

action between double bond and methylene units (type A), and the other is that between two methylene units (type B). For instance, **2a** has one type A and two type B interactions, while **2b** has two type A and one type B interactions, as summarized in the fourth column of Table I. According to the PMO analysis of propylene,¹⁴ the sum of all the π -type orbital interaction energies present in type A interaction is positive. Namely, the net result of conjugation between the double bond and the methylene units is not stabilizing but destabilizing. An example of type B interaction is found in ethane, the π -type orbitals of which are shown in Figure 2. The PMO analysis of ethane¹⁴ shows that the net result of all the π -type orbital interactions present in type B interaction is destabilizing as well. In addition, type B interaction is found to be more destabilizing than type A interaction due essentially to the fact that the overlap between two neighboring π_{CH_2} orbitals is greater than that between π_{CH_2} and π_{CC} .¹⁴ As summarized in the fourth column of Table I for each isomeric series of the alkenes **1**, **2**, or **3**, the number of type A interactions increases but that of type B interactions decreases with alkyl substitution. Since type A interaction is less repulsive than type B interaction, the thermodynamic stability of the alkene is expected to increase with alkyl substitution. The π_{CC} orbital of a double bond is raised by type A interaction, so the raising of the alkene HOMO is expected to increase with alkyl substitution as well.

The last column of Table I lists the total π -type orbital interaction energy ΔE^* for each alkene. By employing the PMO method,^{14,15} this energy was estimated as the orbital energy difference defined in eq 1, where the first sum-

$$\Delta E^* = 2 \sum_i^{\text{occ}} e_i^*(\text{alkene}) - 2 \sum_i^{\text{occ}} e_i^*(\text{fragments}) \quad (1)$$

mation includes all the occupied π -type orbitals of a given alkene while the second summation includes those of the alkene fragments (i.e., the double bond and methylene units of the alkene).¹⁷ As expected from the above discussion, the interaction energy ΔE^* becomes less repulsive as the number of alkyl substituents increases in each isomeric series of the alkenes **1**, **2**, or **3**.

Concluding Remarks

Alkyl substitution enhances the thermodynamic stability of an alkene and raises the HOMO level of the alkene as well. These two effects are accounted for by noting that the net result of conjugation between double bond and methylene units is destabilizing in nature, as is that between two methylene units, but the former is less destabilizing.

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Registry No. **1a**, 106-98-9; **1b**, 624-64-6; **2a**, 109-67-1; **2b**, 646-04-8; **2c**, 513-35-9; **3a**, 592-41-6; **3b**, 13269-52-8; **3c**, 616-12-6; **3d**, 563-79-1.

(17) Within the framework of SCF MO theory, orbital energy variation is caused not only by orbital interaction but also by potential change.¹⁵ In the Fock matrix partitioning method of defining fragment orbitals,^{14,15} which was adopted in the present work, the effect of potential change is incorporated into fragment orbital energies.¹⁵ Thus, eq 1 measures the orbital energy change induced by orbital interaction.

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Retro-Diels-Alder, γ -Hydrogen Rearrangement, and Decarboxylation Reactions. Pathways for Fragmentation in the Collision Activated Dissociation Mass Spectra of Ketones and Carboxylic Acid ($M - 1$)⁻ Ions

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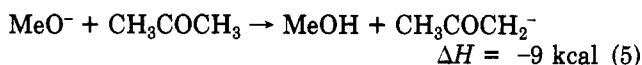
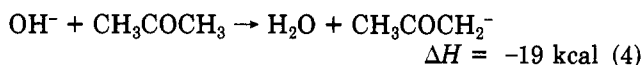
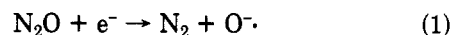
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Fragment ions observed in the collision activated dissociation mass spectra of ketone ($M - 1$)⁻ ions can be explained by either a retro-Diels-Alder reaction or a γ -hydrogen (McLafferty) rearrangement.¹ Here we present evidence in support of the postulated mechanisms for these novel fragmentation pathways of negative ions.

Collision activated dissociation mass spectra were obtained on a triple quadrupole mass spectrometer that has been described in detail elsewhere.¹ This instrument employs a chemical-ionization source, three quadrupole mass filters, and a conversion dynode electron multiplier detector.²

Negative ion mass spectra were generated under chemical-ionization conditions with either $\text{CH}_4/\text{N}_2\text{O}$ or $\text{MeOH}/\text{N}_2\text{O}$ mixtures as the reagent gas.³ The anions OH^- and MeO^- are produced as shown in eq 1-3 and were



employed as the chemical-ionization reactant ions in the present work. Both of these species function as strong Brønsted bases in the gas phase and abstract protons from the carbon α to the carbonyl group in ketones (eq 4 and 5).⁴

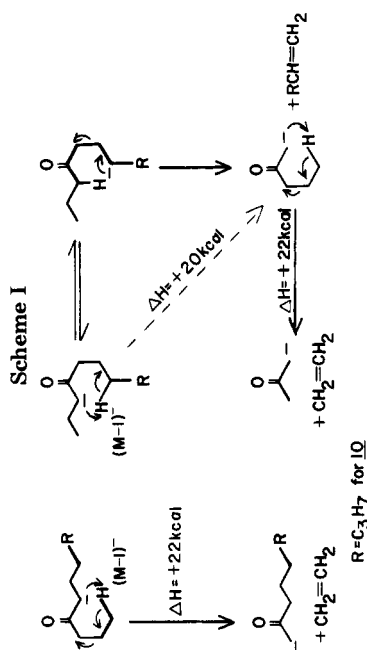
Collision activated dissociation mass spectra were obtained by using the first quadrupole mass filter to mass select the parent ($M - 1$)⁻ ion and transmit it to the second quadrupole. The chamber containing this latter quadrupole was filled with nitrogen to a pressure of 2-6 mtorr, and the quadrupole was operated with only rf voltage on the rods. In this mode of operation, the quadrupole functions as a highly efficient collision cell and both focuses and transmits ions of all possible m/z values. When the parent ($M - 1$)⁻ ion enters the second quadrupole, it suffers

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(2) Stafford, G. C.; Reeher, J.; Smith, R.; Story, M. *Dyn. Mass Spectrom.* **1978**, **5**, 55-57.

(3) Smit, A. L. C.; Field, F. H. *J. Am. Chem. Soc.* **1977**, **99**, 6471-6483.

(4) Enthalpy changes for the reaction channels discussed in this paper are estimated from heats of formation and proton affinity data that are either taken from ref 4a,b or estimated by the group equivalent method of ref 4c: (a) Rosenstock, H. M.; Draxl, K.; Steiner, B. W.; Herron, J. T. *J. Phys. Chem. Ref. Data, Suppl.* **1977**, **6**, 774-783. (b) Bartmess, J. E.; McIver, R. T. "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Chapter 11. (c) Benson, S. W. "Thermochemical Kinetics", 2nd ed.; Wiley-Interscience: New York, 1976.

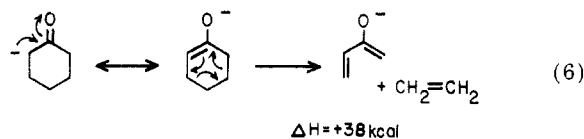
Table I. Collision Activated Dissociation Mass Spectra of Ketone ($M - 1$)⁻ Ions

compd	mol wt	no.	parent ion (P) ^a (m/z)	% total sample ion current						others (m/z)
				P^a	$P - H_2$	$P - HD$	$P - RC_2H_3$ (m/z , R)	$MeCOCH_2^-$ (d_n)		
cyclohexanone	98	1	($M - 1$) ⁻ (97)	57.8	38.4					41 (0.9)
		2	($M-d_3 - 1$) ⁻ (100)	38.5	48.1	2.7				41 (1.5)
		3	($M - 1$) ⁻ (111)	32.8	56.5					
		4	($M-d_2 - 1$) ⁻ (113)	29.7	50.8	10.1				
		5	($M - 1$) ⁻ (153)	63.2	15.5					41 (2.9)
2-decanone	156	6	($M - 1$) ⁻ (155)	77.8	1.6					69 (4.4), 83 (0.3), 127 (0.8), 139 (1.9)
		7	($M-d_4 - 1$) ⁻ (159)	72.8	0.7					42 (0.4), 71 (0.2), 72 (3.2), 73 (1.2), 129 (0.4), 139 (0.7), 140 (2.4)
3-decanone	156	8	($M - 1$) ⁻ (155)	78.7	2.0					83 (3.8), 125 (0.8), 127 (1.1)
		9	($M-d_3 - 1$) ⁻ (158)	79.2	0.7	0.7				84 (0.3), 85 (2.2), 86 (0.6), 125 (0.2), 126 (0.3), 127 (0.1), 128 (0.7), 129 (0.1)
4-decanone	156	10	($M - 1$) ⁻ (155)	60.6	2.9				2.8	41 (0.1), 69 (0.4), 71 (0.1), 97 (2.4), 111 (1.2), 139 (3.0)
		11	($M-d_3 - 1$) ⁻ (158)	71.3	0.9	0.5			1.7, 0.2 (d_2)	42 (0.1), 72 (0.1), 74 (0.1), 98 (0.1), 99 (1.0), 111 (0.2), 112 (0.6), 140 (0.1), 141 (1.4)
5-decanone	156	12	($M - 1$) ⁻ (156)	80.6	1.7				0.5	42 (0.1), 83 (0.8), 97 (0.6), 98 (0.2), 111 (1.1), 112 (0.1), 125 (0.1), 127 (1.3)
		13	($M-d_3 - 1$) ⁻ (158)	81.6	1.3	0.2			0.2	42 (0.1), 84 (0.7), 98 (0.3), 99 (0.1), 128 (0.5), 129 (0.3)

^a P refers to the parent ion, i.e., the ion undergoing collision activated dissociation.

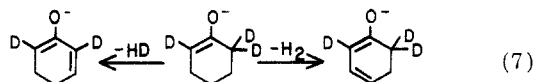
collisions with nitrogen molecules, becomes vibrationally excited, and dissociates to smaller charged fragments. Collectively, these fragments are then transmitted to the third quadrupole analyzer where they undergo mass analysis to produce the collision activated dissociation mass spectrum.

Data obtained from collision activated dissociation of the $(M-1)^-$ ion from cyclohexanone (1) indicate the loss of both hydrogen and ethylene.¹ Olefin elimination is thought to occur by a retro-Diels-Alder reaction as shown in eq 6.⁴ Loss of ethylene and 3,3-dimethylbutene from



the $(M-1)^-$ ions of 2-methylcyclohexanone (3) and 4-*tert*-butylcyclohexanone (5), respectively, is consistent with the postulated fragmentation pathway. When $N_2O/MeOD$ is employed as the chemical-ionization reagent gas, the ketone $(M-1)^-$ ions undergo ion molecule isotope-exchange reactions in the ion source and incorporate deuterium at the carbon α to the carbonyl group.⁵ As shown in Table I, the $(M-d_3-1)^-$ ion, 2, from cyclohexanone and the $(M-d_2-1)^-$ ion, 4, from 2-methylcyclohexanone both show only loss of ethylene- d_0 under collision activated dissociation conditions. This result is also in agreement with a mechanism involving a retro-Diels-Alder reaction pathway for the elimination of olefins from ketone $(M-1)^-$ ions.

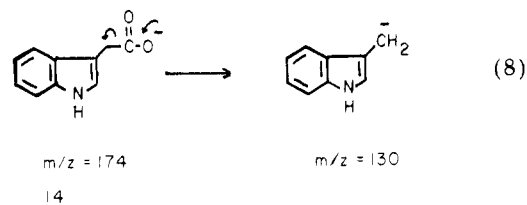
Results from the ion molecule isotope exchange experiments also provide information on the pathway for elimination of hydrogen from ketone $(M-1)^-$ ions. Loss of H_2 rather than HD or D_2 is the dominant but not exclusive result when the deuterium-labeled ions 2 and 4 undergo collision activated dissociation. Products consistent with the deuterium-labeled experiments are shown in eq 7.



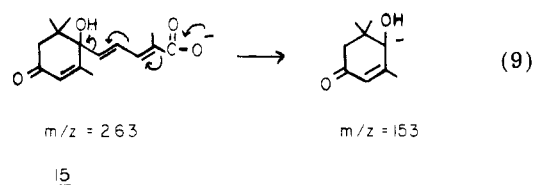
Like their cyclic analogues, acyclic ketone $(M-1)^-$ ions also eliminate hydrogen and olefins under collision activated dissociation conditions. The latter process is thought to involve migration of a γ -hydrogen to the carbanion α to carbonyl group through a cyclic transition state containing six atoms (Scheme I).¹ Consistent with this postulate is the finding that alkene elimination does not occur from the $(M-1)^-$ ion of 3-methyl-2-butanone.¹ Loss of one and two olefins occurs from the $(M-1)^-$ ions of 4-decanone and 5-decanone, respectively. As indicated in Table I, consecutive losses of olefins are not observed from the $(M-1)^-$ ions of 2- and 3-decanone.

Deuterium incorporation into the ketone $(M-1)^-$ ions by the gas-phase ion molecule isotope-exchange procedure provides additional information on the rearrangement pathway. Undeuterated olefins are the dominant, but not exclusive, reaction products in the fragmentation of ions 7, 9, 11, and 13 in Table I. Incorporation of one and two deuteriums into the olefin product also occurs to a small extent. The appearance of one but not two deuteriums in the olefin product can be explained if the first step in the γ rearrangement is reversible. No explanation is offered for the formation of small amounts of dideuterated alkene products.

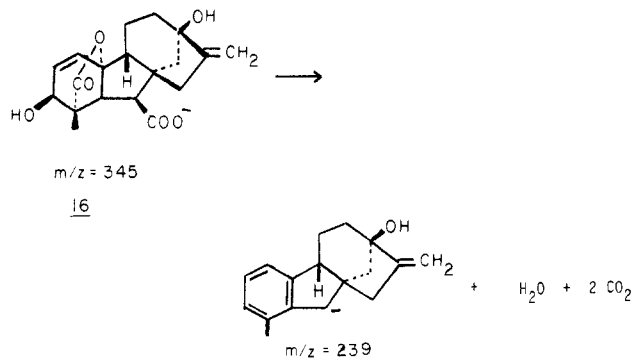
Under collision activated dissociation conditions many simple carboxylate anions suffer loss of CO_2 (44 amu). This is a particularly facile process if the resulting charged fragment is an aromatic or benzylic anion. In the case of the plant hormone indoleacetic acid (14), more than 80% of the ion current in the collision activated dissociation mass spectrum of the $(M-1)^-$ ion is carried by the $(M-1-44)^-$ ion at m/z 130 (eq 8). The undissociated parent is the only other ion in the spectrum.



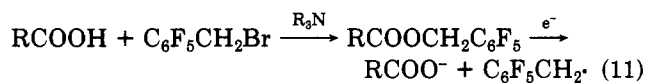
Two other plant hormones suffer decarboxylation under collision activated dissociation conditions but do so as part of a more complex pathway. Five ions are observed in the collision activated dissociation mass spectrum of the abscisic acid $(M-1)^-$ ion, 15: m/z (percent total ion current) 263 (24.0), 219 (16.8), 204 (6.3), 201 (4.8), 153 (48.1). A possible pathway for formation of the most abundant ion in the spectrum is shown in eq 9.



Aliphatic carboxylate anions are generally resistant to fragmentation under the low-energy collision conditions (10–30 eV) employed in our present triple quadrupole instrument. The $(M-1)^-$ ion of gibberellin A_3 (16) is an interesting exception to this generalization. The most abundant ion in its collision activated dissociation mass spectrum, aside from the parent ion at m/z 345, occurs at m/z 239 and is formed by loss of H_2O and two molecules of CO_2 . A possible pathway for this process is shown in eq 10. Gibberellins with saturated A rings also undergo this reaction but with much lower efficiency.



Parent $(M-1)^-$ ions from the above acids can be formed by either direct reaction with OH^- in the gas phase or by ionization of the corresponding pentafluorobenzyl esters under electron-capture negative ion conditions (eq 11).



The latter pathway facilitates detection of these acids at levels more than 100 times lower than that which can be achieved under conventional electron-impact or positive

ion chemical-ionization conditions.⁶

Acknowledgment is made to the U.S. Army Research Office (Grant No. DAAG29-80-C-0101) for their support

(6) Hunt, D. F.; Crow, F. W. *Anal. Chem.* 1978, 50, 1781-1784.

of this research.

Registry No. Cyclohexanone, 108-94-1; 2-methylcyclohexanone, 583-60-8; 4-*tert*-butylcyclohexanone, 98-53-3; 2-decanone, 693-54-9; 3-decanone, 928-80-3; 4-decanone, 624-16-8; 5-decanone, 820-29-1; 1*H*-indole-3-acetic acid, 87-51-4; abscisic acid, 21293-29-8; gibberellin A₃, 77-06-5.

Communications

A New Approach for Stereoselective Synthesis of γ -Butyrolactones

Summary: Diethylaluminum chloride promotes 1,4-cycloaddition of α,β -unsaturated carbonyl compounds with isocyanides to afford unsaturated *N*-substituted iminolactones, which are stereoselectively converted to γ -butyrolactones via hydrogenation on Pd/C and then acid hydrolysis.

Sir: Recently, an interest in some biologically active sesquiterpenes having a α -methylene- γ -butyrolactone moiety¹ has been intensified, which has rapidly increased needs for the synthetic methods of them. One of the key points of the synthesis is the stereoselective construction of ring-fused γ -butyrolactones.¹ Herein, we report a unique and versatile approach for stereoselective synthesis of ring-fused γ -butyrolactones via Lewis acid catalyzed 1,4-cycloadditions of isocyanides **2** to α,β -unsaturated carbonyl compounds **1**, which lead to unsaturated *N*-substituted iminolactones **3** as shown in Scheme I. The cycloaddition of isocyanides **2** with α,β -unsaturated carbonyl compounds **1** was most efficiently induced by diethylaluminum chloride and ethylaluminum dichloride,² which are also notable catalysts in Snider's work³ on the reactions of α,β -unsaturated carbonyl compounds with olefins.

A representative procedure for the cycloaddition of isocyanide **2** with α,β -unsaturated carbonyl compound **1** is as follows. To a stirring solution of 730 mg (4.8 mmol) of pulegone (**1b**) and 238 mg (5.8 mmol) of methyl isocyanide in 10 mL of tetrahydrofuran was dropwise added a solution of 0.65 mL (4.81 mmol)⁴ of diethylaluminum chloride in 10 mL of tetrahydrofuran at 5–10 °C, and then the mixture was stirred at room temperature for 12 h. The reaction mixture was poured into cold aqueous K₂CO₃ and extracted with ether. The ether extract was evaporated and distilled with a Kugelrohr apparatus to furnish bicyclic unsaturated *N*-methyliminolactone **3b** in 85% yield [**3b**: bp 60–65 °C (0.1 mmHg)];⁵ IR (neat) 1734, 1702 cm⁻¹; NMR (CDCl₃ with Me₄Si) δ 1.01 (d, 3 H), 1.16 (s, 6 H), 0.7–2.5 (m, 7 H), 3.01 (s, 3 H)]. Some syntheses of unsaturated

(1) Grieco, P. A. *Synthesis* 1975, 67.

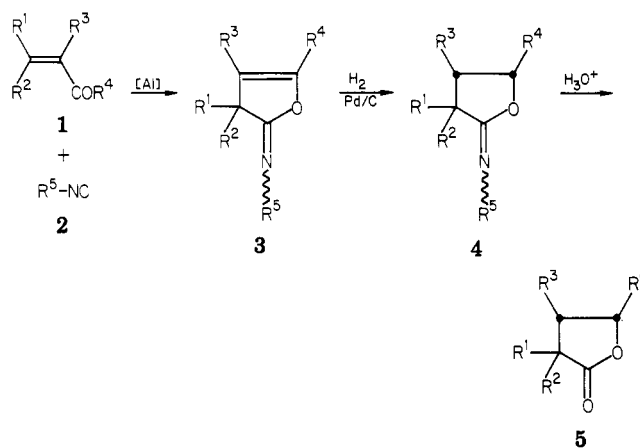
(2) The cycloadditions of isocyanides with α,β -unsaturated carbonyl compounds were also promoted by AlCl₃ and BF₃·OEt₂ but with much less efficiency.

(3) Snider, B. B.; Rodini, D. J.; van Straten, J. *J. Am. Chem. Soc.* 1980, 102, 5872.

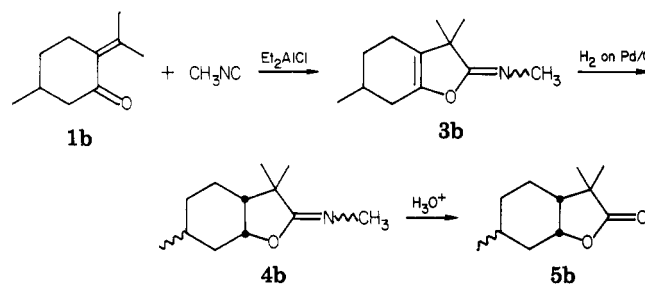
(4) The cycloaddition of isocyanide with α,β -unsaturated carbonyl compound was very sluggish in the presence of 10–20 mol % of diethylaluminum chloride.

(5) **3b**: Anal. Calcd for C₁₂H₁₉NO: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.81; H, 9.77; N, 7.27.

Scheme I



N-substituted iminolactones **3** and **6**⁶ are summarized in Table I.



The present cycloadditions work well with crowded β,β -disubstituted α,β -unsaturated carbonyl compounds (runs 1–4). Thus, the reaction⁷ of 8-methyl- Δ^8 -octal-1-one (**1c**) with *tert*-butyl isocyanide provided tricyclic unsatu-

(6) All new compounds reported gave satisfactory IR and NMR spectra and combustion analyses. Analytical data for selected products are as follows. **3a**: IR (neat) 1725, 1686 cm⁻¹; NMR (CDCl₃ with Me₄Si) δ 1.31 (s, 6 H), 1.75 (d, 3 H, $J_{H-H} = 1.3$ Hz), 2.06 (s, 3 H), 4.83 (q, 1 H, $J_{H-H} = 1.3$ Hz), 6.6–7.2 (m, 4 H). Anal. Calcd for C₁₄H₁₇NO: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.23; H, 8.11; N, 6.44. **3c**: IR (neat) 1736, 1708 cm⁻¹; NMR (CDCl₃ with Me₄Si) δ 1.18 (s, 3 H), 1.27 (s, 9 H), 0.7–2.5 (m, 13 H). Anal. Calcd for C₁₆H₂₂NO: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.79; H, 9.98; N, 5.90. **6f**: IR (neat) 1687 cm⁻¹; NMR (CDCl₃ with Me₄Si) δ 1.31 (d, 3 H, $J_{H-H} = 6.6$ Hz), 1.43–2.50 (m, 8 H), 3.04 (s, 3 H), 4.55–5.23 (m, 1 H). Anal. Calcd for C₁₀H₁₅NO: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.81; H, 9.03; N, 8.66. **3g**: IR (neat) 1720, 1611 cm⁻¹; NMR (CDCl₃ with Me₄Si) δ 1.17 (s, 3 H), 1.26 (s, 9 H), 1.57 (s, 3 H), 1.64 (s, 3 H), 1.1–2.2 (m, 4 H), 4.83–5.18 (m, 1 H), 5.18 (d, 1 H, $J_{H-H} = 3.3$ Hz), 6.59 (d, 1 H, $J_{H-H} = 3.3$ Hz). Anal. Calcd for C₁₅H₂₅NO: C, 76.55; H, 10.71; N, 5.95. Found: C, 76.60; H, 10.66; N, 5.80.

(7) The reaction was performed by adding slowly *tert*-butyl isocyanide in benzene to a mixture of **1c** and diethylaluminum chloride in benzene at 5–10 °C.