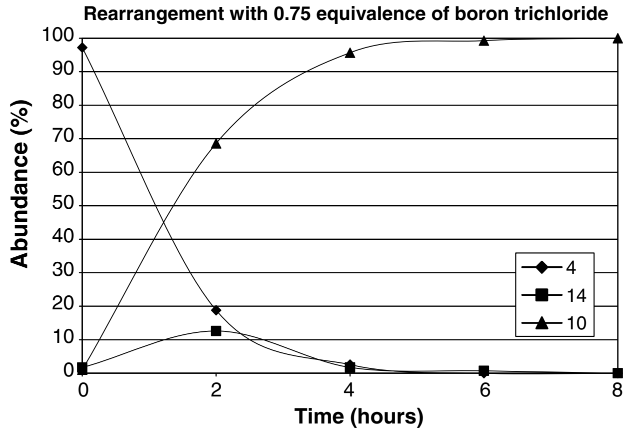


Fig. 5. Time profile rearrangement of 4-iodo-1-vinylcubane (**4**) to 4-vinyl-trans-β- iodostyrene (**10**) using 0.75 equiv BCl_3.

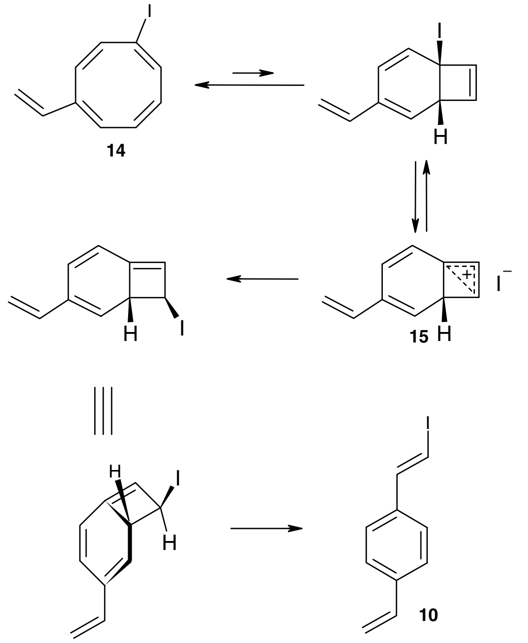
octatetraene, **14**, into **10**. (Fig. 3) (4-vinyl-trans-β-iodostyrene (**10**) appears at 15.1 min).

The addition of 25% and 75% of the Lewis acid BCl_3, dramatically increased the rate of the reaction for complete conversion after only 12 (Fig. 4) and 8 h (Fig. 5), respectively. The reactions were monitored every 2 hours and it was observed that there was no significant amount of **14** at any time interval. Cope reported the use of acids to accelerate the conversion of halogenated cyclooctatetraene to *trans*-β-halostyrene however, in their study the acid sources were carboxylic acids only.[21] They noted a positive relationship between acid strength and rearrangement;[21] it was theorized that the ionization step forming **15** (Scheme 3) would be accelerated in the presence of an acid.

Scheme 3 illustrates a proposed mechanism using **14** as the model cyclooctatetraene. The coordination of iodine with a Lewis acid should increase the rate of formation of **15** and ultimately the overall rate of the reaction. In all the three cases the rate was first order with respect to the disappearance of 4-iodo-1-vinylcubane (**4**).

What remained unknown was whether the initial conversion of **4**→**14** was also being accelerated by the use of the Lewis acid. The reverse reaction (**14**→**4**) is not possible and the non-Lewis acid assisted reaction requires 36 h for complete disappearance of **4** (Fig. 3); thus any reaction proceed at a more rapid rate must therefore be catalyzing the first step as well. Upon addition of a Lewis acid, the reaction was completed in less than 36 h, thus the acid must play two roles: initially, to assist in the ring opening (Scheme 2) as well as with the cyclooctatetraene rearrangement (Scheme 3).

This is the first reported example of a cubane derivative undergoing cage-opening to a cyclooctatetraene derivative without the assistance of rhodium(I). The initial product continued to rearrange to the much more stable styrene derivative. Work is currently underway to examine the use of other Lewis acids as well as the incorporation of different halides on the cube backbone. In addition, we are attempting to isolate cyclooctatetraene, **14**, in order to determine the kinetic nature of both steps in the cage-opening/rearrangement pathway.



Scheme 3. Proposed mechanism of cyclooctratetraene, **14**, to 4-vinyl-trans-β-iodo-styrene (**10**).

Acknowledgements

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18. *4-Iodo-1-vinylcubane* (**4**). Yield 88%. White solid with mp 77–79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.09 (m, 3H), 4.19 (m, 3H), 4.92 (dd, 1H, $J = 1.95$, 17.10 Hz), 5.06 (dd, 1H, $J = 1.95$, 10.60 Hz), 6.05 (dd, 1H, 10.60, 17.10 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 39.18, 50.49, 54.31, 60.34, 113.15, 136.66. Elemental Anal. Calcd $C_{10}H_9I$: C, 46.90; H, 3.54, Found: C, 47.22; H, 3.45.
19. *4-Vinyl-trans-*β*-iodostyrene* (**10**). White solid with mp 101–102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.27 (dd, 1H, $J = 0.60$, 10.80 Hz), 5.75 (dd, 1H, $J = 0.60$, 17.10 Hz), 6.67 (dd, 1H, 10.80, 17.10 Hz), 6.81 (d, 1H, 14.70 Hz), 7.24 (d, 2H, 8.40 Hz), 7.35 (d, 2H, 8.40 Hz), 7.39 (d, 1H, 14.70 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 114.28, 126.03, 126.43, 136.09, 136.87, 137.40, 144.36, 149.69. Elemental Anal. Calcd $C_{10}H_9I$: C; 46.90; H, 3.54. Found: C, 47.04; H 3.22.
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22. Injection volume: 5 μL; injection rate: 5 μL/s; injection temperature: 150 °C; column flow; 1.0 mL/min; column temperature: 40–290 °C at 10 °C/min; FID detector temperature: 290 °C.