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ON THE MECHANISM OF THE LEWIS ACID CATALYZED CYCLOCONDENSATION OF ALDEHYDES WITH SILOXYDIENES

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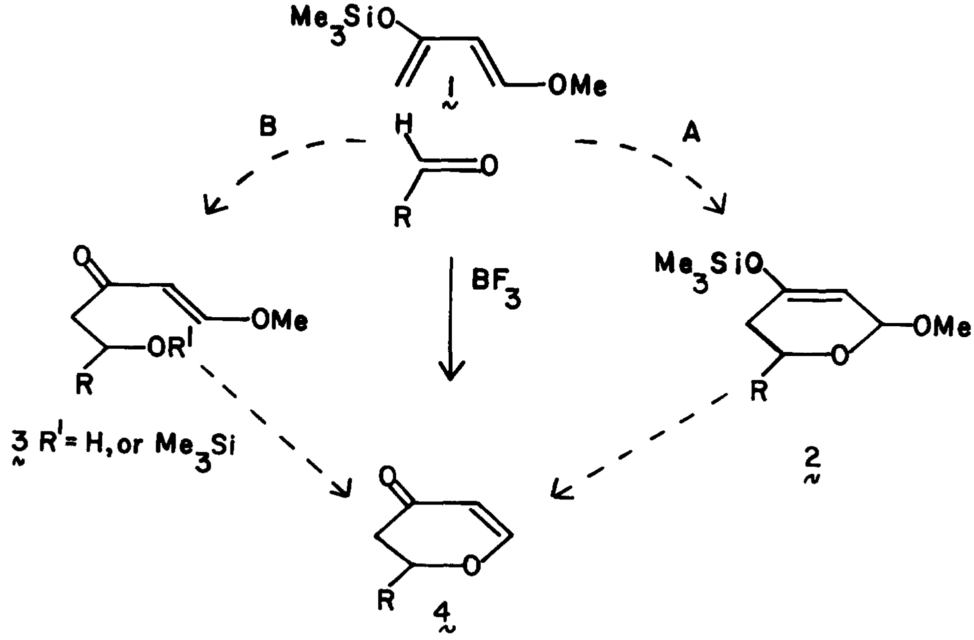
Abstract· Competing cycloaddition versus aldolization-cyclization processes are demonstrated in the formation of 6-styryl-5,6-dihydro-γ-pyrone *via* the BF_3 catalyzed reaction of cinnamaldehyde with *trans*-1-methoxy 3-trimethylsilyloxy-1,3-butadiene

We have reported on the Lewis Acid mediated cyclocondensations of siloxydienes such as **1** with a diverse range of aldehydes to afford 5,6-dihydro-γ-pyrones of the type **4** [1] With unsaturated aldehydes (R = vinyl or styryl) cyclocondensation occurs to the apparent exclusion of the classical Diels-Alder process, which is the sole observed reaction under thermal conditions [2] In this Letter, we provide some insights into the mechanism of the cyclocondensation process.

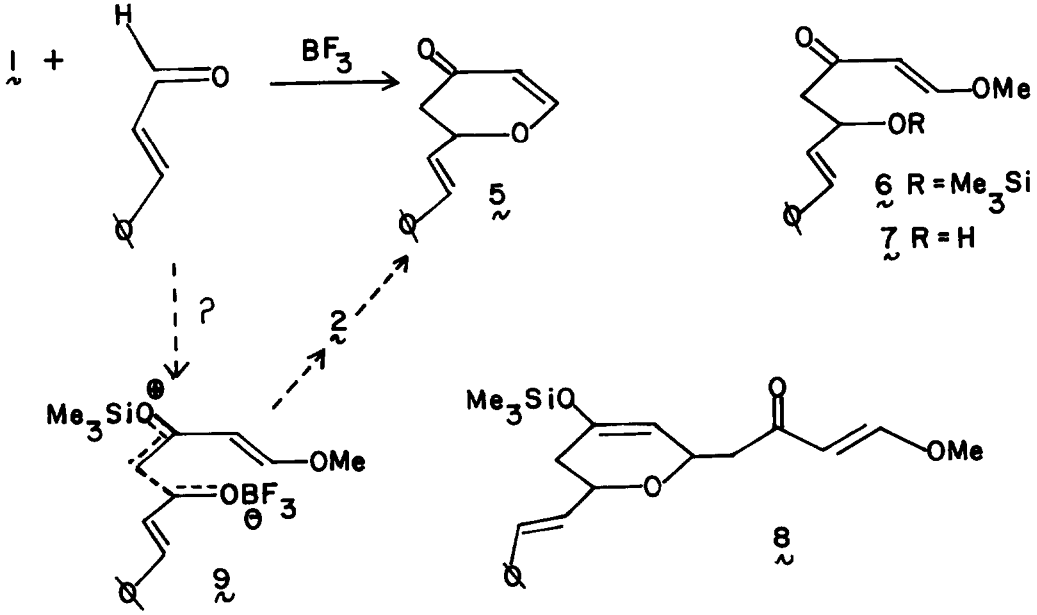
The first question to be addressed in this connection is whether **4** arises from a *bona fide* cycloaddition process (path A) or whether it is the consequence of a Mukaiyama-like aldol reaction,[3] followed by cyclization (path B) For the moment, an intermediate of the type **2** has not been demonstrated in these reactions.



On reaction of **1** with cinnamaldehyde under standard conditions (1 eq. each of aldehyde, and boron trifluoride etherate, 0.1 M diethyl ether at -78°C) for 4 hr. followed by quenching (aq. sodium bicarbonate), there was obtained a 72% yield of isolated homogeneous **5**. The same reaction conditions, but with quenching (aq. sodium bicarbonate -78 → 0°) after 5 min. afforded **5** (38%), starting aldehyde (12%), the two Mukaiyama-like products, **6** and **7** (40% combined)[5] and a *bis* adduct **8**[4,6] (6%). *Despite repeated efforts at early quenching, the yield of **5** could not be suppressed below ca. 40%.*

When either **6** or **7**, in pure form, was re-subjected to the "standard" conditions (see above), each underwent conversion to **5**. After 4 hr., the conversion of **6** → **5** is 75%. In the case of hydroxyenone **7**, the yield after 1.5 hrs. is 70%. However, the rates of these cyclizations are too slow to account for the substantial (*ca.* 40%) formation of **5** which occurs even after 5 minutes.

Thus at least under these conditions, two distinct pathways are discerned. One involves a BF_3 mediated Mukaiyama-like reaction (with or without accompanying silyl transfer (*cf.* **6** and **7**)), followed by slow conversion to **5**. There is an alternate rapid route to **5** which does not pass through detectable intermediates such as **3**. A strong inference for the existence of a cyclocondensation process, presumably leading to a system of the type **2**, has thus been provided.



We emphasize that in drawing this inference we avoid conjectures about the degree of concertedness of the cycloaddition reaction For instance, the existence of species of the type 9 are not excluded by the expression "cycloaddition" Analogous species may well be involved in the Lewis Acid mediated "conventional" Diels-Alder reaction

Further investigations directed to this question, using other substrates under different conditions have provided more evidence in favor of a cycloaddition process These findings as well as new synthetic applications of the reaction will be described in due course

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References

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2 Danishefsky, S., Kerwin, J F., Jr Manuscript submitted for publication

3 *cf* Mukaiyama, T , Nasasaka, K., Banno, K Chem Lett , 1973, 1011 J Am Chem Soc , 1974, 96, 7503. These authors generally use titanium tetrachloride catalysis.

4 Satisfactory IR, NMR and mass spectral data were obtained for the following compounds 5 IR ν ($CHCl_3$) 1680 and 1600 cm^{-1}, ^1H NMR (90 MHz, $CDCl_3$) δ 7.38 (6 H, m), 6 78 (1 H, d, J = 16 Hz), 6.32 (1 H, dd, J = 16, 6 Hz), 5 45 (1 H, d, J = 6 Hz), 5 02 (1 H, m), 2 55 (2 H, m), ^{13}C NMR (22.5 MHz, $CDCl_3$) 191.9, 163 1, 135.8, 133 8, 128.9, 128.7, 127 0, 125.4, 107.4, 79 8, 42 1, m/e 200 (M^+). 6 IR ν ($CHCl_3$) 1695, 1670, 1630, 1600, 1250 and 840 cm^{-1}, ^1H NMR (90 MHz, $CDCl_3$) δ 7 51 (1 H, d, J = 13 Hz) 7 32 (5 H, m) 6.59 (1 H, d, J = 16 Hz), 6 22 (1 H, dd, J = 16, 6 Hz) 5 60 (1 H, d, J = 13 Hz), 4 81 (1 H, m), 3 68 (3 H, s) 2.83 (1 H, dd, J = 15, 8 Hz), 2 55 (1 H, dd, J = 15, 5 Hz), ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 197 0, 163 2, 136 7, 132.0, 129.3, 128 4, 127 4, 126 3, 102 4, 70.3, 57.3, 49 5, 0 1, m/e 304 (M^+). 7 IR ν ($CHCl_3$) 3500 (br) 1680, 1650, 1620 and 1600 cm^{-1}, ^1H NMR (90 MHz, $CDCl_3$) δ 7 67 (1 H, d, J = 13 Hz), 7 34 (5 H, m), 6.70 (1 H, d, J = 16 Hz), 6 36 (1 H, dd, J = 16, 6 Hz), 5 61 (1 H, d, J = 13 Hz), 4 76 (1 H, m), 3 73 (3 H, S), 3 56 (1 H, brs, D_2O exch.) 2 77 (2 H, d, J = 6 Hz), ^{13}C NMR (22 5 MHz, $CDCl_3$) δ 199 0, 163,6, 136 6, 130 6, 130 0, 128 4, 127 5, 126 4, 105 9, 68 7, 57.5, 47 0, m/e 232 (M^+) 8 IR ν ($CHCl_3$) 1685, 1670, 1620, 1600, 1250 and 840 cm^{-1}, ^1H NMR

(90 MHz, CDCl$_3$) δ 7.61 (1 H, d, J = 13 Hz), 7.33 (5 H, m), 6.63 (1 H, d, J = 16 Hz), 6.23 (1 H, dd, J = 16 Hz), 6.23 (1 H, dd, J = 16, 5 Hz) 5.57 (1 H, d, J = 13 Hz), 4.83 (1 H, bs). 4.77 (1 H, m), 4.41 (1 H, m), 3.60 (3 H, s), 2.81 (1 H, dd, J = 14, 7 Hz), 2.50 (1 H, dd, J = 14, 6 Hz), 2.12 (2 H, d, J = 6 Hz), ^{13}C NMR (22.5 MHz, CDCl$_3$) δ 197.1, 163.1, 147.9, 136.7, 131.3, 128.9, 128.6, 127.7, 126.5, 106.2, 105.3, 69.9, 69.1, 57.5, 47.1, 35.3, 0.3, m/e 372 (M$^+$).

5. The ratio of 6:7 was variable, and may reflect the extreme ease of converting 6 → 7, either in the reaction, or on workup.
6. Compound 8 was synthesized independently (72%) from the reaction 5 + 1 with BF$_3$. Its relative stereochemistry is undetermined.

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