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# ACID CATALYZED INTRAMOLECULAR DIELS-ALDER REACTIONS IN LITHIUM PERCHLORATE-DIETHYL ETHER: ACID PROMOTED MIGRATION OF TERMINAL DIENES PRIOR TO [4+2] CYCLOADDITION IN CONFORMATIONALLY RESTRICTED SUBSTRATES

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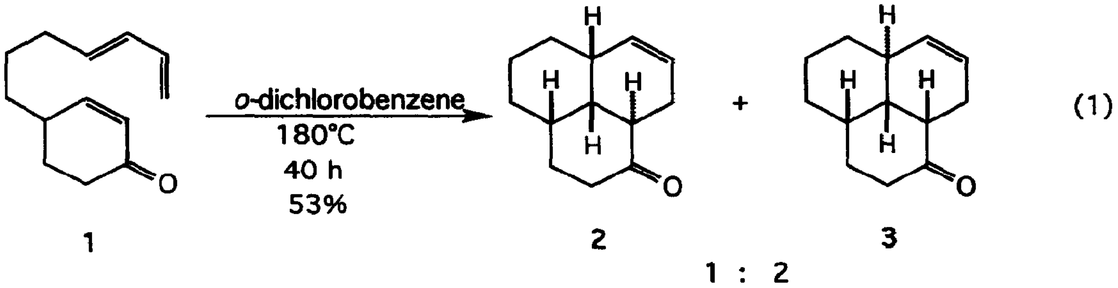
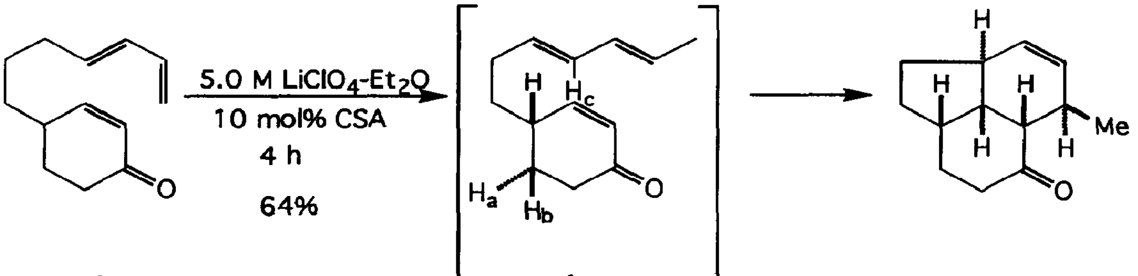
**Abstract:** Use of 10 mol% camphorsulfonic acid in 5.0 M lithium perchlorate-diethyl ether to promote intramolecular Diels-Alder reactions of conformationally restricted substrates, wherein the substrates possess a terminal diene unit, gives rise to tandem diene migration - [4+2] cycloaddition.

We have recently shown that catalytic camphorsulfonic acid in lithium perchlorate-diethyl ether can have a dramatic effect on the rates of intramolecular Diels-Alder reactions.[1,2] We wish to report that use of catalytic acid in 5.0 M lithium perchlorate-diethyl ether to promote intramolecular Diels-Alder reactions of conformationally restricted substrates possessing terminal dienes results in acid catalyzed migration of the diene prior to [4+2] cycloaddition.

In an attempt to accelerate and improve upon the endo/exo selectivity observed for the thermal intramolecular cycloaddition of substrate 1[3] (Equation 1),[4] the reaction of 1 was examined in lithium perchlorate-diethyl ether. Unfortunately there was no observable reaction at ambient temperature in 5.0 M lithium perchlorate-diethyl ether. However, exposure (4 h) of a 0.01 M solution of 1 in 5.0 M lithium

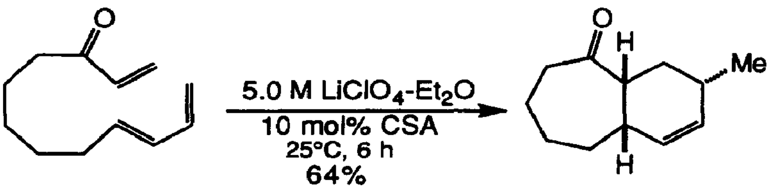


perchlorate-diethyl ether containing 10 mol% camphorsulfonic acid (0.5 M in tetrahydrofuran) gave rise to a single reaction product in 64% yield. Much to our surprise, the cycloadduct was neither **2** nor **3**, but the exo derived tricyclic ketone **5**.[5] The formation of **5** undoubtedly arises via competitive protonation of the terminal diene and subsequent loss of a proton leading to the migrated diene **4** which undergoes very facile intramolecular cycloaddition relative to **1**. The absence of any endo cycloadduct derived from **4** is undoubtedly due to a serious interaction between $H_a$ and $H_c$ in the endo transition state.



**1** **4** **5**

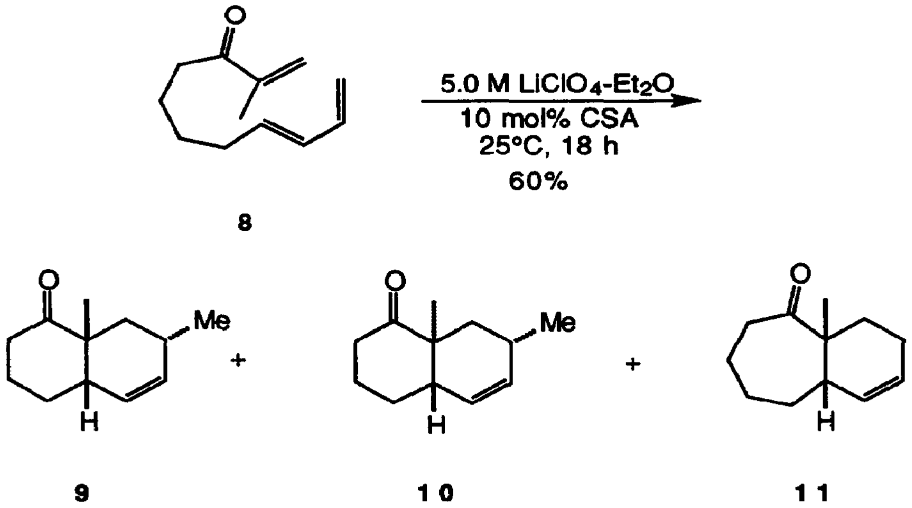
The acid promoted migration of terminal dienes in lithium perchlorate-diethyl ether prior to intramolecular [4+2] cycloaddition appears to be general in conformationally restricted substrates. For example treatment of a 0.05 M solution of trienone **6**[6] in 5.0 M lithium perchlorate-diethyl ether with 10



**6** **7**

mol% camphorsulfonic acid (0.5 M in tetrahydrofuran) for 6 h afforded the known 6,7 *cis*-fused cycloadduct **7**[1a] in 65% yield. Approximately 6% of the 6,8 *cis*-fused cycloadduct was isolated. The corresponding *trans*-fused cycloadducts were not detected. Attempts to improve the yield of **7** by employing more acid were not successful. For example, use of 20 mol% camphorsulfonic acid in 5.0 M lithium perchlorate-diethyl ether gave rise to only a 46% yield of **7**, along with a 4% yield of the 6,8 *cis*-fused cycloadduct. Efforts to promote the cycloaddition of **6** in 1.0 M lithium perchlorate-diethyl ether containing 5-20 mol% camphorsulfonic acid lead to less satisfactory results. The Diels-Alder reactions were slowed appreciably and the yields of 7 were modest (35-38%).

Similar results were obtained with the equally demanding substrate 8.[9] Treatment of a 0.05 M solution of 8 in 5.0 M lithium perchlorate-diethyl ether with 10 mol% camphorsulfonic acid (0.5 M in THF) at ambient temperature for 18 h affords as the major product the known 6,6 *cis*-fused cycloadduct 9[1a]



(40%) along with equal amounts of the 6,6 *trans*-fused product 10[1a] (10%) and the 6,7 *cis*-fused adduct 11[1a] (10%).

The strategy of using catalytic acid in highly polar media such as 5.0 M lithium perchlorate-diethyl ether to promote diene migration prior to [4+2] cycloaddition in conformationaly restricted substrates should be of general interest to those engaged in organic synthesis.

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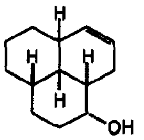
1984, *32*, 1; Roush, W.R. in *Comprehensive Organic Synthesis*; Trost, B.M.; Fleming, I. Eds; Pergamon: Oxford, **1991**, vol. 5, chapter 4.4, pp 513-550.

3. Substrate **1** was prepared according to the general procedure of Stork [Stork, G.; Danheiser, R.L. *J. Org. Chem.*, **1973**, *38*, 1775].

4. Under the conditions of the thermal reaction, one observes equilibration adjacent to the carbonyl in the endo adduct leading to the formation of **2**. The structure of **2** was established by reduction ($NaBH_4$, MeOH) to the crystalline alcohol *i*, mp 90-92°C, whose structure was determined by single-crystal x-ray analysis. The structure of cycloadduct **3** follows from an x-ray of the derived [(a) $NaBH_4$, MeOH; (b) NBS, $CCl_4$] bromo ether *ii*, mp 78-79°C.



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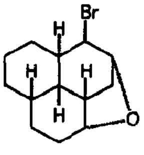
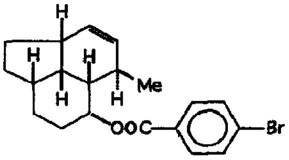


*ii*

5. The structure of **5** was determined by single-crystal x-ray analysis of *p*-bromobenzoate *iii*, mp 75-77°C, which was prepared in straightforward fashion from **5**.



*iii*

6. Prepared from 7,9-decadienal[7] by treatment with vinyl magnesium bromide in tetrahydrofuran followed by oxidation with triphenylbismuth carbonate.[8]

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9. Prepared from 6,8-nonadienal[7] by treatment with 2-propenyl magnesium bromide in tetrahydrofuran followed by PCC oxidation.

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