40244-98-2; **10**, 66271-50-9; **11**, 22818-69-5; **12**, 29559-25-9; **13**, 1781-70-0; **14**, 7214-61-1; 2,2-dimethyl-1-tridecanal, 76173-57-4; *tert*-butyl 2,2,3,3-tetramethyl-4-oxobutanoate, 76173-37-0; 2-methyl-2-(1-cyanocyclohex-1-yl)propanal, 76173-58-5; 3,5-bis(trifluoromethyl)-α,α-dimethylbenzeneacetaldehyde, 76173-59-6; α,α-dimethyl-4-(phenylsulfonyl)benzeneacetaldehyde, 76173-61-0; 3-phenyl-2,2,3-trimethylbutanal, 76173-62-1; 1-octanal, 124-13-0; 1-decanal, 112-31-2; 10-undecenal, 112-45-8; 1-hexadecanal, 629-80-1; benzenepropanal, 104-53-0; *p*-bromobenzaldehyde, 1122-91-4; cyclododecanone, 830-13-7; acetophenone, 98-86-2; $KMnO_4$, 7722-64-7.

Alkylaluminum Halide Induced Cyclization of Unsaturated Carbonyl Compounds

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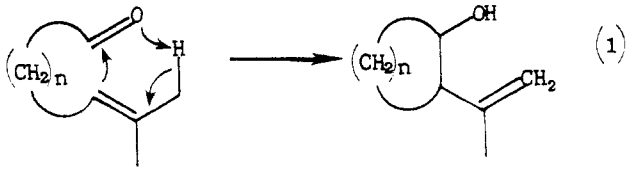
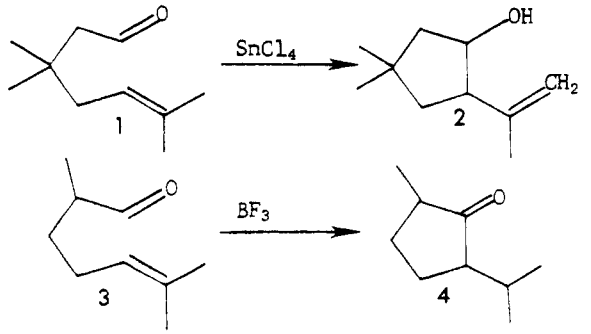
2,6-Dimethyl-5-heptenal (**3**) and 5-octenal (**24**) undergo concerted ene reactions with 1 equiv of Me_2AlCl and cation-olefin cyclizations with 2 equiv of Me_2AlCl, $MeAlCl_2$, or $EtAlCl_2$ to give a zwitterion which reacts to give several products including an ene adduct. 3,7-Dimethyl-6-octenal (**12**) and (*Z*)- and (*E*)-6-nonenal (**18** and **19**) undergo only ene reactions with all catalysts. The enones **31** and **32** formed by reaction of **3** and **12** with acetonylidenetriphenylphosphorane react analogously to **3** and **12** in the presence of Lewis acid. The effect of ring size on the nature of these cyclizations is explained on the basis of thermodynamic and kinetic data.

Lewis acid induced cyclization of unsaturated carbonyl compounds is an attractive method for the synthesis of highly functionalized cyclic compounds.[2,3] Type I intramolecular ene reactions[4] to give cyclohexanols (eq 1, n = 4) are well-known. These reactions proceed at 150–300 °C



(1)

or with Lewis acid catalysis[3] at room temperature. In a detailed study of the scope of this reaction, Andersen reported the first example of the synthesis of a cyclopentanol via this type of ene reaction (eq 1, n = 3).[5] Treatment of **1** with 0.1 equiv of $SnCl_4$ for <15 min at 0 °C gives an 85% yield of **2** as an 80:20 cis–trans mixture. This reaction may not be general, since treatment of the closely related aldehyde **3** with 2.9 equiv of $BF_3{\cdot}Et_2O$ for 1 h at 25 °C gives the cyclopentanone **4**.[6]



We set out to determine the reasons for the differing behavior of **1** and **3** under apparently similar conditions and to try to develop procedures which would allow us to control the course of the reaction. The use of alkylaluminum halides as the Lewis acid catalysts has provided a tool to study this problem. We have recently exploited these reagents as unique Lewis acids which are also Brønsted bases.[7] Proton-catalyzed side reactions are minimized by the use of these reagents. Furthermore, $RAlCl_2$, $R_3Al_2Cl_3$, R_2AlCl, and R_3Al constitute a series with perdictably decreasing Lewis acidity.

Results and Discussion

Reactions of 3 and 12. The reactions of 2,6-dimethyl-5-heptenal (**3**) indicate that the nature of the reaction can be controlled by variation of the strength and amount of Lewis acid.[8] Most remarkably, we have found that both concerted and stepwise ene reactions of **3** occur, giving adducts with different stereochemistry.

Treatment of **3** with 1.0 equiv of Me_2AlCl at −78 °C gives primarily **5a** and **5b** in a 4:1 ratio. The detailed results are shown in Table I. (In the text **3**–**11** refer to the alcohol or carbonyl compound obtained after workup from the structures shown in Scheme I). At 0 °C, no starting material is recovered, but the reaction is less selective. We believe that **5** is formed by a concerted process since concerted thermal ene reactions of 1,6-dienes have been shown to give mainly cis-substituted cyclopentanes.[2,9]

Treatment of **3** with 2 equiv of Me_2AlCl gives the more electrophilic aldehyde, $(Me_2AlCl)_2$ complex, or a species stoichiometrically equivalent to it.[10] This complex reacts

(1) Address correspondence to this author at the Department of Chemistry, Brandeis University, Waltham, MA 02254.

(2) For a review of intramolecular ene reactions see: Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476.

(3) For a review of Lewis acid catalyzed ene reactions see: Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426.

(4) This very useful terminology for classifying intramolecular ene reactions according to the connectivity of the ene and enophile components is discussed in ref 2.

(5) Andersen, N. H.; Ladner, D. W. *Synth. Commun.* **1978**, *8*, 449 and references cited therein. See also: Paquette, L. A.; Han, Y.-K. *J. Am. Chem. Soc.* **1981**, *103*, 1835.

(6) Kulkarni, B. S.; Rao, A. S. *Org. Prep. Proc. Int.* **1978**, *10*, 73. Related reactions are known: Sakai, K.; Ide, J.; Oda, O.; Nakamura, N. *Tetrahedron Lett.* **1972**, 1287. Baldwin, J. E.; Lusch, M. J. *J. Org. Chem.* **1979**, *44*, 1923. Cookson, R. C.; Smith, S. A. *J. Chem. Soc., Chem. Commun.* **1979**, 145.

(7) Snider, B. B.; Rodini, D. J.; Karras, M.; Kirk, T. C.; Deutsch, E. A.; Cordova, R.; Price, R. T. *Tetrahedron* **1981**, *37*, 3927.

(8) For a preliminary report see: Karras, M.; Snider, B. B. *J. Am. Chem. Soc.* **1980**, *102*, 7951.

(9) McQuillin, F. J.; Parker, D. G. *J. Chem. Soc., Perkin Trans. 1* **1974**, 809.

(10) Alkylaluminum halides often disproportionate in the presence of a deficit of base. Disproportionation is more favored for $RAlCl_2$ than for R_2AlCl.[11,12] Analysis in this case is complicated by lack of data on the relative rates of cyclization and disproportionation.

(11) Mole, T.; Jeffery, E. A. "Organoaluminum Compounds"; Elsevier: Amsterdam, 1972; p 32.

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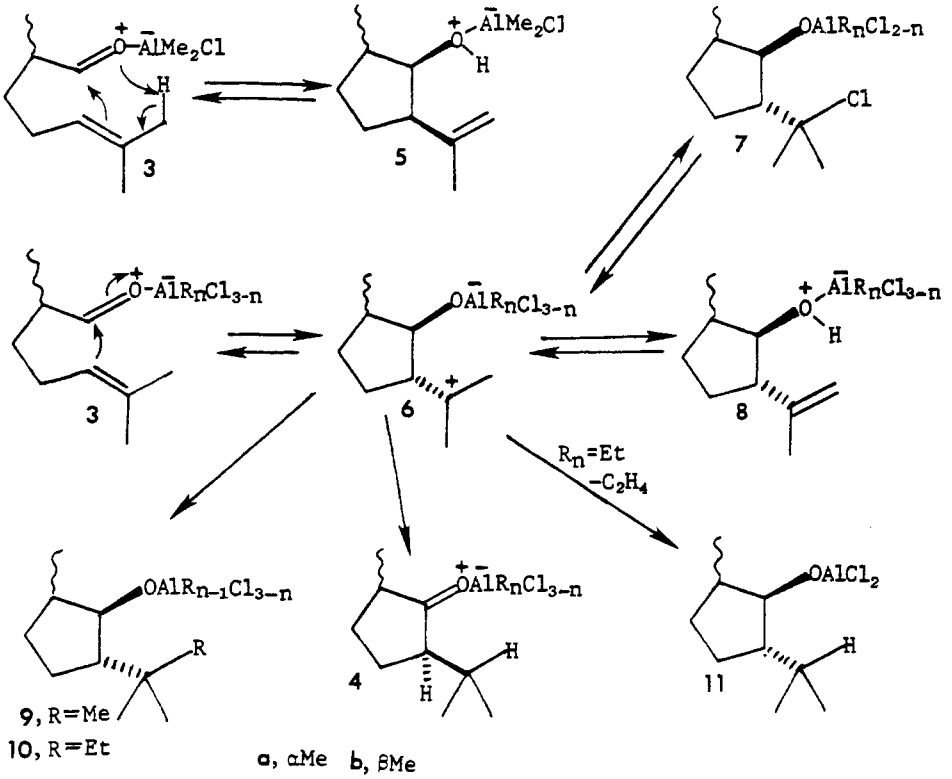
Table I. Cyclization of 2,6-Dimethyl-5-heptenal (3)

run	Lewis acid (equiv)	temp, °C (time, h)	% yield[a] 4a (4b)	5a (5b)	7a	8a (8b)	9a/10a	11a
1	Me_2AlCl (1)[b]	−78 (1.3)		24 (6)				
2	Me_2AlCl (2)	−78 (4.0)		1	75			
3	Me_2AlCl (2)	0 (4.0)	22 (2)	7 (2)		34 (1)	30	
4	$MeAlCl_2$ (2)	−78 (0.2)	72 (6)	4 (1)		9 (1)	4	
5	$EtAlCl_2$ (2)	−78 (0.2)	8 (3)				14	73
6	$EtAlCl_2$ (2)	0 (1.0)	43 (4)				7	41

[a] Determined by GC analysis. All compounds were isolated by preparative GC or column chromatography on silica gel and fully characterized. [b] 60% unreacted 3 was present.

Scheme I



rapidly at −78 °C to give the zwitterion **6**. At −78 °C, an irreversible 1,5 chloride shift to give chloroalkoxide **7** is the major process. At 0 °C, the 1,5 chloride shift is apparently reversible, so that products obtained from **6** by three competing irreversible reactions are obtained. A 1,5 methyl shift gives **9**,[13] a reversible 1,5 proton shift gives **8**, which irreversibly loses CH_4, and two 1,2 hydride shifts give **4**. The formation of **8** by a stepwise ene reaction confirms that the cis adduct **5** results from a concerted ene reaction. The reactions of **3**·$(Me_2AlCl)_2$ are consistent with our general observation that enhancing the electrophilicity of an enophile accelerates stepwise reactions more than concerted reactions.

Treatment of **3** with 2 equiv of $MeAlCl_2$ at −78 °C gives mainly **4**. This is readily understood in terms of the differences between $MeAlCl_2$ and Me_2AlCl. The greater Lewis acidity of $MeAlCl_2$ leads to a faster cyclization, makes **7** unstable, even at −78 °C, and also makes the oxygen of **6** less basic, decreasing the rate of the 1,5 proton shift which gives **8**. The methyl group of $MeAlCl_2$ is both less basic and less nucleophilic than those of Me_2AlCl. Therefore, the 1,5 methyl shift to give **9** is slower, and reversion of **8** to **6** can compete with the irreversible loss of CH_4 from **8**.

Addition of 2 equiv of $EtAlCl_2$ to **3** at −78 °C gives mainly the reductive cyclization product **11**. At 0 °C, **4** and **11** are formed in equal amounts. Ketone **4** is not an intermediate in the formation of **11** since is is not reduced by $EtAlCl_2$. Apparently zwitterion **6** reacts via hydrogen delivery from the β-hydrogen of the ethyl group to give **11** and C_2H_4, possibly through an eight-membered-ring transition state. The selective formation of **11** at lower temperature is consistent with this cyclic mechanism which has a more negative $\Delta S^{\ddagger}$ than the formation of **4** from **6**. The vastly different reactions with $EtAlCl_2$ and $MeAlCl_2$ were not anticipated. However, ethylaluminum compounds are more nucleophilic than methylaluminum compounds, and β-hydride delivery to the electrophilic site can be the major reaction of ethylaluminum compounds.[14]

In all cases stepwise reaction appears to proceed exclusively or predominantly through the trans,trans zwitterion **6a**. No **7b**, **9b**, **10b**, or **11b** is detected, and only small amounts of **4b** and **8b** are formed. Ketone **4** is ~95% **4a** which is consistent with reaction proceeding through **6a**

(12) Nixon, A.; Childs, R. F. *J. Poly. Sci., Poly. Chem. Ed.* **1980**, *18*, 1499.

(13) Addition of the methyl group of Me_3Al to carbenium ions generated by addition to carbon–carbon double bonds has been observed: Yamamoto, H.; Nozaki, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 169.

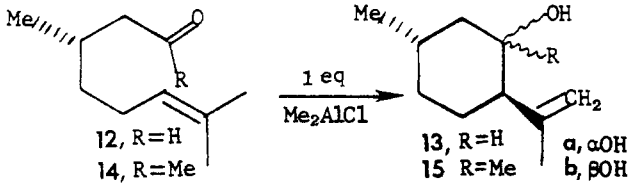
(14) See ref 11 and: Ashby, E. C.; Noding, S. A. *J. Org. Chem.* **1979**, *44*, 4792.

and indicates that equilibration does not occur since a 70:30 mixture of **4a** and **4b** is present at equilibrium.[15] The selective formation of **6a** may be due to kinetic or thermodynamic control since formation of **6** from **3** is reversible. Treatment of chloro alcohol **7** with 1 equiv of Et_2AlCl and 1 equiv of $EtAlCl_2$ at −78 °C gives the chloroalkoxide **7** which would be obtained from **3**·$(EtAlCl_2)_2$. This species reacts to give **3**, **4**, **10a**, and **11a** in yields of 5%, 15%, 25%, and 54%. This demonstrates that **7** can revert to **6** and that **6** can revert to **3**.

The stereochemical assignments of **5** and **7**–**11** are based on analysis of the NMR data. Ene adducts **5** and **8** were distinguished by the pattern of the olefinic protons. A cis-2 substituent splits the olefinic methylene group of an isopropenylcyclopentane into two singlets and shifts the allylic methyl group downfield.[5,9] Cis adducts **5a** and **5b** absorb at δ 4.85, 4.99, and 1.81 and at δ 4.87, 5.01, and 1.82, respectively, while trans adducts **8a** and **8b** absorb at δ 4.82 (2 H) and 1.74 and at δ 4.80 (2 H) and 1.70, respectively.

The **a** and **b** series were established by the chemical shift and coupling pattern of the proton α to the hydroxyl group.[16] In **8a** this hydrogen is shielded by the two substituents cis to it and absorbs at δ 3.42 as a doublet of doublets with J = 8 and 8 Hz. In **8b**, with only one cis substituent, this hydrogen absorbs at δ 3.93 as a doublet of doublets with J = 6.3 and 6.3 Hz. In **5a** this hydrogen absorbs at δ 3.74 as a broad doublet with J = 4.6 Hz. In **5b** with no cis substituents this hydrogen absorbs at δ 3.93 as a doublet of doublets with J = 2.9 and 3.1 Hz. The chemical shifts and coupling patterns for this proton in **7a**, **9a**, **10a**, and **11a** are analogous to those of **8a**.

Citronellal (**12**) does not show a similar variation in reactivity, giving, under all of the above conditions, mixtures of isopulegol (**13a**) and neoisopulegol (**13b**) with traces of the other two stereoisomers, as previously reported with other Lewis acids.[17]

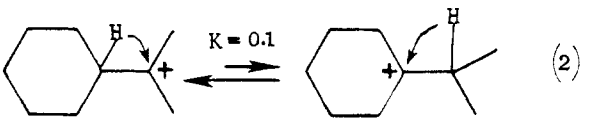


The difference in reactivity between **3** and **12** is due at least in part to the equilibrium constants for the two ene reactions. Using Benson's group additivity rules, we calculate ΔH = −5.0 kcal/mol and ΔS = −10.3 eu for the ene reaction of **3** to give **5** or **8** and ΔH = −11.6 kcal/mol and ΔS = −18.9 eu for the ene reaction of **12** to give **13**.[18] Although these values are only estimates, the difference between the two reactions is probably quite accurate since it is due primarily to the differences between the ΔH and ΔS corrections for cyclopentane and cyclohexane rings which have been determined from many examples. Cyclohexane is strain free while cyclopentane has a ring strain of 6.3 kcal/mol. The flexibility of the cyclopentane ring leads to a less negative ΔS for the formation of **5** and **8** than for **13**.

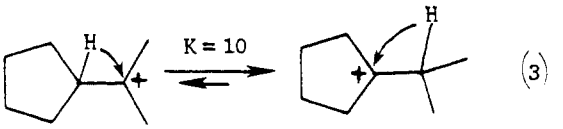
These values suggest that **3** should exist in equilibrium with **5** and **8** at 25 °C and that at slightly elevated temperatures **3** is the more stable species. We have observed partial reversion of **5**, but not **8**, to **3** during GC at 125 °C. This is expected since **5**, but not **8**, can give **3** by a concerted retro-ene reaction. Treatment of **5a** with BF_3·Et_2O at 0 °C gives **4**, presumably via **3**. This explains Kulkarni and Rao's observations.[6] Although **5** may have been formed on treatment of **3** with BF_3·Et_2O, it is present in equilibrium with **3** which is converted irreversibly to **4**. Use of Me_2AlCl makes the isolation of ene adducts **5** and **8** possible by irreversible deprotonation of the alcohol with loss of CH_4 to give the stable aluminum alkoxide. Andersen has observed similar reversion of **2**, especially the cis isomer,[5] to the aldehyde **1** at slightly elevated temperatures. The geminal methyl groups of **2** stabilize the cyclic structure relative to the aldehyde **1** and allow the isolation of **2** at 0 °C.

The absence of methanes in all reactions of **12** indicates that the 1,5 proton shift is much faster than two 1,2 hydride shifts in the six-membered-ring case, if in fact there is a stepwise component to the ene reaction giving **13**.

Saunders has shown that the thermodynamics of 1,2 hydride shifts favor the exocyclic carbenium ion in the cyclohexane case (eq 2) but the endocyclic carbenium ion



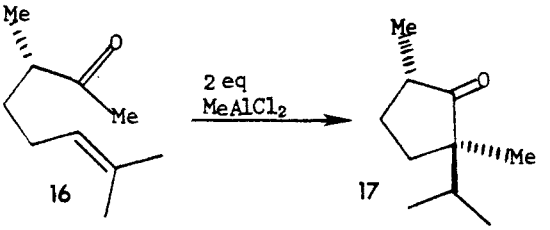
(2)



(3)

in the cyclopentane case (eq 3).[19] These thermodynamic differences will undoubtedly be translated into large rate differences for the initial 1,2 hydride shift in the zwitterionic intermediate.

Reactions of 14 and 16. The corresponding ketones **14** and **16** react analogously to **12** and **3**. Treatment of **16** with 2 equiv of $MeAlCl_2$ at 0 °C gives a 60% yield of **17**.



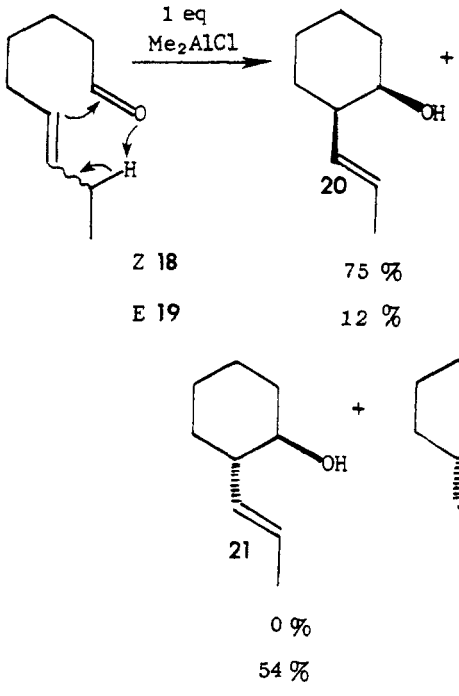
The stereochemistry of **17** is inferred from mechanistic considerations and the NMR absorption of the 2-methyl group at δ 0.91 which suggests shielding by a 5-methyl group cis to it.[16,20] Due to the decreased electrophilicity of the ketone carbonyl group, **16** reacts only at 0 °C while **3** reacts at −78 °C. Use of $EtAlCl_2$ or BF_3 gives complex mixtures while use of Me_2AlCl leads to the aldol dimer.

The ketone **14** gives a 58% yield of a 4.5:1 mixture of **15a** and **15b** and 20% of the aldol dimer on treatment with 1 equiv of Me_2AlCl at 25 °C for 24 h. The isolation of a tertiary alcohol in the presence of a Lewis acid is remarkable and is presumably due to the rapid loss of CH_4 from the alcohol–Me_2AlCl complex to give the aluminum alkoxide, which is stable. Me_2AlCl is especially useful for the intramolecular ene reactions of ketones since the adducts are often not stable at the temperatures required for

(15) Sisido, K.; Kurozumi, S.; Utimoto, K.; Isida, T. *J. Org. Chem.* **1966**, *31*, 2795.
(16) Rei, M.-H. *J. Org. Chem.* **1978**, *43*, 2173.
(17) Nakatani, Y.; Kawashima, K. *Synthesis* **1978**, 147 and references cited therein.
(18) Benson, S. W. "Thermochemical Kinetics", 2nd ed.; Wiley: New York, 1976.
(19) Saunders, M., Yale University, Personal communication, 1980.
(20) House, H. O.; Trost, B. M. *J. Org. Chem.* **1965**, *30*, 1341, 2502.

uncatalyzed thermal reactions. For instance, Conia has reported that pyrolysis of **14** for 46 h at 350 °C gives a 50% yield of 2,4-dimethylisopropylbenzene, which he proposes arises via dehydration and dehydrogenation of the ene adduct **15**.[21]

Reaction of 18, 19, and 24. Cyclizations of **18**, **19**, and **24** were examined to determine the suitability of the less reactive 1,2-disubstituted double bond as the nucleophilic component and to explore the effect of double bond stereochemistry on the stereochemistry of the ene adduct. The *Z* isomer **18** gives exclusively the cis-substituted ene adduct **20** with 1 equiv of Me_2AlCl for 2 h at 0 °C while

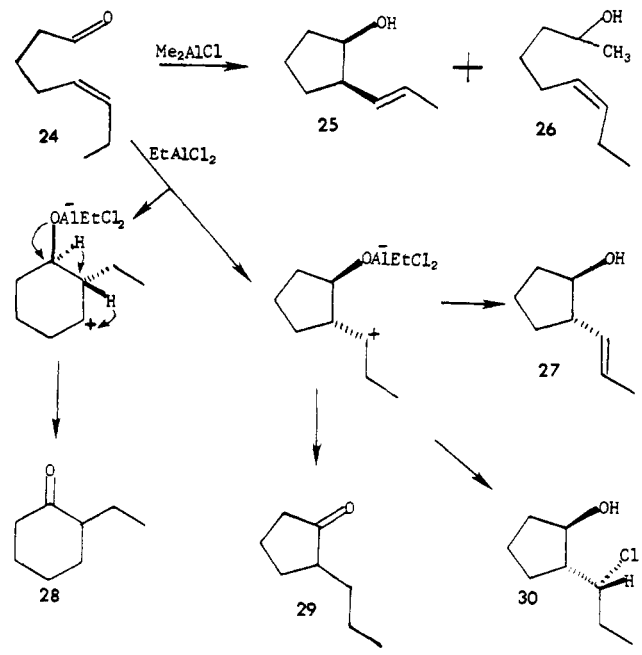


the *E* isomer **19** gives mainly the trans-substituted isomers **21** and **22**. Due to the less nucleophilic double bond of **18** and **19**, reaction is much slower than with **12**, and methyl addition to the aldehyde competes to give 15–20% of 7-decen-2-ol (**23**), although this can be prevented by proper choice of conditions (vide infra.)

The exclusive formation of **20** from **18** is due to geometrical constraints on the transition state. The ene reaction of **19** is less selective but gives mainly the trans isomers **21** and **22**. This type of ene reaction offers a promising route to 2-(1-alkenyl)cyclohexanols with control of stereochemistry.

Treatment of **24** with 0.9 equiv of Me_2AlCl at 0 °C under standard conditions (ca. 0.4 M) gives a 37% yield of **25** and a 48% yield of *Z*-6-nonen-2-ol (**26**; see Scheme II). The ratio of **25** to **26** can be improved by careful modification of the reaction conditions. The ene reaction is a unimolecular reaction of the aldehyde–Me_2AlCl complex. Methyl addition is a bimolecular reaction involving the above complex and a second molecule of Me_2AlCl. The unimolecular reaction is favored at lower concentration. The bimolecular reaction will be favored at lower temperatures because of its larger negative $\Delta S^{\ddagger}$. Excess Me_2AlCl will also favor methyl addition. Thus, reaction of **24** with 0.9 equiv of Me_2AlCl at higher dilution (ca. 0.04 M) and higher temperature (25 °C) gives a 66% yield of **25** and a 24% yield of **26**. Under these conditions **18** gives a 93% yield of **20** with only 2% of **23**.

Scheme II



Under the optimal conditions discussed above the ene reaction of **18** is 90% complete in 3 min. The ene reaction of **24** is 27% complete after 3 min, 57% complete after 12 min, and 90% complete after 28 min. The greater extent of methyl addition to **24** is consistent with this rate data. As reported by Andersen,[5] the ene reactions of aldehydes to give six-membered rings are faster than those which give five-membered rings.

In contrast, in all carbons systems, ene reactions which give five-membered rings are much faster.[2] This order is observed in most cyclization reactions due to the less negative $\Delta S^{\ddagger}$ for formation of five-membered rings. Due to the greater stability of the carbonyl double bond, the ene reactions of aldehydes are less exothermic than those of all carbon systems. The transition state therefore is more product-like, and the strain energy of the cyclopentane affects $\Delta G^{\ddagger}$. This effect is exacerbated by the use of Lewis acid catalysis which leads to a very unsymmetrical transition state with C–C bond formation almost complete and C–H bond formation just beginning.[3,22]

Reaction of **24** with 2 equiv of $EtAlCl_2$ at 0 °C for 2 h gives 29% of **25**, 17% of *trans*-2-[(*E*)-1-propenyl]cyclopentanol (**27**), 9% of 2-ethylcyclohexanone (**28**), 19% of 2-propylcyclopentanone (**29**), and 26% of *trans*-2-(1-chloropropyl)cyclopentanol (**30**). Under these conditions, a five-membered ring zwitterion, analogous to **6**, is formed which gives rise to **27** by a 1,5 proton shift, **29** by two 1,2 hydride shifts and **30**, as a single diastereomer, by a 1,5 chloride shift. A six-membered ring zwitterion gives **28** by two 1,2 hydride shifts.

Enal **24** behaves analogously to **3**, undergoing both concerted and stepwise ene reactions which give **25** and **27**, respectively. The substitution pattern of the double bond allows the formation of two zwitterionic intermediates. Geometric constraints preclude the formation of products other than **28** from the six-membered-ring intermediate.

The stereochemistry of ene adducts **20–22**, **25**, and **27** can be easily determined by the chemical shift of the proton α to the alcohol group. In cis isomers **20** and **25**

(21) Rouessac, F.; Le Perchec, P.; Conia, J.-M. *Bull. Soc. Chim. Fr.* **1967**, 818.

(22) Stephenson, L. M.; Orfanopoulos, M. *J. Org. Chem.* **1981**, *46*, 2200.

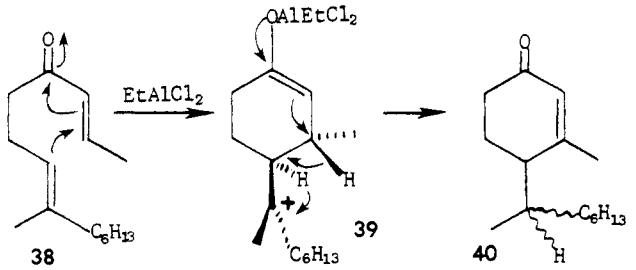
this proton absorbs at δ 3.81 and 4.1 while in trans isomers **21**, **22**, and **27** the substituent shields the hydrogen so that it absorbs at δ 3.17, 3.21, and 3.75.[16,23]

Reactions of Enones 31, 32, and 38. We have previously reported cyclizations analogous to the conversion of **3** to **4** using α,β-unsaturated ketones as the electrophilic component.[24] Enones **31** and **32** react similarly to aldehydes **3** and **12**. Treatment of **31** with 0.9 equiv of Me_2AlCl gives **33** in 20% yield and **34** in 10% yield (Scheme III). Alcohol **33** is formed by two sequential ene reactions[25] in which the double bond and then the carbonyl group act as enophile. Dihydropyran **34** is formed by an inverse electron demand Diels–Alder reaction.[26] All of these reactions may be concerted. Treatment of **31** with 2 equiv of Me_2AlCl for 1 h at 0 °C gives a 48% yield of **35** as a mixture of all four isomers. Enone **35** is strictly analogous to **4**.

The homologous ketone **32** gives a 13% yield of **36** and a 58% yield of **37** with 0.1 equiv of Me_2AlCl for 12 h at −15 °C and a 58% yield of **36** with 2 equiv of Me_2AlCl for 1 h at 0 °C. Treatment of **32** with $BF_3{\cdot}Et_2O$ gives, as has been previously reported,[27] a 70% yield of **37**. Diels–Alder adduct **37** is the kinetic product. In the presence of Lewis acid it reverts to **32** by a retro-Diels–Alder reaction or opens to a zwitterion which undergoes a 1,5 proton shift to give the initial ene adduct. The stability of **33** and **36** in the presence of Lewis acid is due to their in situ protection as aluminum alkoxides.

The cyclizations of **31** and **32** are therefore analogous to those of **3** and **12** but are complicated by the formation of Diels–Alder adducts **34** and **37**, which appear to be formed by reversible, concerted reactions.[26] The only other reaction of **32** is two sequential ene reactions to give **36**, while **31** gives **33** under conditions where **3** gave **5** and gives **35** under conditions where **3** underwent stepwise reactions.

The cyclization of **38** was examined to determine the nature of these zwitterionic intermediates.[24] Treatment of **38** with 1.5 equiv of $EtAlCl_2$ at 0 °C for 10 min gives



38 39 40

a quantitative yield of **40** as 1:1 mixture of stereoisomers. Bond rotation of ether 60 or 120° in the zwitterionic intermediate **39** takes place to align the hydrogen with the vacant π orbital. Either there is no preference or the intermediate is long-lived enough so that all stereochemical information is lost.

Conclusion

These results elaborate some the the factors controlling product distribution in the cyclization of unsaturated aldehydes. They will allow these reactions to be used more reliably in organic synthesis and will be applicable to a variety of other Lewis acid catalyzed reactions.

Experimental Section

NMR spectra were taken on Varian A-60, Perkin-Elmer R-32, and JEOL FX-90Q spectrometers. IR spectra were recorded on a Perkin-Elmer 283 spectrometer. Mass spectra were recorded on AE1-MS9, Du Pont 21-490, and Hewlett-Packard 5992 spectrometers. Combustion analyses were performed by Galbraith Laboratories. All GC analyses were carried out on a 9 ft × 0.25 in. 10% DEGS on Chromosorb PNAW (60/80 mesh) column with a flow rate of 60 mL/min. CH_2Cl_2 was dried by distillation from CaH_2. All reactions were run under nitrogen in flame-dried glassware. Reagents were added via dry syringes through septa.

Lewis Acids. $BF_3{\cdot}Et_2O$ was distilled and stored under N_2. $AlCl_3$ was purified by sublimation twice in vacuo and was stored and handled under N_2. $EtAlCl_2$ and Me_2AlCl were obtained from Texas Alkyls as solutions in heptane. $EtAlCl_2$ was also obtained pure and diluted with pentane for use when separation of products from heptane was a problem. $MeAlCl_2$ was obtained by adding 18.1 mL of 1.14 M (14.6% w/w) Me_2AlCl in heptane (20.4 mmol) to 2.72 g of $AlCl_3$ (20.4 mmol) under N_2.[28] The mixture was heated at 80 °C until all the $AlCl_3$ dissolved. Dry heptane (17.6 g) was added to give a solution which was 13.9% w/w $MeAlCl_2$ in heptane. The density was determined to be 0.75 g/mL. Therefore the concentration is 0.92 M.

Starting Materials. 2,6-Dimethyl-5-heptenal (**3**) was obtained from Givaudan Corp. and was purified by chromatography on silica gel. 6-Methyl-5-hepten-2-one and ene adducts **5** and **8** were present as impurities. Ketones **14** and **16** were prepared by addition of MeMgCl to **12** and **3** followed by Jones oxidation of the resulting alcohol. (*Z*)-6-Nonenal (**18**) was obtained from Bedoukian Research Inc. It contained 8% of the *E* isomer. (*E*)-6-Nonenal (**19**) was prepared as follows. Addition of EtMgBr to 2,3-dichlorotetrahydropyran followed by reduction with sodium in ether gave (*E*)-4-heptenol.[29] This was converted to the bromide with PBr_3 and coupled with the lithium salt of 5,6-dihydro-2,4,4,6-tetramethyl-4*H*-1,3-oxazine.[30] Reduction with $NaBH_4$ and hydrolysis with oxalic acid[30] gave **19** which contained 7% of the *Z* isomer. (*Z*)-5-Octenal (**24**) was prepared by oxidation of (*Z*)-5-octenol with pyridinium chlorochromate with sodium acetate as a buffer. (*Z*)-5-Octenol was obtained from Bedoukian Research Inc.

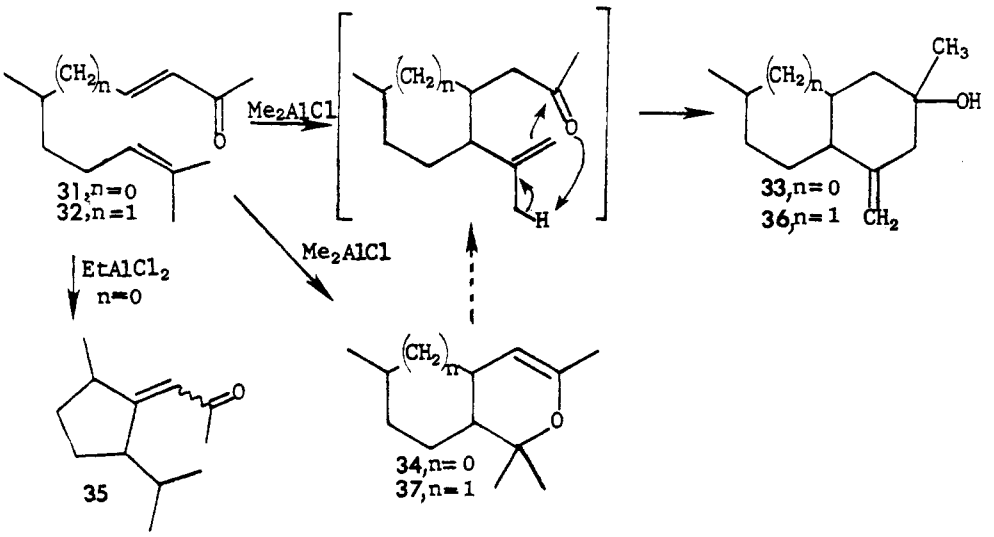
Enones **31** and **32** were prepared from **3** and **12** by reaction with acetonylidentriphenylphosphorane. Enone **38** was prepared as follows. Addition of Me_3Al and $ZrCp_2Cl_2$ to 1-octyne followed by addition of butyllithium and quenching with paraformaldehyde gave (*E*)-3-methyl-2-nonen-1-ol.[31] This was converted to the allylic bromide with PBr_3. This was coupled with the lithium salt of 5,6-dihydro-2,4,4,6-tetramethyl-4*H*-1,3-oxazine.[30] Reduction with $NaBH_4$ and hydrolysis with oxalic acid[30] gave (*E*)-5-methyl-4-undecenal which was converted to **38** as previously described for related aldehydes.[24] The stereochemical purity of **38** was confirmed by ^1H NMR (which showed a single allylic methyl group at δ 1.49) and ^{13}C NMR, which showed only 15 peaks.

Cyclizations of 2,6-Dimethyl-5-heptenal (3). Run 1. Me_2AlCl (1.30 mL of a 1.14 M solution in heptane, 1.48 mmol) was added to a solution of **3** (213 mg, 1.52 mmol) in 4.5 mL of CH_2Cl_2 at −78 °C in a flame-dried flask under nitrogen. The reaction mixture was stirred for 1.3 h and quenched by slow addition to rapidly stirred 25% aqueous potassium hydroxide solution (15 mL). Pentane (10 mL) was added. The organic layer was washed with saturated $NaHCO_3$ solution, water, and brine, dried (Na_2SO_4), and evaporated at reduced pressure to give 203 mg of product which NMR and GC showed to consist of 60% recovered **3**, 24% of **5a**, and 6% of **5b**.

Run 2. Reaction with 2.7 mL of Me_2AlCl solution for 4 h at −78 °C gave 220 mg of product which was ca. 75% **7a** by NMR

(23) Crandall, J. K.; Arrington, J. P.; Hen, J. *J. Am. Chem. Soc.* **1967**, *89*, 6208.
(24) Snider, B. B.; Rodini, D. J.; Van Straten, J. W. *J. Am. Chem. Soc.* **1980**, *102*, 5872.
(25) Snider, B. B.; Deutsch, E. A. *J. Org. Chem.* **1982**, *47*, 2682.
(26) Snider, B. B.; Dunčia, J. V. *J. Org. Chem.* **1980**, *45*, 3461 and references cited therein.
(27) Naves, Y.-R.; Ardizio, P. *Bull. Soc. Chim. Fr.* **1953**, 494.
(28) Grosse, A. V.; Mavity, J. M. *J. Org. Chem.* **1940**, *5*, 106. Reinheckel, H.; Haage, K. *J. Prakt. Chem.* **1966**, *33*, 70.
(29) Crombie, L.; Harper, S. H. *J. Chem. Soc.* **1950**, 1707. Jacobson, M. *J. Am. Chem. Soc.* **1950**, *72*, 1489. Jacobson, M.; Keiser, I.; Chambers, D. L.; Miyashita, D. H.; Harding, C. *J. Med. Chem.* **1971**, *14*, 236.
(30) Meyers, A. I.; Nabeya, A.; Adickes, H. W.; Politzer, I. R.; Malone, G. R.; Kovelesky, A. C.; Nolen, R. L.; Portnoy, R. C. *J. Org. Chem.* **1973**, *38*, 36.
(31) Okukado, N.; Negishi, E.-I. *Tetrahedron Lett.* **1978**, 2357.

Scheme III



analysis. Purification by chromatography on silica gel (9:1 and then 4:1 pentane–ether) gave 144.6 mg (54%) of pure **7a**: NMR ($CDCl_3$) δ 3.60 (dd, 1, J = 7.3, 7.3 Hz), 2.31 (s, 1, OH), 1.5–2.1 (m, 6), 1.62 (s, 3), 1.54 (s, 3), 1.03 (d, 3, J = 6.2 Hz); ^{13}C NMR ($CDCl_3$) δ 81.7, 74.5, 58.7, 42.9, 31.8, 30.5, 30.3, 25.5, 17.3; IR (neat) 3400, 2960, 2880, 1460, 1390, 1375, 1110, 1070, 1035, 760 cm^{-1}; MS, m/e 140 (M^+ – HCl), 125, 123, 122, 109, 107, 83, 82, 81, 69, 67, 55. Anal. Calcd for $C_9H_{17}ClO$: C, 61.18; H, 9.70; Cl, 20.07. Found: C, 59.15; H, 9.11; Cl, 19.26.

Runs 3, 4, and 6 were carried out as described for run 1 to give the results shown in Table I.

Run 5. $EtAlCl_2$ (1.7 mL of a 1.17 M solution in pentane, 1.99 mmol) and **3** (0.148 g, 1.05 mmol) in 3.0 mL of CH_2Cl_2 for 1 h at −78 °C gave 0.145 g of product which consisted of the mixture indicated in Table I. Purification by chromatography on silica gel (2:1 pentane–ether) gave pure **11a**: 80 mg (51%); NMR ($CDCl_3$) δ 3.28 (dd, 1, J = 7.0, 7.0 Hz), 1.77 (s, 1, OH), 1.4–1.9 (m, 3), 1.1–1.4 (m, 4), 1.01 (d, 3, J = 6.2 Hz), 0.96 (d, 3, J = 6.2 Hz), 0.86 (d, 3, J = 6.4 Hz); IR (neat) 3340, 2950, 2870, 1460, 1385, 1370, 1080, 1060, 1020 cm^{-1}; MS, m/e (relative intensity) 142 (M^+, 67), 127 (35), 124 (22), 109 (64), 99 (27), 95 (36), 85 (60), 82 (70), 81 (78), 71 (100); GC t_R = 16.0 min (125 °C); mol wt calcd for $C_9H_{18}O$ 142.1358, found 142.1354.

The remaining products listed in Table I were isolated from the above reactions by preparative GC.

The spectral data for **4a** are identical with those previously reported for the trans isomer:[15] GC t_R = 9.9 and 10.5 min (125 °C) for **4a** and **4b**, respectively.

The spectral data for **5a** follow: NMR ($CDCl_3$) δ 4.99 (br s, 1), 4.85 (br s, 1), 3.74 (br d, 1, J = 4.6 Hz), 2.45 (m, 1), 1.9–2.2 (m, 1), 1.4–1.9 (m, 4), 1.81 (s, 3), 1.52 (s, 1, OH), 1.01 (d, 3, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 144.2, 112.2, 79.1, 50.9, 41.3, 31.3, 26.6, 23.4, 20.2; IR (neat) 3440, 3090, 2960, 2870, 1650, 1455, 1378, 1070, 1030, 960, 890 cm^{-1}; MS, m/e 140 (M^+), 125, 122, 107, 93, 83, 82, 69; GC t_R = 15.6 min (125 °C); mol wt calcd for $C_9H_{16}O$ 140.1201, found 140.1194.

The spectral data for **5b** follow: NMR ($CDCl_3$) δ 5.01 (br s, 1), 4.87 (br s, 1), 3.93 (dd, 1, J = 2.9, 3.1 Hz), 2.50 (m, 1), 1.4–2.2 (m, 5), 1.82 (s, 3), 1.28 (s, 1, OH), 1.07 (d, 3, J = 6.4 Hz); ^{13}C NMR ($CDCl_3$) δ 144.5, 111.7, 75.2, 53.1, 39.7, 29.9, 25.3, 23.6, 14.5; IR ($CDCl_3$) 3600, 3090, 2970, 2880, 1650, 1450, 1375, 1070, 880 cm^{-1}; GC t_R = 14.6 min (125 °C); mol wt calcd for $C_9H_{16}O$ 140.1201, found 140.1207.

The spectral data for **8a** follow: NMR ($CDCl_3$) δ 4.82 (br s, 2), 3.42 (dd, 1, J = 8.8, 8.1 Hz), 2.38 (ddd, 1, J = 8.8, 8.8, 8.8 Hz), 1.3–2.1 (m, 6), 1.74 (s, 3), 1.09 (d, 3, J = 6.2 Hz); IR (neat) 3380, 3090, 2950, 2870, 1645, 1455, 1375, 1030–1100, 885 cm^{-1}; GC t_R = 21.9 min (125 °C); mol wt calcd for $C_9H_{16}O$ 140.1201, found 140.1203.

The spectral data for **8b** were determined from a 3:1 mixture with **8a**: NMR ($CDCl_3$) δ 4.8 (br s, 2), 3.93 (dd, 1, J = 6.3, 6.3 Hz), 2.3 (m, 1), 1.3–2.1 (m, 6), 1.7 (s, 3), 1.03 (d, 3, J = 7.7 Hz); IR is the same as for **8a**; GC t_R = 25.9 min (125 °C).

The spectral data for **9a** follow: NMR ($CDCl_3$) δ 3.41 (br, 1, $w_{1/2}$ = 15 Hz), 1.45–1.9 (m, 6), 1.35 (br, 1), 1.03 (d, 3, J = 6.2 Hz), 0.92 (s, 9); IR ($CDCl_3$) 3615, 2960, 2910, 2870, 1450, 1365, 1035 cm^{-1}; MS, m/e 156 (M^+), 141, 123, 109, 95–99, 83, 82, 81, 71, 70, 69, 67, 58, 57, 56, 55; GC t_R = 18.9 min (125 °C); mol wt calcd for $C_{10}H_{20}O$ 156.1514, found 156.1518. These data are identical with those previously reported.[32]

The spectral data for **10a** follow: NMR ($CDCl_3$) δ 3.44 (dd, 1, J = 6.7, 6.7 Hz), 1.5–1.9 (m, 5), 1.1–1.5 (m, 4), 1.02 (d, 3, J = 6.2 Hz), 0.88 (s, 3), 0.84 (t, 3, J = 7 Hz), 0.82 (s, 3); IR ($CHCl_3$) 3615, 2960, 2880, 1460, 1385, 1375, 1363, 1200, 1100 cm^{-1}; MS, m/e 170 (M^+), 155, 153, 152, 151, 141, 137, 123, 110, 109, 97, 95, 83, 82, 81, 71, 70, 69, 67; GC t_R = 34.7 min (125 °C); mol wt calcd for $C_{11}H_{22}O$ 170.1671, found 170.1673.

Cyclization of 16. Treatment of ketone **16** (295 mg, 1.91 mmol) with $MeAlCl_2$ (4.2 mL of 0.92 mL in heptane, 3.8 mmol) in CH_2Cl_2 (6 mL) at 0 °C for 4 h as described above for run 1 gave 290 mg of product which was shown by NMR and GC analysis to consist of **17** (ca. 65%) and five minor components. Preparative GC gave 47 mg of **17** and 7 mg of 3,7,7-trimethyl-2-octanone.

The spectral data for **17** follow: NMR ($CDCl_3$) δ 1.3–2.2 (m, 6), 1.08 (d, 3, J = 6.4 Hz), 0.91 (s, 3), 0.85 (d, 3, J = 6.8 Hz), 0.74 (d, 3, J = 6.6 Hz); IR ($CDCl_3$) 2970, 2940, 2880, 1730 cm^{-1}; GC t_R = 11.9 min (125 °C). The mass spectral data are identical with those previously reported.[33]

The spectral data for 3,7,7-trimethyl-2-octanone follow: NMR ($CDCl_3$) δ 2.5 (m, 1), 2.16 (s, 3), 1.1–1.9 (br m, 6), 1.09 (d, 3, J = 6.8 Hz), 0.86 (s, 9); IR ($CDCl_3$) 2960, 2940, 2880, 1710 cm^{-1}; GC t_R = 15.1 min (125 °C).

Cyclization of 14. Treatment of **14** (256 mg, 1.52 mmol) with Me_2AlCl (1.30 mL of a 1.14 M solution in heptane, 1.48 mmol) in CH_2Cl_2 (4.5 mL) for 2.5 h at −78 °C and then 10 h at 25 °C as described above for run 1 gave 252 mg of product. Column chromatography on silica gel (15:1 hexane–EtOAc) gave 28 mg (11%) of **15b**, 120 mg (47%) of **15a**, and 50 mg (20%) of the aldol dimer.

The spectral data for **15a**[34] follow: NMR ($CDCl_3$) δ 4.91 (br s, 1), 4.74 (br s, 1), 2.06 (s, 1, OH), 2.04 (dd, 1, J = 11.4, 4.6 Hz), 1.75 (s, 3), 1.2–1.7 (m, 7), 1.09 (s, 3), 0.87 (d, 3, J = 5.9 Hz); ^{13}C NMR ($CDCl_3$) δ 146.3, 113.6, 72.2, 54.7, 50.5, 34.9, 30.2, 28.4, 22.9, 22.7, 22.3; IR (neat) 3450 (br), 3080, 2950, 2920, 2860, 1640, 1455, 1375, 1150, 1110, 1050, 1025, 915, 885 cm^{-1}; GC t_R = 20.8 min (135 °C).

The spectral data for **15b**[34] follow: NMR ($CDCl_3$) δ 4.90 (br s, 1), 4.76 (br s, 1), 1.3–2.2 (m, 9), 1.83 (s, 3), 1.14 (s, 3), 0.88 (d, 3, J = 6.2 Hz); IR (neat) 3500 (br), 3070, 2950, 2920, 2860, 1640, 1455, 1375, 1285, 1155, 1105, 1030, 940, 910, 885 cm^{-1}; GC t_R =

(32) Varech, D.; Jacques, J. *Bull. Soc. Chim. Fr.* **1969**, 3505.
(33) Doering, W. v. E.; Willcott, M. R., III; Jones, M., Jr. *J. Am. Chem. Soc.* **1962**, *84*, 1224.
(34) Watanabe, S. *J. Sci. Hiroshma Univ., Ser. A: Phys. Chem.* **1973**, *37*, 91.

14.4 min (135 °C).

The spectral data for the aldol dimer follow: NMR ($CDCl_3$) δ 5.1 (m 2), 3.89 (br s, 1, OH) 2.55 (s, 2), 2.2–2.4 (m, 2), 1.75–2.15 (m, 6), 1.67 (s, 6), 1.59 (s, 6), 1.1–1.5 (m, 6), 1.20 (s, 3), 0.8–1.1 (m, 6); MS, m/e 336 (M^+).

Cyclization of 18. Me_2AlCl (1.7 mL of a 1.14 M solution in heptane, 1.9 mmol) was added to **18** (184 mg, 1.3 mmol; 92% **18**, 8% **19**) in 4 mL of CH_2Cl_2 at 0 °C. The reaction was stirred for 2.5 h and worked up as described above for run 1 to give 180 mg of product which NMR and GC analysis showed to be 75% **20**, 4% **21**, 1% **21**, 1% **22**, and 16% (*Z*)-**23**. The minor isomers **21** and **22** arose from **19** present in the starting material.

Chromatography on silica gel (4:1 pentane–ether) gave 80 mg (44%) of pure **20** and 35 mg (17%) of (*Z*)-**23**.

The spectral data for **20** follow: NMR ($CDCl_3$) δ 5.55 (m, 2), 3.81 (m, 1), 2.18 (m, 1), 1.72 (m, 3, virtually coupled), 1.2–1.9 (m, 9); IR ($CHCl_3$) 3560, 2980, 2930, 2850, 1445, 1387, 1378, 1200–1270, 1080, 1045, 970 cm^{-1}; GC t_R = 30.5 min (120 °C); mol wt calcd for $C_9H_{16}O$ 140.1201, found 140.1206.

Repetition of the reaction in 40 mL of CH_2Cl_2 at 25 °C for 2 h gave 181 mg which was shown by GC to be 90% **20**, 1–2% (*Z*)-**23**, and 6% **21** from **19**.

Cyclization of 19. Me_2AlCl (0.44 mL of a 1.14 M solution in heptane, 0.49 mmol) was added to **19** (68 mg, 0.49 mmol, 93% **19**, 7% **18**) in 2 mL of CH_2Cl_2 at 0 °C. The reaction was stirred for 2 h and worked up to give 69 mg of product which was shown by GC and NMR to consist of 15% **20**, 46% **21**, 8% **22**, and 15% (*E*)-**23**. Pure **21** and **22** were isolated by preparative GC.

The spectral data for **21** follow: NMR ($CDCl_3$) δ 5.58 (dq, 1, J = 15.3, 5.9 Hz), 5.29 (dd, 1, J = 15.3, 8.4 Hz), 3.17 (ddd, J = 4.1, 9.5, 9.5 Hz), 1.5–2.2 (m, 5), 1.9 (s, 1, OH), 1.71 (d, 3, J = 5.9 Hz), 0.9–1.5 (m, 4); IR (neat) 3400, 3030, 2940, 2860, 1450, 1030–1060, 967 cm^{-1}; MS, m/e 140 (M^+), 123, 122, 111, 109, 107, 93–98, 91, 81, 79, 70–67, 55; GC t_R = 27.7 min (120 °C); mol wt calcd for $C_9H_{16}O$ 140.1201, found 140.1199.

The spectral data for **22** follow: NMR ($CDCl_3$) δ 5.67 (dq, 1, J = 10.8, 6.8 Hz), 5.24 (ddq, 1, J = 10.8, 9.9, 1.6 Hz), 3.21 (ddd, 1, J = 4.1, 9.0, 9.0 Hz), 1.5–2.5 (m, 6), 1.70 (dd, 3, J = 6.7, 1.6 Hz), 1.1–1.5 (m, 4); IR ($CHCl_3$) 3580, 2990, 2925, 2860, 1600, 1445, 1200–1270, 1110, 1045, 1015, 925, 850 cm^{-1}; GC t_R = 25.0 min (120 °C); mol wt calcd for $C_9H_{16}O$ 140.1201, found 140.1203.

Cyclization of 24. Me_2AlCl (1.75 mL of a 1.14 M solution in heptane, 2 mmol) was added to **24** (259 mg, 2 mmol) in 6 mL of CH_2Cl_2 at 0 °C. The reaction mixture was stirred 2 h and worked up to give 260 mg of product which was shown by GC and NMR analysis to consist of 37% of **25** and 48% of **26**. If the solvent is not removed at 0 °C some of ene adduct **25** is lost. Pure samples of **25** and **26** were isolated by preparative GC.

The spectral data for **25** follow: NMR ($CDCl_3$) δ 5.52–5.66 (m, 2), 4.08–4.13 (m, 1), 2.36 (br s, 1), 1.44–1.76 (m, 10); IR ($CDCl_3$) 3620, 3575, 3030, 1665, 970 cm^{-1}; GC t_R = 12.4 min (125 °C); MS, m/e (relative abundance) 126 (3, M^+), 111 (3), 109 (3), 108 (33), 98 (17), 97 (16), 95 (5), 93 (35), 91 (7), 84 (15), 83 (24), 82 (39), 81 (13), 80 (8), 79 (24), 78 (4), 77 (11), 71 (6), 70 (37), 69 (19), 68 (24), 67 (100), 65 (9), 57 (34), 55 (54), 54 (14), 53 (27), 43 (29), 42 (20), 41 (76), 39 (61), 31 (18), 29 (51), 28 (14), 27 (62).

Repetition of the reaction in 60 mL of CH_2Cl_2 for 4 h at 25 °C gave 250 mg of product which was shown by GC analysis to consist of 60% of **25** and 24% of **26**.

$EtAlCl_2$ (2.61 mL of a 1.53 M solution in heptane, 4 mmol) was added to **24** (259 mg, 2 mmol) in 6 mL of CH_2Cl_2 at 0 °C. The reaction was stirred 12 min and worked up to give 270 mg of crude product which was shown by GC analysis to consist of 29% of **25**, 17% of **27**, 9% of **28**, 19% of **29**, and 26% of **30**. Pure samples were obtained by preparative GC.

The spectral data for **27** follow: NMR ($CDCl_3$) δ 5.11–5.68 (m, 2), 3.69–3.84 (m, 1), 0.90–2.35 (m, 11); IR ($CDCl_3$) 3610, 3010, 1685, 965 cm^{-1}; GC t_R = 16.4 min (125 °C); MS, m/e (relative abundance) 126 (2, M^+), 111 (2), 110 (1), 109 (2), 108 (28), 98 (13), 97 (14), 95 (5), 93 (29), 91 (6), 84 (15), 83 (23), 82 (38), 81 (15), 79 (23), 77 (10), 71 (7), 70 (37), 69 (18), 68 (23), 67 (100), 65 (9), 58 (16), 57 (39), 55 (56), 53 (26), 43 (30), 42 (20), 41 (77), 39 (60), 31 (21), 29 (56), 28 (14), 27 (63).

The spectral data for **28** follow: NMR ($CDCl_3$) δ 1.08–2.40 (m, 11), 0.79–0.98 (m, 3); IR ($CDCl_3$) 1710, 1155, 1080 cm^{-1}; GC t_R = 8.8 min (125 °C); MS, m/e (relative abundance) 127 (2), 126 (31, M^+), 111 (8), 99 (6), 98 (92), 97 (29), 84 (16), 83 (45), 82 (24), 71 (5), 70 (25), 69 (24), 68 (8), 67 (28), 59 (5), 57 (7), 56 (27), 55 (100), 53 (11), 42 (66), 41 (90), 39 (55), 31 (17), 29 (46), 28 (21), 27 (72).

Ketones **28** and **29** could not be separated by preparative GC. The IR spectra of the mixture showed carbonyl stretched at 1710 and 1730 cm^{-1}. The ketones were separated by analytical GC and characterized by GC/MS. The large peaks at m/e 98 and 84 in **28** and **29**, respectively, arise from McLafferty rearrangement and confirm the structure assignment.

The spectral data for **29** follow: NMR ($CDCl_3$) δ 1.08–2.40 (m, 11), 0.79–0.98 (m, 3); IR ($CDCl_3$) 1730, 1155, 1080 cm^{-1}; GC t_R = 8.8 min (125 °C); MS, m/e (relative abundance) 127 (1), 126 (15, M^+), 98 (1), 97 (5), 85 (6), 84 (100), 83 (36), 79 (1), 70 (7), 89 (10), 67 (9), 56 (16), 55 (48), 53 (7), 43 (8), 42 (39), 41 (53), 40 (8), 39 (35), 29 (27), 28 (17), 27 (53).

The spectral data for **30** follow: NMR ($CDCl_3$) δ 3.38–3.62 (m, 2), 2.65 (br s, 1), 1.13–2.06 (m, 9), 0.89 (t, 3, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 75.6, 74.0, 45.0, 33.2, 30.5, 25.8, 22.9, 10.2; IR ($CDCl_3$) 3580, 1070, 1035 cm^{-1}; GC t_R = 37.5 min (125 °C); MS, m/e (relative abundance) 162 (1, M^+), 146 (1), 144 (4), 126 (5), 118 (2), 116 (6), 111 (5), 109 (18), 108 (28), 98 (34), 97 (22), 95 (9), 93 (20), 83 (12), 82 (60), 81 (13), 79 (31), 78 (12), 77 (8), 75 (7), 70 (27), 69 (21), 67 (35), 57 (100), 55 (46), 53 (21), 44 (20), 43 (27), 41 (65), 39 (44), 29 (59), 27 (58).

The ^{13}C NMR spectra confirms that this is a single diastereomer. Its structure is tentatively assigned based on mechanistic arguments.[35]

Cyclization of 31 with 0.9 Equiv of Me_2AlCl. Me_2AlCl (1.11 mL of a 1.14 M solution, 1.26 mmol, 0.9 equiv) was added to a solution of **34a** (250 mg, 1.4 mmol) in 5 mL of CH_2Cl_2. This solution was stirred for 8 h at 25 °C. A normal workup gave 250 mg of crude material. Purification of 200 mg of the crude material on silica gel (1:1 pentane–ether) gave 0.024 g (10.5%) of **34** and 0.043 g (19%) of **33**.

The spectral data for **33** follow: NMR (CCl_4) δ 4.68 (br s, 2), 2.63–1.08 (m, 10), 2.13 (br s, 2), 1.22 (s, 3), 0.98 (d, 3, J = 7 Hz); IR (neat) 3458, 3080, 1652 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.76; H, 11.37.

The spectral data for **34**, which consists of two isomers in a ca. 1:1 ratio, follow: NMR (CCl_4) δ 4.20 and 4.13 (2 br s, 1), 2.52–1.07 (m, 7), 1.6–1.7 (br s, 3), ~1.18 (4 s, 6), ~0.97 (2 d, 3, J = 7 Hz); IR (neat) 1678, 1140 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O$: C, 79.44; H, 11.18. Found: C, 79.82; H, 11.22.

Cyclization of 31 with 2 Equiv of Me_2AlCl. Me_2AlCl (2.45 mL of a 1.14 M solution, 2.80 mmol, 2 equiv) was added to a solution of **34a** (250 mg, 1.4 mmol) in 5 mL CH_2Cl_2. This solution was stirred at 0 °C for 1 h. Normal workup gave 250 mg of crude material. Purification of 190 mg on silica gel (4:1 pentane–ether) gave 91 mg (48%) of **35**, as a mixture of all four isomers: NMR (CCl_4) δ 5.96 (m, 1); IR (neat) 1690, 1608 cm^{-1}. A small amount of the β,γ-unsaturated isomer was present as determined by the NMR absorption at δ 3.43 and a shoulder in the IR at 1710 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.66; H, 11.18.

Cyclization of 32 with 0.1 Equiv of Me_2AlCl. Me_2AlCl (0.12 mL of a 1.14 M solution, 0.14 mmol, 0.1 equiv) was added to a solution of **34b** (250 mg, 1.4 mmol) in 5 mL of CH_2Cl_2. This solution was stirred at −15 °C for 12 h. A normal workup gave 250 mg of crude material. Purification of 180 mg on silica gel (4:1 pentane–ether) gave 104 mg (58%) of **37** and 24 mg (13%) of **36**.

The spectral data for **37** which is an ~4:1 mixture of isomers follows: NMR (CCl_4) δ 4.10 and 4.04 (2 br s in 1:4 ratio, 1), 2.56 (m, 1), 2.05–0.95 (m, 8), 1.64 (d, 3, J = 2 Hz), 1.18 (s, 3), 1.16 (s, 3), 0.82 (d, 3, J = 7 Hz); IR (neat) 1670 cm^{-1}. Adduct **37** is identical with an authentic sample prepared by treatment of **32** with $BF_3{\cdot}Et_2O$ in benzene.[27]

The spectral data for **36** follow: NMR ($CDCl_3$) δ 4.67 (s, 2), 2.15 (br s, 2), 2.1–1.02 (m, 9) 1.17 (s, 6), 0.89 (d, 3, J = 7 Hz); IR 3450, 3088, 1648, 1072 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: 80.21; H, 11.52.

(35) Cis addition to the double bond is observed in related intermolecular reactions: Snider, B. B.; Rodini, D. J.; Kirk, T. C.; Cordova, R. C. *J. Am. Chem. Soc.* **1982**, *104*, 555.

Cyclization of 32 with 2.0 Equiv of Me_2AlCl. Me_2AlCl (2.28 mL of a 1.14 M solution, 2.6 mmol, 2 equiv) was added to a solution of **32** (250 mg, 1.3 mmol) in 5 mL of CH_2Cl_2. This solution was stirred at 0 °C for 1 h. Normal workup gave 250 mg of crude material. Purification of 210 mg on silica gel (2:1 pentane–ether) gave 120 mg (58%) of **36**.

Cyclization of 38. Addition of $EtAlCl_2$ (0.3 mL of a 1.53 M solution in heptane, 0.45 mmol) to a solution of enone **38** (100 mg, 0.45 mmol) in 3 mL of CH_2Cl_2 at 25 °C. The reaction was stirred 1.5 h at 25 °C. TLC showed no reaction had occurred so an additional 0.15 mL of $EtAlCl_2$ solution was added. The reaction was complete in 10 min. Normal workup gave 97.3 mg of **40** as a 1:1 mixture of isomers which was chromatographically pure: NMR ($CDCl_3$) δ 5.91 (br s, 1), 2.5–1.8 (m, 4) 1.90 (br s, 3), 1.24 (br, 12), 0.93 (d, 0.5 × 3, J = 7 Hz), 0.80 (br t, 3, J = 6 Hz), 0.69 (d, 0.5 × d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 199.3, 164.7, 164.5, 128.6, 128.4, 45.5, 43.2, 36.2, 36.0, 35.0, 33.7, 33.2, 32.3, 31.7, 31.4, 29.4, 29.3, 27.9, 27.5, 23.0, 22.6, 22.5, 21.4, 18.2, 15.1, 13.9; IR (neat) 1670, 1618 cm^{-1}.

To ensure that isomerization of **40** had not occurred after cyclization, **38** (50 mg, 0.22 mmol) in 1.5 mL of $EtAlCl_2$ was treated with $EtAlCl_2$ (0.30 mL of a 1.53 M solution in heptane, 0.45 mmol, 2 equiv) at −78 °C. The reaction mixture was stirred for 5 h at −78 °C and quenched to give 49 mg (99%) of a 1:1 mixture of recovered **38** and **40**. NMR analysis indicated that **40** was present as a 1:1 mixture of isomers.

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Registry No. **3**, 106-72-9; **4a**, 66575-33-5; **4b**, 66575-34-6; **5a**, 83026-65-7; **5b**, 83059-39-6; **7a**, 81980-08-7; **8a**, 83059-40-9; **8b**, 83059-41-0; **9a**, 25073-02-3; **10a**, 81980-09-8; **11a**, 82009-61-8; **12**, 106-23-0; **14**, 3664-64-0; **14** (dimer), 83026-79-3; **15a**, 76156-38-2; **15b**, 76189-17-8; **16**, 504-37-0; **17**, 76123-37-0; **18**, 2277-19-2; **19**, 2277-20-5; **20**, 76123-38-1; **21**, 76156-39-3; **22**, 76156-40-6; (*E*)-**23**, 83026-66-8; (*Z*)-**23**, 81980-06-5; **24**, 41547-22-2; **25**, 83026-67-9; **26**, 79925-78-3; **27**, 83059-42-1; **28**, 4423-94-3; **29**, 1193-70-0; **30**, 83026-68-0; **31**, 83026-69-1; **32**, 19870-49-6; **33**, 83026-70-4; **34**, 83026-71-5; **35**, 83026-72-6; **36**, 83026-73-7; **37**, 83026-74-8; **38**, 83026-75-9; **40** (isomer 1), 83026-76-0; **40** (isomer 2), 83026-77-1; 3,7,7-trimethyl-2-octanone, 83026-78-2; Me_2AlCl, 1184-58-3; $MeAlCl_2$, 917-65-7; $EtAlCl_2$, 563-43-9.

Conformational Dependence in the Mass Spectrum of Cyclohexanecarboxaldehyde

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The mass spectrum of cyclohexanecarboxaldehyde (**1**) was shown to fit a composite of the mass spectra of the equatorial and axial conformers. By comparison of the fragmentation processes from $1^{+\cdot}$ with the processes from the fixed conformers corresponding to $1^{+\cdot}$, the processes involving hydrogen abstraction by the oxygen atom as the initial step were attributed to the axial conformer, and the processes involving initial ring bond cleavage were attributed to the equatorial conformer. The abundant α-cleavage ion at 50 eV was attributed to both conformers, analogous to its occurrence in the fixed conformers. The loss of C_2H_4O from $1^{+\cdot}$ was found to be loss of CH_3CHO and thus was attributed to equatorial $1^{+\cdot}$. Initial hydrogen abstraction in axial $1^{+\cdot}$ was found to occur at a faster rate than initial ring bond stretching, whereas in equatorial $1^{+\cdot}$ initial ring bond stretching was found to occur at a faster rate than conversion to axial $1^{+\cdot}$.

The McLafferty rearrangement in the molecular ions of nonfixed conformers of cyclohexyl acetate and diethyl cyclohexylmalonates was found to occur from the two chair forms in the same proportion as that in which the two chair forms existed before ionization, on the basis of the known stereoselectivity of the fixed conformers.[1] The γ-hydrogen abstraction process was proposed to be faster than chair-to-chair interconversion.[1] The McLafferty rearrangement from both chair forms would be expected to be of very low activation energy, similar to the McLafferty rearrangement in the propyl acetates, where the experimental and calculated appearance energies were equal to the ionization energy.[2] There was no need for internal excitation of the molecular ion, in agreement with the extremely low relative abundance of the molecular ion.[2] In contrast, an activation energy would be expected for the chair-to-chair interconversion in the molecular ions of the cyclohexyl acetates and corresponding cyclohexylmalonates.[3]

In this study of the fragmentation processes of the molecular ion of cyclohexanecarboxaldehyde (**1**), only the axial conformer has the required geometry for hydrogen abstraction in a six-membered transition state, and further rearrangement is required for fragmentation. However, by comparison to the mass spectra of analogous fixed conformers and cyclohexane, the fragmentation processes of $1^{+\cdot}$ were found to be consistent with a dependence on the initial stereochemistry of the aldehyde.

Results

In Table I are given data on the primary product ions and neutral fragments from $1^{+\cdot}$. The empirical structures of the product ions were confirmed by high-resolution mass spectroscopy. For the estimation of product ion energy levels, with various structures for the ions and neutral

(1) Rej, R. N.; Bacon, E.; Eadon, G. *J. Am. Chem. Soc.* **1979**, *101*, 1668.
(2) Benoit, F. N.; Harrison, A. G.; Lossing, F. P. *Org. Mass Spectrom.* **1977**, *12*, 78.
(3) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. "Conformational Analysis"; Wiley: New York, 1965.

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