Tetrahedron Letters, Vol.31, No.16, pp 2243-2246, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

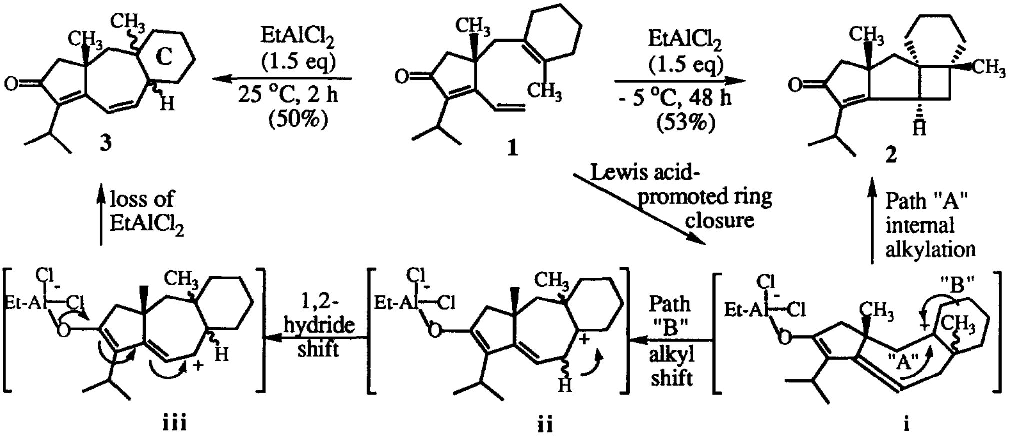
Intramolecular Reactions of Unactivated Alkenes with Conjugated Dienones

George Majetich* and Vikram Khetani
Department of Chemistry, *The University of Georgia*
Athens, Georgia 30602

Summary: Lewis acid- or Amberlyst resin-promoted cyclizations of unactivated alkenes with 3-vinylcycloalkenones afford a variety of polycyclic systems.

Although Lewis acid-catalyzed reactions of alkenes with simple and conjugated carbonyl compounds have been extensively studied,[1] in only one case have dienones been used as electrophiles.[2] In the course of our dolastane work[3] we found that treatment of trienone **1** with excess ethylaluminum dichloride at low temperatures gave tetracyclic enone **2** in 53% yield, while reaction at room temperature led to a comparable yield of tricyclic dienone **3** (Eq. 1).[4] Both products can be derived from the zwitterion **i**, which forms upon initial ring closure. At low reaction temperatures intermediate **i** undergoes intramolecular alkylation to give a cyclobutane (Path "A"). This process corresponds to a non-photochemical 2+2 cycloaddition.[5] In contrast, at higher temperature **i** first undergoes an alkyl shift (**i**→ **ii**, i.e., Path "B") and then a 1,2-hydride shift to generate dienone **3**.

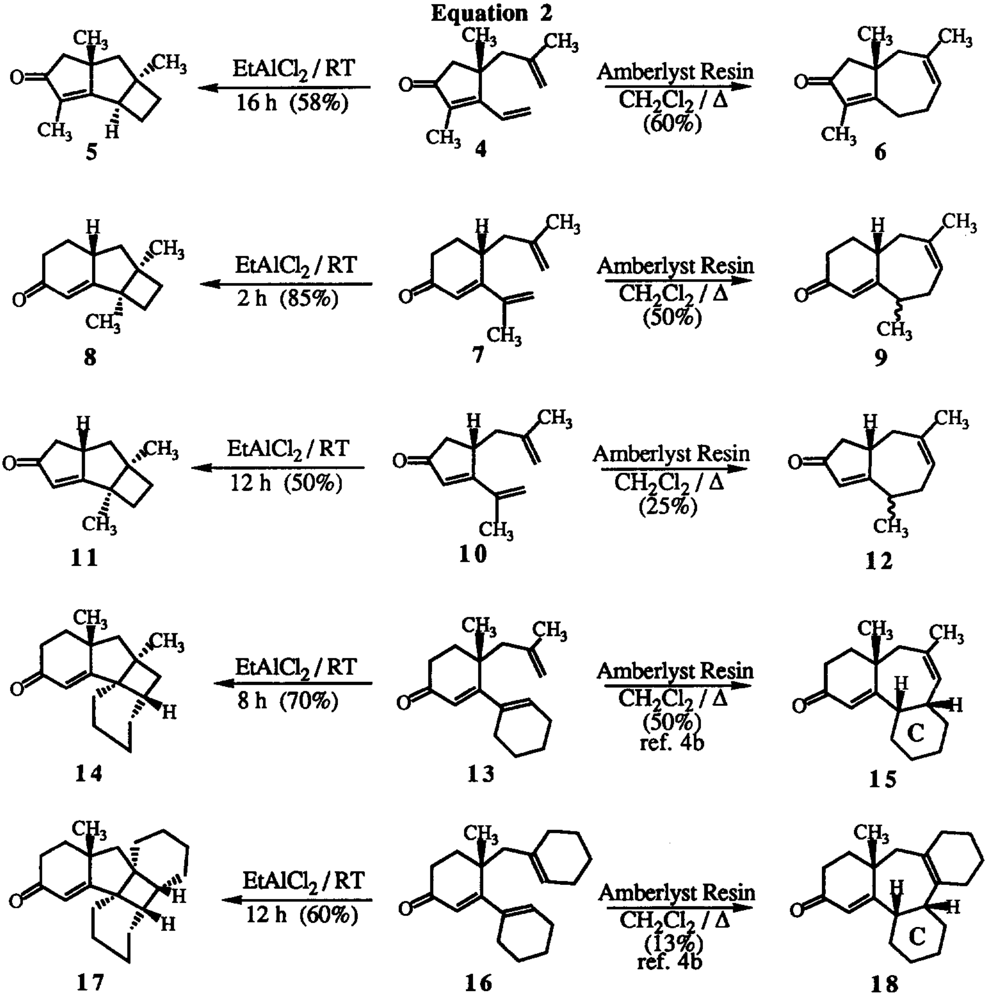
Equation 1



We have found Amberlyst resins[6] useful for the initiation of other cation-olefin cyclizations.[7] The novelty of the results described above prompted us to probe the utility of cation-dienone cyclizations for the formation of polycyclic systems, and to compare the effect of Lewis acid catalysts with acidic resins.

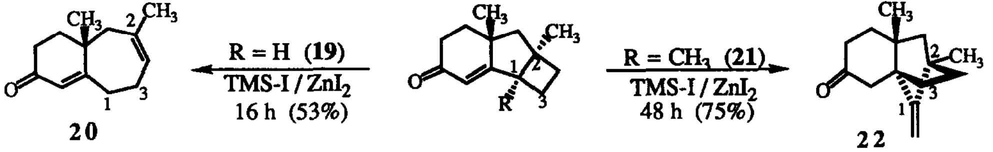
Equation 2 summarizes the profound catalyst dependency exhibited in the cyclizations of a series of trienones. In each Lewis acid-catalyzed case only a single cyclobutane containing polycycle was formed. Ethylaluminum dichloride was the reagent of choice among the various Lewis acids examined, even though >1.2 equivalents were routinely required. Note that the cyclization of **16** generates a pentacyclic product with remarkable efficiency. On the other hand, use of < 0.05 equivalents of the strongly acidic Amberlyst resins led to the formation of polycyclic enones; adducts containing either a cyclobutane ring or a conjugated dienone moiety were not detected.

Equation 2



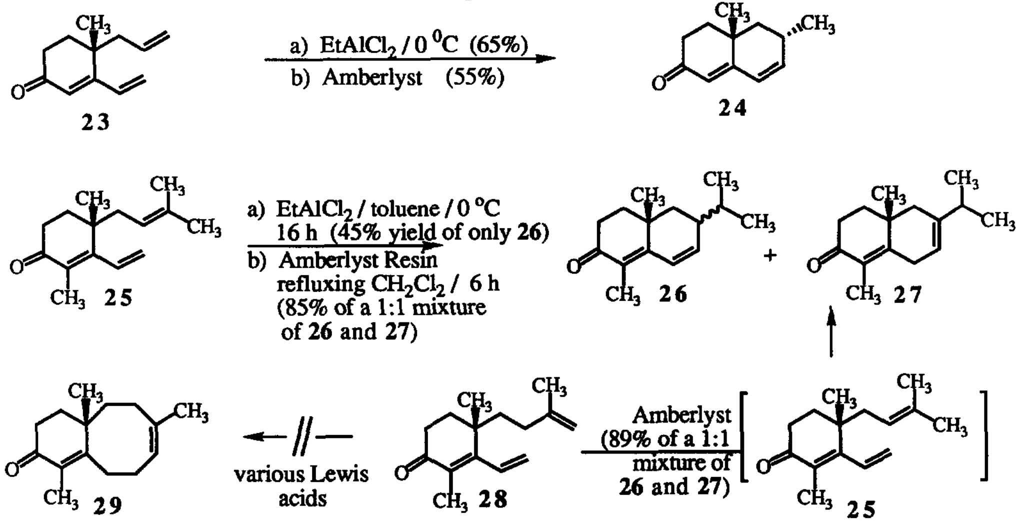
We felt that formation of the cyclobutane adducts shown above was a kinetically favored process and that varying the strength or amount of Lewis acid (or reaction temperatures) would lead to opening of the cyclobutane ring. Contrary to our expectations, cyclobutanes **5**, **8**, **11**, **14** and **17** were inert to strong Lewis acids such as $TiCl_4$, $MgBr_2$, $AlCl_3$ or $EtAlCl_2$ under a variety of vigorous reaction conditions, yet cyclobutanes **19** and **21** reacted cleanly upon prolonged exposure to TMSI to give enone **20** and ketone **22**, respectively (Eq. 3).[8,9]

Equation 3



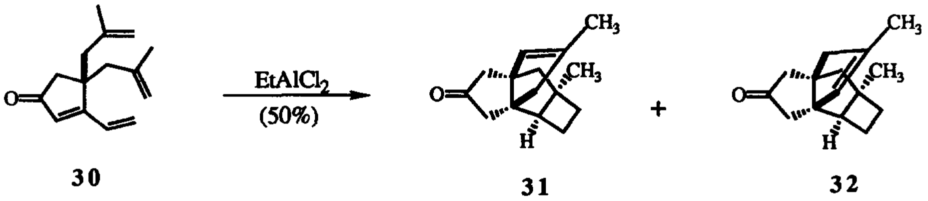
Cation-dienone cyclizations are also useful for the annulation of cyclohexane rings (Eq. 4). For example, trienones **23** and **25** form decalins, with either Lewis acid or Amberlyst catalysis, by means of a series of hydride shifts. The reactions of substrate **28** are particularly noteworthy. Although unreactive upon treatment with various Lewis acids, **28** rapidly rearranges *in situ* with Amberlyst catalysis to generate trienone **25**, affording the identical 1:1 mixture of decalins **26** and **27**.

Equation 4



Finally, this new annulation strategy is also applicable to polyene-like cyclizations as typified by the cyclization of substrate **30** (Eq. 5).

Equation 5

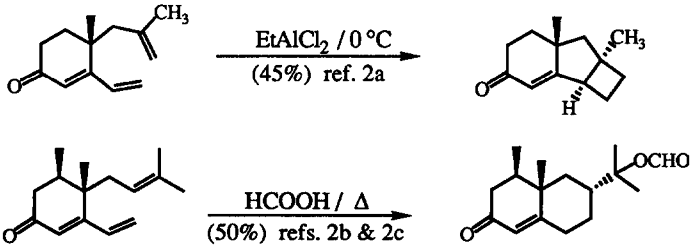


In conclusion, Amberlyst catalyzed reactions are useful for the formation of six and seven-membered rings, while the Lewis acid-catalyzed reactions of olefin-dienones provide rapid access to cyclobutane-containing polycycles. Further studies on the mechanism and synthetic applications of these reactions are in progress.

Acknowledgments: Support from the National Institute of General Medical Sciences through research grant 1 R01 GM39752 is gratefully acknowledged. Special thanks are extended to Mr. Derric Lowery and Mr. Sunil Patel for technical assistance in the early stages of this work.

References and Notes:

1. a) Snider, B. Acc. Chem. Res. **1980**, *13*, 426. b) Snider, B.B.; Rodini, D.J.; Straten, J. v. J. Am. Chem. Soc. **1980**, *102*, 5872. c) Snider, B.B.; Cartaya-Marin, C.P.; J. Org. Chem. **1984**, *49*, 153. d) Snider, B.B. Kirk, T.C. J. Am. Chem. Soc. **1983**, *105*, 2364. e) Snider, B.B.; Karras, M.; Price, R.T.; Rodini, D.J. J. Org. Chem. **1982**, *47*, 4538.
2. For the only Lewis acid catalyzed reaction of a conjugated dienone with an unactivated olefin, see: a) Majetich, G.; Defauw, J.; Ringold, C. J. Org. Chem. **1988**, *53*, 50-68. For two proton-catalyzed examples, see: b) Dastur, K.P. J. Am. Chem. Soc. **1974**, *96*, 2605. c) Heathcock, C.H.; Graham, S.L.; Pirrung, M.C.; Plvac, F.; White, C.T. In "The Total Synthesis of Natural Products"; ApSimon, J., Ed.; Wiley-InterScience, New York, 1983; Vol. V, pp 184.



3. G. Majetich, J.-S. Song, C. Ringold, and G. A. Nemeth, "A Direct Stereoselective Synthesis of (±)-14-Deoxyisoamijiol," the preceding Letter.
4. a) All structures drawn here represent racemates, only one enantiomer being drawn. b) The spectroscopic data obtained for all new compounds [^{1}H NMR, ^{13}C NMR, IR and MS] were fully consistent with the assigned structures. The three exceptions to this statement are compounds **3** (Eq. 1),**15** (Eq. 2) and **18** (Eq. 2) in which the stereochemistry of the "C" ring fusion is uncertain. Sterochemical assignments are based on DIFNOE experiments. c) Reaction conditions have not been optimized. d) All yields are isolated yields.
5. For other examples of non-photochemical 2 + 2 cycloadditions of acyclic enones and alkenes, see: Engler, T. A.; Ali, M.H.; Velde, D.V. Tetrahedron Lett. **1989**, *30*, 1761.
6. Amberlyst 15(wet) Ion-exchange resins [Aldrich].
7. Unpublished results of Mr. Derric Lowery.
8. a) Crimmins, M.T.; Gould, L.D. J. Am. Chem. Soc. **1987**, *109*, 6199. b) Cargill, R.L.; Dalton, J.R.; O'Connor, S.; Michels, D.G. Tetrahedron Lett. **1978**, 4465.
9. In the rearrangement of **21**, migration of the anti periplanar carbon-C(1)-C(2) bond to the silylated enone intermediate results in a tertiary carbonium ion, which leads to double bond formation. In the case of enone **19**, a comparable Michael-like rearrangement would produce a less stable secondary carbonium ion; this consequently favors the fragmentation of the C(1)-C(2) bond and forms an alternate tertiary cation and subsequently dienone **20**.
10. Surprisingly, alkynes and aromatic rings are not nucleophilic enough to undergo Lewis acid-initiated cyclization with dienones.

(Received in USA 3 January 1990)