

Chemoselectivity in the Reactions of Acetylketene and Acetimidoylketene: Confirmation of Theoretical Predictions

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Acetylketene (**1**) was generated by flash pyrolysis of 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**6**). The selectivities of **1** toward a number of representative functional groups were measured for the first time in a series of competitive trapping reactions. The trend in reactivities toward **1** follows the general order amines > alcohols ≫ aldehydes ≈ ketones and can be rationalized by considering both the nucleophilicity and the electrophilicity of the reacting species. Alcohols show significant selectivity based on steric hindrance, with MeOH ≈ 1° > 2° > 3°. These selectivities are consistent with the activation energies and the pseudopericyclic transition structure previously calculated for the addition of water to formylketene. The results, presented here, of *ab initio* transition structure calculations for the addition of ammonia to formylketene are qualitatively consistent with the experimental trends as well. *N*-Propylacetacetimidoylketene (**2**) was generated by the solution pyrolysis of *tert*-butyl *N*-propyl-3-amino-2-butenolate (**9a**) and showed similar selectivity toward alcohols as opposed to ketones and similar steric discrimination toward alcohols. This is again in agreement with previous *ab initio* calculations. Taken together, these experimental trends in the reactivities of both **1** and **2** toward a variety of reagents provide strong, although indirect support for the planar, pseudopericyclic transition structures for these reactions which are predicted by *ab initio* calculations.

Introduction

The chemistry of α -oxo ketenes (e.g., **1**) has been extensively studied, both experimentally¹ and theoretically.^{1c,2} These reactive intermediates may be generated both thermally and photochemically and have been identified in solution and in argon matrices. They add a variety of polar reagents, including alcohols, ketones, and amines, as described below. These ketenes have found application in the synthesis of macrocyclic lactones and amides as well as 4*H*-4-pyranones.³ The closely related acetimidoylketenes (e.g., **2**) have also been studied,

although less intensively.^{2c,4} Despite this interest, there have been no systematic studies of the trends in the reactivities of these substituted ketenes.



An unusual and mechanistically important aspect of the reactivity of both of these ketenes is their tendency to participate as the four-center partner in [4 + 2]⁵ reactions, as opposed to the [2 + 2] reactions typical of ketenes.⁶ For example, hydration of acetylketene (**1**) in water has recently been shown to occur extremely rapidly ($k = 1.5 \times 10^6 \text{ s}^{-1}$, eq 1).¹⁰ The observations that the *Z*-enol **3h** is the initial product both in solution¹¹ and in matrix isolation experiments¹² are in agreement with *ab initio* calculations^{2c,13} which indicate that **3h** is formed

(5) Because there are multiple electron pairs on some atoms, and because there is not a loop of interacting orbitals, we use the designation [4 + 2] to indicate the number of atoms from each component and do not necessarily imply a cycloaddition. Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper and Row Publishers: New York, 1987; pp 840–841.

(6) There have been extensive studies of ketene reactivity in [2 + 2] reactions^{1b} including competition reactions of the type reported here.^{1b,7} However, the [4 + 2] reactions of acetylketenes are mechanistically quite different. There is a recent report⁸ of a competitive [2 + 2] reaction between butylamine and ethanol with a photogenerated dienylylketene. However, in a related study, the photochemical addition of alcohols to 2*H*-pyran-2-one was shown to be independent of the ketene intermediate.⁹

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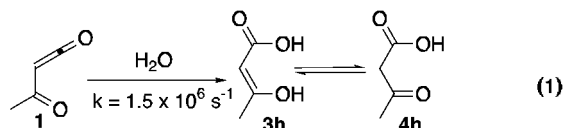
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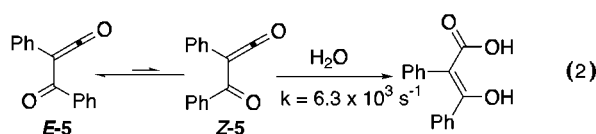
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via a [4 + 2] transition state where the water adds to the *Z*-conformation of **1**. The more stable keto tautomer (**4h**) is subsequently formed via a slower process.^{10,11}

Two substituents on formylketene have been calculated to significantly destabilize the *Z*-conformation required for a [4 + 2] reaction, due to steric hindrance.^{2b} Thus it would be expected that the [4 + 2] hydration of phenylbenzoylketene (**5**), via the less stable *Z*-conformation, would be significantly slower than **1**, as is indeed observed ($k = 6.29 \times 10^3 \text{ s}^{-1}$, eq 2).^{1f} However, these [4 + 2] reactions of both **1** and **5** are significantly faster than the uncatalyzed hydration of ketene ($\Delta H^\ddagger = 10.3 \text{ kcal/mol}$, $\Delta S^\ddagger = -15 \text{ eu}$)¹⁴ which must proceed via a [2 + 2] mechanism.



We have predicted, based on *ab initio* calculations, that the additions of water and formaldehyde to formylketene and to acetimidoylketene would be facile. The very low barriers were shown to be the consequence of the unusual, essentially planar transition states (see Figure 1).^{2c,4j} The term pseudopericyclic¹⁵ has been used to describe such reactions, highlighting the absence of the loop of interacting orbitals which characterize typical pericyclic transition states. Unfortunately, there are no product analysis methods which would experimentally probe the transition state geometries in these systems.¹⁶ For example, there are no stereochemical consequences of such a planar transition state which are retained in the product.¹⁷

Our calculations did offer testable predictions, however. The additions of water and formaldehyde to formylketene were predicted to have barriers of 6.3 and 10.6 kcal/mol, respectively, at the MP4(SDQ)/6-31G**//MP2(FULL)/6-31G* + ZPE level.^{2c} Similarly, the additions of water and formaldehyde to acetimidoylketene were calculated to have barriers of 6.3 and 10.6 kcal/mol, respectively, at the MP4(SDQ)/6-31G**//MP2/6-31G** + ZPE level.^{4j} The barrier height and vibrational frequencies can be used to calculate the rates of these reactions. From the data in ref 2c, the gas phase reaction of water and (*Z*)-formylketene at 25 °C is predicted to have a bimolecular rate constant of $k = 4.17 \times 10^6 \text{ s}^{-1} \text{ M}^{-1}$.¹⁸ Extrapolating to aqueous solution, the observed first-order rate constant for hydration of formylketene would be $k_{\text{obs}} = 2.3 \times 10^8 \text{ s}^{-1}$ ($k_{\text{obs}} = k[\text{H}_2\text{O}]$). This may be

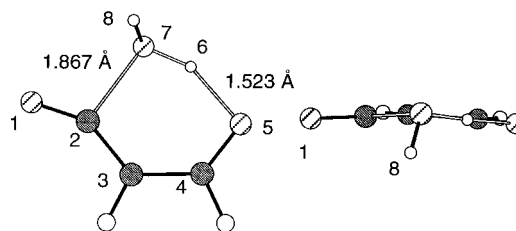


Figure 1. MP2/6-31G*-optimized geometry of the transition structure for the addition of water to formylketene from reference 2c. The two views are rotated by 90°. Carbons are shaded, hydrogens are open, and oxygens are striped. Partial bonds are hollow.

compared to the somewhat slower experimental rate for the hydration of acetylketene (**1**) ($k_{\text{obs}} = 1.5 \times 10^6 \text{ s}^{-1}$, eq 1).¹⁰ Given greater stabilization of acetylketene (**1**)^{2a,21} and the uncertainties of transferring a gas-phase rate constant to aqueous solution, these numbers are in good agreement. Thus, the recent measurement of rate of hydration of **1** supports the validity of our previously calculated planar, pseudopericyclic transition state.

Furthermore, the calculations predicted that there should be significant differences in the barrier heights for the additions of an alcohol and a ketone to each of these ketenes. Measurements of the relative rates would be sufficient to verify this prediction. Agreement between the theoretical and experimental barriers would provide additional indirect support for the pseudopericyclic transition structures as well as demonstrate a potentially synthetically useful selectivity.

We therefore undertook a systematic study of competitive reactions²² of both acetylketene and *N*-propylacetimidoylketene with a variety of polar reagents with the twin aims of providing fundamental reactivity information on these ketenes and as a test of the validity of our predictions regarding these pseudopericyclic transition structures. The reactions indeed show significant and potentially useful selectivity in some cases and are in accord with our earlier predictions. We also report *ab initio* calculations on the addition of ammonia to formylketene, which are in qualitative agreement with the experimental results.

Results and Discussion

Acetylketene (1) Reactivity. Pyrolysis of trimethyldioxinone (**6**) is a convenient source of acetylketene (**1**, Scheme 1) for both spectroscopic studies and preparative reactions.^{1a,24a} In the absence of trapping agents, this reaction is reversible, although the ketene will also undergo dimerization to **7**. However, **1** reacts rapidly

(18) MP4(SDQ)/6-31G* energies, MP2(FULL)/6-31G* zero-point energies (ZPE) scaled by 0.9646¹⁹ and the MP2(FULL)/6-31G* vibrational frequencies scaled by 0.9427,¹⁹ give ΔH^\ddagger and ΔS^\ddagger ²⁰ from which the rate was calculated. The presence of the *E*-conformation was ignored in this calculation.

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(22) When the mechanism is complex, competitive reactions can sometimes require care in interpretation.²³ However, these are well understood mechanisms: formation of **1** from **6** and **4** have been shown to be unimolecular.²⁴

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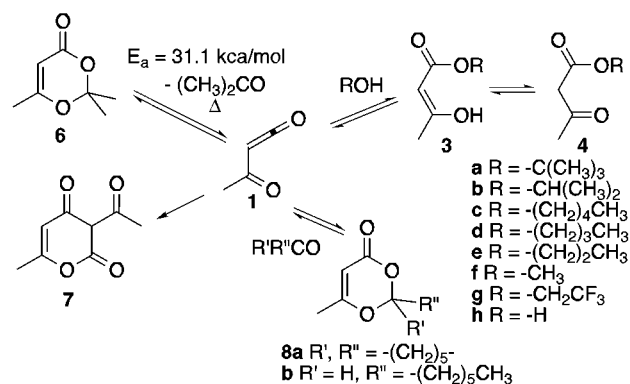
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(16) The initial formation of *Z*-enol products is consistent with either planar or non-planar (Diels–Alder-like) [4 + 2] transition states.

(17) Indirect evidence to support a planar transition state is found in the reluctance of α -oxo ketenes to undergo intramolecular cyclizations with a tethered alcohol unless the tether is quite long. Chen, C.; Quinn, E. K.; Olmstead, M. M.; Kurth, M. J. *J. Org. Chem.* **1993**, *58*, 5011–5014.

Scheme 1



with added polar reagents, including alcohols, ketones, imines, nitriles, and other ketenes as shown in Scheme 1. On a preparative scale, these reactions are conveniently carried out by refluxing **6** and an excess of the reagent in toluene.^{24a} Analytical samples of **4a–e** and **8a** were prepared via this method.

Preliminary competition reactions were carried out in this manner and gave results similar to those obtained using flash pyrolysis (FP).²⁵ However, to avoid the reversibility of the trapping reactions under the solution pyrolysis conditions, in the competition experiments reported here, **1** was generated by FP. A mixture of **6** and two traps was dripped through the pyrolysis tube and collected in a liquid nitrogen cooled trap.²⁶ As the homogeneous pyrolysate thawed and warmed to room temperature, acetylketene (**1**) would have reacted irreversibly with the trapping agents. The trapping reagents were usually used in excess to ensure that their concentrations remained relatively constant. Thus the product ratio reflects the kinetic selectivity toward a known ratio of trapping reagents, admittedly at an unknown temperature. In this work, methanol, 1-propanol, 1-butanol, 1-pentanol, 2-propanol, 2-methyl-2-propanol, 2,2,2-trifluoroethanol, cyclohexanone, heptanal, and 1-propylamine were used as competitive trapping reagents. The results are reported in Table 1.

When **6** was subjected to flash pyrolysis in the presence of cyclohexanone, a high yield of the adduct (**8a**) between acetylketene (**1**) and cyclohexanone was obtained. However, when acetylketene (**1**) was trapped with a 1:1 mixture of 1-pentanol and cyclohexanone, the β -keto ester (**4c**) was formed to the virtual exclusion of **8a**. Indeed, even when a 20-fold excess of cyclohexanone was used, **4c** remained the nearly exclusive product. It was gratifying to observe such a high and potentially useful selectivity, in confirmation of our earlier theoretical prediction.

Importantly, there is no selectivity between an aldehyde (heptanal) and a ketone (cyclohexanone). This is likely a consequence of the concerted nature of the transition state. Although aldehydes are generally more susceptible to nucleophilic attack, the ketone oxygen is more nucleophilic. These two effects apparently offset

Table 1. Results of Competitive Reactions of Pairs of Reagents with Acetylketene (**1**) Generated by Flash Pyrolysis of **6**^a

reactants		mole ratio 6:A:B	products ^b		mole ratio X:Y
A	B		X	Y	
CH ₃ (CH ₂) ₄ OH	(CH ₃) ₃ COH	1:5:5	4c	4a	8.2:1.0
CH ₃ (CH ₂) ₄ OH	(CH ₃) ₂ CHOH	1:5:5	4c	4b	3.0:1.0
CH ₃ (CH ₂) ₂ OH	CH ₃ OH	1:6:6	4e	4f	1.0:1.1
CH ₃ (CH ₂) ₄ OH	CF ₃ CH ₂ OH	1:5:5	4c	8g	6.2:1.0
CH ₃ (CH ₂) ₄ OH	cyclohexanone	1:1:1	4c	8a	≈800:1
CH ₃ (CH ₂) ₄ OH	cyclohexanone	1:1:20	4c	8a	300:1
cyclohexanone	heptanal	1:10:10	8a	8b	1.0:1.0
CH ₃ (CH ₂) ₃ OH	CH ₃ (CH ₂) ₂ NH ₂	1:4:4	9c	11	1.0:2.3

^a Results are an average of three separate reactions. ^b The quantities of the enol tautomers **3** are included.

one another, leading to the similar rates of reaction.²⁷ In the literature, reagents which add to acetylketene are commonly described as nucleophiles; this result clearly indicates the importance of both nucleophilic and electrophilic sites on the reagent. We note that this reaction could not be carried out in a static system due to decomposition of the aldehyde; the authentic material (**8b**) was also synthesized by preparative FP.

From the data in Table 1, it is clear that steric hindrance can also lead to synthetically useful selectivities in the reactions of alcohols with acetylketene. Although there is essentially no selectivity between methanol and 1-propanol (the product ratio **4f:4e** is 1.1:1), there is greater selectivity between a 1° and a 2° alcohol (**4c:4b** is 3.0:1.0) and even more between a 1° and a 3° alcohol (**4c:4a** is 8.2:1).²⁸ Such a steric effect is consistent with the calculated concerted transition state (Figure 1). There is significant bond formation between the nucleophilic alcohol oxygen and the electrophilic central ketene carbon (C₂) which brings the carbon of the alcohol (which would correspond to H₈ in Figure 1) close to the ketene oxygen (O₁).

The geometry of the calculated transition structure in Figure 1 indicates that there is substantial proton transfer as well. Thus it was anticipated that changes in the nucleophilicity of the alcohol oxygen as well as the acidity of the alcohol hydrogen would have significant influences on the reactivity. Trifluoroethanol (TFE) was investigated because it is more acidic but less nucleophilic than primary alcohols. As seen in Table 1, butanol reacted with **1** 6.2 times faster than did TFE. This suggests that of the two opposing effects the reduced nucleophilicity of TFE was most significant. This is consistent with the transition structure in Figure 1, in which nucleophilic attack of the alcohol oxygen (O₇) on the ketene carbon (C₂) is more advanced, while proton (H₆) transfer to the carbonyl oxygen (O₅) is less so.

On the basis of this result, the reactivity of **1** with an amine was also investigated. It was anticipated that an

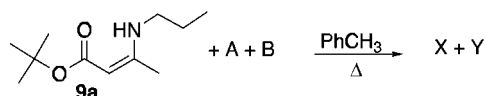
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(26) Similar FP conditions give complete conversion of **3b** and **6** to **1** and the corresponding alcohol or ketone, as detected by matrix isolation FT-IR.¹² Thus we expect that the ketene reached the cold trap.

(27) We have recently compared the *ab initio* transition structures for the [3 + 2] cycloadditions of formaldehyde and acetone to nitrosoketene. Although bond formation at the carbon of acetone is less than that in formaldehyde, both are concerted reactions, and the barriers are similar. Ham, S.; Birney, D. M. *Tetrahedron Lett.* **1997**, *38*, 5925–5928.

(28) There is at least one other example in which an α -oxo ketene reacted preferentially with a secondary alcohol in the presence of a tertiary one.^{3a}

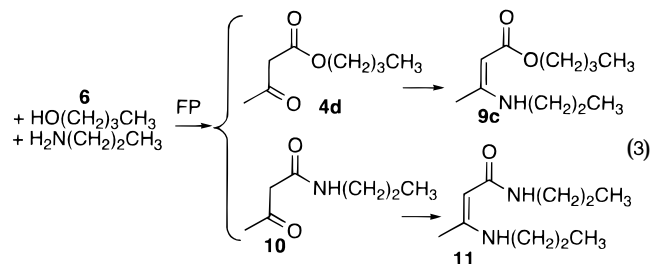
Table 2. Results of Competitive Reactions of Pairs of Reagents with Acetimidoylketene (2) Generated by Pyrolysis of 9a in a Closed Vessel in Toluene Solution^a

reactants		mole ratio 9a:A:B	conv ^b %	products		mole ratio X:Y
A	B			X	Y	
CH ₃ (CH ₂) ₃ OH	(CH ₃) ₂ CHOH	1:10:10	0.8% ^c	9c	9b	(25.1 ± 0.8):1.0
CH ₃ (CH ₂) ₃ OH	CH ₃ OH	1:50:50	0.7% ^d	9c	9d	1.0:(1.04 ± 0.04)
CH ₃ (CH ₂) ₃ OH	CF ₃ CH ₂ OH	1:10:10	0.7% ^e	9c	9e	(21.2 ± 2.4):1.0
CH ₃ (CH ₂) ₃ OH	cyclohexanone	1:0:solvent	no reaction			

^a Results are an average of three separate reactions. Product ratios were determined by GC, with the injector temperature 125 °C, oven temperature 80 °C, then 10 °/min to 180 °C. ^b % conversion of starting material. ^c 2 h at 128 °C. ^d 2 h at 124 °C. ^e 1 h at 126 °C.

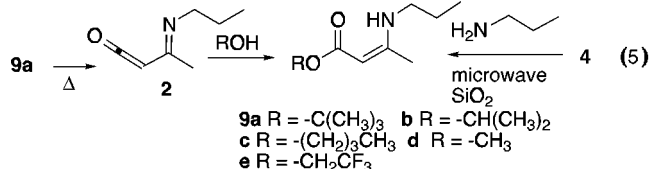
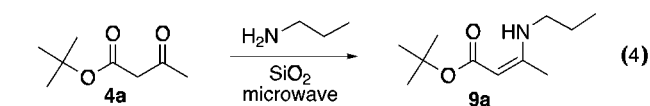
amine, being more nucleophilic than alcohol (although also less acidic), would be predicted to react more rapidly than an alcohol.

α -Oxo ketenes are known to react with primary and secondary amines,^{1a,3b,11b} although this reaction has not been extensively studied. When **6** was pyrolyzed in the presence of excess 1-butanol and 1-propylamine, a mixture of **9c** and **11** was obtained (eq 3). A control



experiment was performed to ensure that the enamines **9c** and **11** were formed from the β -keto ester **4d** and the β -keto amide **10**. When a mixture of **4d** and **10** was subjected to the workup and analysis conditions, amide **11** and ester **9c** were obtained in the same ratio as the starting materials.²⁹ There was no trans-esterification. Thus the 1:2.3 ratio of **9c** to **11** reflects the relative reactivities of acetylketene (**1**) toward the alcohol and the amine. The more nucleophilic amine was indeed more reactive.

Acetimidoylketene (2) Reactivity. A nitrogen analog of **6** is not readily available; to generate acetimidoylketene (**2**), we turned to the pyrolysis of enamino ester **9a**. Pyrolysis of other enamino esters has previously been shown to produce acetimidoylketenes.³⁰ The enamino ester **9a** was conveniently prepared by microwave irradiation of **4a** and 1-propylamine on silica gel (eq 4).³¹ Authentic samples of the products from competition reactions could be prepared either by thermolysis of **9a** with an appropriate alcohol or by microwave-

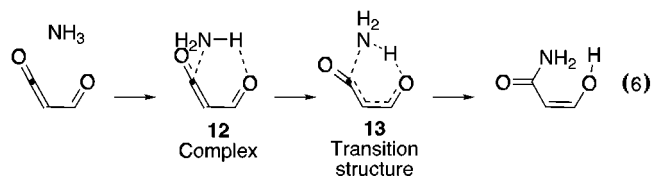


induced reaction of **4** with propylamine (eq 5). The sensitivity of **9a–e** to hydrolysis to give **4** made FP

difficult. Therefore the competition reactions reported here were performed in solution, with analysis at low conversion (<1%) to minimize back reactions. The results reported in Table 2 were similar to those obtained by FP of acetylketene (**1**) (vide supra). Methanol and 1-butanol reacted at essentially the same rate, giving a 1.04:1 ratio of products (**9d:9c**). 2-Propanol reacts more slowly than 1-butanol due to steric hindrance; the selectivity of **2** (**9c:9b** is 25.1:1) is in fact greater than the analogous reactions of **1**. This enhanced selectivity is not predicted by the calculated transition structures for the addition of water to formylketene^{2c} and acetimidoylketene;^{4j} the O₁–H₈ distance (H₈ corresponds to the α -carbon of the alcohols) is slightly shorter in the former (2.695 vs 2.722 Å). Pyrolysis of the precursor **9a** generates 2-methyl-2-propanol, so that competition with this alcohol is not possible. The acetimidoylketene (**2**) is more sensitive to the nucleophilicity of the reagent than is acetylketene (**1**), as 1-butanol reacts 21.2 times faster than does TFE.

Calculations from this laboratory had predicted that alcohols should react much faster with **2** than ketones.^{4j} Heating **9a** in neat cyclohexanone gave only starting material, under conditions where the reaction was observed with other traps. It is reasonable to assume that **2** and 2-methyl-2-propanol were indeed formed from **9a**, but that **2** reacted faster with the alcohol than with cyclohexanone. Efforts are underway to prepare an alternative precursor which will enable a quantitative comparison to be made. Qualitatively, it is clear that even a sterically encumbered alcohol such as 2-methyl-2-propanol is more reactive toward **2** than is cyclohexanone, as was predicted by *ab initio* calculations.^{4j}

Ab Initio Calculations on the Addition of Ammonia to Formylketene. The higher reactivity of **1** toward an amine as compared to an alcohol was not unexpected, because of the greater nucleophilicity of the amine. However, to complement the previous *ab initio* studies,^{2c} the barrier for the addition of ammonia to formylketene (eq 6) was calculated. A transition struc-



ture (**13**) was located at the MP2/6-31G* level, as was a tight molecular complex (**12**) which was a minimum on the potential energy surface (Figure 2). The transition structure **13** is completely planar, as by now expected for a pseudopericyclic reaction.^{2c,d,4j,32} There is no pos-

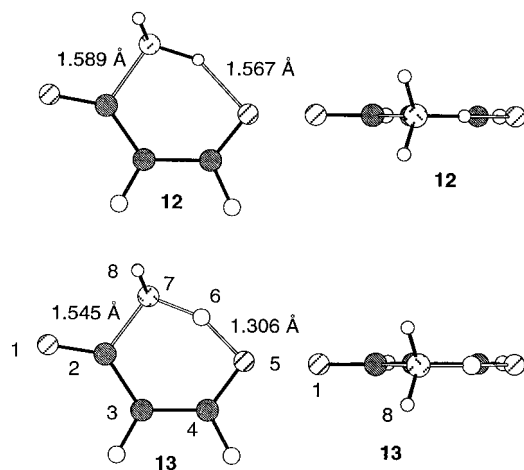


Figure 2. MP2/6-31G*-optimized geometries for the complex between formylketene and ammonia (**12**) and for the transition structure (**13**) for the addition reaction between the two. The two views are rotated 90° from each other. Atom shading is as in Figure 1, with nitrogen cross-hatched.

Table 3. Relative Energies (kcal/mol) and Entropies of Minima and the Transition Structure in the Addition of Ammonia to Formylketene, at the MP2/6-31G*-Optimized Geometry

level of theory	formylketene + NH ₃	12	13	product
RHF/6-31G* ^a	3.4	0.0	2.7	-18.5
MP2/6-31G*	5.2	0.0	0.8	-10.0
MP3/6-31G*	4.7	0.0	0.6	-15.5
MP4(SDQ)/6-31G*	10.2	0.0	1.1	-13.5
MP4(SDQ) + ZPE ^{b,c}	8.2	0.0	-0.9 ^d	-12.6
-TΔS ^{b,e}	-16.4	0.00	0.4	0.3

^a At the RHF/6-31G* geometry ^b From the MP2/6-31G* frequency calculations. ^c Zero-point energy scaled by 0.9646. ^d Note that the calculated energy of **13** is **below** that of the complex **12**. See text for further discussion. ^e At 110° C.

sibility for developing amide resonance between the ketene carbonyl and the ammonia nitrogen. It is also a very late transition structure, with both the C₂-N₇ and O₅-H₆ bonds (Figure 2) much more formed than the corresponding C₂-O₇ and O₅-H₆ bonds in the reaction with water (Figure 1).^{2c}

The relative energies are presented in Table 3.³³ The barrier between the two structures is only 1.1 kcal/mol at the MP4(SDQ)/6-31G**//MP2/6-31G* level. However, this small enthalpic barrier vanishes when the zero-point vibrational energy correction (ZPE) is applied.³⁴ A significant entropic barrier to the cycloaddition remains. The calculated enthalpic barrier for the addition of water (6.3 kcal/mol)^{2c} is significantly higher than that calculated for ammonia. This is consistent with the qualitative trend observed in the reactivity of **1** toward propylamine and 1-butanol. However, the calculated low or nonexistent enthalpic barrier for the cycloaddition of ammonia to formylketene from the complex **12** would predict much

(29) Subjecting this mixture to the pyrolysis conditions would have regenerated the ketene **1** from **9c** and possibly from **11** as well.

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(33) The energy of isolated formylketene and ammonia is higher than that of the transition structure **13**, although the complex **12** is below **13** (without the ZPE correction). Less extreme examples are also found in the addition of water to formylketene^{2c} and in other gas phase reactions. (Chandrasekhar, J.; Smith, S. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1985**, *107*, 154-163.)

greater selectivity for an amine than is observed in solution. One factor which likely contributes to this discrepancy is that in solution the reactivity of 1-propylamine would presumably be reduced by the presence of hydrogen bonds to the amine which would need to be broken during the addition to **1**.

Conclusions. For the first time, acetylketene (**1**) and acetimidoylketene (**2**) have both been shown to react selectively with alcohols in the presence of ketones, as was previously predicted by *ab initio* calculations. Both ketenes show significant steric discrimination toward alcohols, with the reactivity preference MeOH ≈ 1° > 2° > 3°. Both ketenes also react more slowly with TFE than with 1-butanol, indicating that the nucleophilicity of the reagent contributes to the selectivity. Consistent with this and with *ab initio* calculations, 1-propylamine reacts more rapidly with **2** than do alcohols. The agreement between the experimental and calculated selectivities is consistent with the proposed planar, pseudopericyclic transition structures, as is the good agreement between the calculated rate of gas-phase hydration of formylketene and that experimentally observed for acetylketene in water. Furthermore, it is anticipated that the selectivities observed will prove synthetically useful.

Experimental Section

NMR spectra were recorded in CDCl₃ (¹H at 200 or 300 MHz and ¹³C at 50 or 75.47 MHz) using CHCl₃ as an internal standard. For ¹H NMR spectra in which the enol tautomer is also observed, only those peaks from the enol which are not obscured by the keto tautomer are reported. Dioxinone **6** was used as supplied. Trapping reagents and solvents were distilled prior to use. Gas chromatographic (GC) analyses were carried out on a Hewlett-Packard 5890A with a flame ionization detector, using a 30 m × 0.53 mm × 0.88 μm film thickness HP-1 (cross-linked methyl silicone gum) and/or HP-5 (cross-linked phenyl methyl silicone) column. Typical GC conditions were as follows: injector 125 °C, oven temperature 65 °C for 2 min, then 8°/min to 180 °C. The injector temperature was set as low as possible, to avoid decomposition. GC response factors were determined using mixtures of known concentrations.

Authentic materials were prepared by either preparative FP or solution pyrolysis. In either case, the crude pyrolysate was purified by column chromatography on silica gel. ¹H and ¹³C NMR spectra were consistent with the proposed structures. Elemental analyses were performed by Desert Analytics and were satisfactory for all compounds except **10** and **11**, which apparently underwent hydrolysis.

Flash Pyrolysis. A mixture of **6** and two trapping agents was slowly dripped through an unpacked vertical seasoned quartz pyrolysis tube at approximately 400 °C and 0.1 Torr (mechanical pump) into a liquid nitrogen cooled trap.³⁵ No reaction was observed without heating. The trap was allowed to warm to room temperature under an inert atmosphere. The products were removed from the trap with a small amount of ether and analyzed by GC, with correction for response factors. The reported results are the average of three separate experiments. In a given competition, the selection of the 1° alcohol (1-propanol, 1-butanol, or 1-pentanol) and/or aldehyde (hexanal or heptanal) was made so that there was no overlap of the product peaks in the GC analysis. The product enones **3** are in equilibrium with the β-keto esters **4** and thus cannot be analyzed individually; however peaks corresponding to both were observed in the GC trace and the uncorrected ratios are

(34) No great significance is necessarily attached to this rather strange result. It may reflect the limitations of single-point energy calculations for low barrier reactions.

(35) This technique has been described as "flash pyrolysis at moderate vacuum".²⁵

reported below. For the reported results of the competition reactions, the integrations of the two tautomers were combined.

For preparative FP, a mixture of **6** and a single trapping agent were mixed and pyrolyzed as above. The product acetone was removed by rotary evaporation, and the residue was subjected to flash chromatography on silica gel, using hexane/ether/ethyl acetate (65:30:5) as the eluent.

Solution Pyrolyses. The precursor (**6** or **9a**) and reagent(s) were placed in a thick-walled glass tube. This was filled with sufficient toluene so that there was minimal dead space when the tube was flushed with nitrogen and sealed with a Teflon "Ace-thread" plug.³⁶ The tube was then heated in an oil bath, behind a blast shield for the time and at the temperature reported in Table 2. (Caution: There is a risk of explosion when heating closed glass containers.) The tube was cooled to room temperature, and the contents were directly injected onto the GC for analysis. For preparative solution pyrolyses, the excess solvent and/or trapping reagents were removed by rotary evaporation. The residue was then subjected to flash column chromatography on silica gel, as above. For compounds **9** and **11**, hexane/ethyl acetate (95:5) was used as the eluent.

Conversion of 4d and 10 to 9c and 11. An ether solution was prepared containing 0.0263 g (1.665×10^{-4} mol) of **4d** and 0.0367 g (2.566×10^{-4} mol) of **10**. The initial molar ratio was 0.649:1. Then 0.1103 g (1.869×10^{-3} mol) of 1-propylamine was added and **9c** and **11** were formed in a 0.653:1 molar ratio as determined by GC.

3-Oxo-2-butenic acid, 1-methylethyl ester (4b): ¹H NMR δ 1.15 (d, 6H, $J = 6.3$ Hz), 2.18 (s, 3H), 3.33 (s, 2H), 4.97 (heptet, 1H, $J = 6.3$ Hz); ¹³C NMR δ 21.5, 29.9, 50.2, 68.7, 166.5, 200.6. **Enol tautomer 3b:** ¹H NMR δ 1.15 (d, 6H, $J = 6.3$ Hz), 1.85 (s, 3H), 4.85 (s, 1H), 4.95 (heptet, 1H, $J = 6.3$ Hz), 12.09 (s, 1H); ¹³C NMR δ 21.0, 21.7, 67.1, 90.0, 172.1, 175.0. GC peak ratio 1:2.9; **4b:3b** 10.0:1 by ¹H NMR.

3-Oxo-2-butenic acid, pentyl ester (4c): ¹H NMR δ 0.80 (t, 3H, $J = 6.7$ Hz), 1.22 (m, 4H), 1.53 (m, 2H), 2.16 (s, 3H), 3.35 (s, 2H), 4.03 (t, 2H, $J = 6.7$ Hz); ¹³C NMR δ 13.7, 22.0, 27.7, 27.9, 29.9, 49.9, 65.3, 167.0, 200.4. **Enol tautomer 3c:** ¹H NMR δ 1.84 (s, 3H), 4.01 (t, 1H, $J = 6.7$ Hz), 4.88 (s, 1H), 12.01 (s, 1H); ¹³C NMR δ 21.0, 63.0, 89.5, 172.5, 175.2. GC peak ratio 1:1.9; **4b:3b** 10.2:1 by ¹H NMR.

3-Oxo-2-butenic acid, butyl ester (4d): ¹H NMR δ 0.89 (t, $J = 7.3$ Hz, 3H), 1.33 (m, 2H), 1.60 (m, 2H), 2.24 (s, 3H), 3.42 (s, 2H), 4.09 (t, $J = 6.7$ Hz, 2H); ¹³C NMR δ 13.60, 18.98, 30.10, 30.42, 50.08, 65.23, 167.16, 200.63. **Enol tautomer 3d:** ¹H NMR δ 1.92 (s, 3H), 4.08 (t, 1H, $J = 6.7$ Hz), 4.94 (s, 1H), 12.08 (s, 1H); ¹³C NMR δ 21.1, 30.6, 63.7, 89.7, 172.5, 175.2. GC peak ratio 1:1.9; **4b:3b** 11.4:1 by ¹H NMR.

3-Oxo-2-butenic acid, propyl ester (4e): ¹H NMR δ 0.82 (t, 3H, $J = 7.3$ Hz), 1.55 (hexet, 2H, $J = 7.3$ Hz), 2.14 (s, 3H), 3.34 (s, 2H), 3.97 (t, 2H, $J = 6.7$ Hz); ¹³C NMR δ 10.0, 21.6, 29.8, 49.8, 67.0, 166.6, 200.4. **Enol tautomer 3e:** ¹H NMR δ 0.82 (t, 3H, $J = 7.3$ Hz), 1.55 (hexet, 2H, $J = 7.3$ Hz), 1.82 (s, 3H), 3.95 (t, 2H, $J = 6.7$ Hz), 4.86 (s, 1H), 11.98 (s, 1H); ¹³C NMR δ 10.0, 20.9, 21.8, 65.2, 89.5, 172.5, 175.2. GC peak ratio 1:1.9; **4b:3b** 8.8:1 by ¹H NMR.

3-Oxo-2-butenic acid, 2,2,2-trifluoroethyl ester (4g): ¹H NMR δ 2.24 (s, 3H), 3.54 (s, 2H), 4.49 (q, 2H, $J = 8.4$ Hz); ¹³C NMR δ 30.0, 49.2, 60.7 (q, $J = 36.9$ Hz), 122.7 (q, $J = 277.1$ Hz), 165.5, 199.2. **Enol tautomer 3g:** ¹H NMR δ 1.96 (s, 3H), 4.47 (q, 2H, $J = 8.4$ Hz), 5.06 (s, 1H), 11.58 (s, 1H); ¹³C NMR δ 21.3, 59.6 (q, $J = 36.6$ Hz), 88.5, 123.2 (q, $J = 277.1$ Hz), 170.7, 177.7. GC peak ratio 1:1.4; **4b:3b** 8.9:1 by ¹H NMR.

4-Methyl-1,5-dioaspiro[5.5]undec-3-en-2-one (8a). Excess cyclohexanone was removed by high-vacuum distillation prior to column chromatography: ¹H NMR δ 1.46 (m, 2H), 1.62 (m, 4H), 1.96 (a sharp singlet overlapping with a small multiplet, 7H), 5.17 (s, 1H); ¹³C NMR δ 20.0, 22.2, 24.6, 33.7, 94.0, 107.0, 161.2, 168.3.

2-Hexyl-6-methyl-1,3-dioxin-4-one (8b). Excess heptanal was removed by high-vacuum distillation prior to column chromatography: ¹H NMR δ 0.84 (t, 3H, $J = 6.7$ Hz), 1.26 (br s, 6H), 1.46 (m, 2H), 1.85 (m, 2H), 1.98 (s, 3H), 5.23 (s, 1H), 5.39 (t, 1H, $J = 5.0$ Hz); ¹³C NMR δ 13.9, 19.3, 22.4, 22.7, 28.7, 31.5, 32.9, 95.8, 100.9, 162.8, 172.1.

3-(Propylamino)-2-butenic acid, 1,1-dimethylethyl ester (9a): 1,1-Dimethylethyl 3-oxopropionate (2.02 g, 0.013 m) and 1-propylamine (0.76 g, 0.013 m) was absorbed on silica gel (2 g) in an open beaker and irradiated in a commercial microwave oven for 2 min.³¹ The product was removed from the silica gel by filtering, using hexane/ethyl acetate (90:10) as the wash solvent. After concentration, the product was obtained by flash chromatography (hexane/ethyl acetate (95:5) on silica gel): ¹H NMR δ 0.93 (t, $J = 8.6$ Hz, 3H), 1.44 (s, 9H), 1.54 (m, 2H), 1.86 (s, 3H), 3.11 (pseudo q, 2H), 4.43 (s, 1H) 8.46 (br s, 1H); ¹³C NMR 11.43, 19.34, 23.78, 28.67, 44.74, 51.51, 83.38, 161.27, 172.00. A small amount of the imine tautomer was also observed in the spectra: ¹H NMR δ 2.20 (s, 3H), 4.54 (s, 2H); ¹³C NMR 27.9, 30.5, 82.0. **9a:imine tautomer** 25:1 by ¹H NMR.

3-(Propylamino)-2-butenic acid, 1-methylethyl ester (9b): ¹H NMR δ 0.94 (t, $J = 7.4$ Hz, 3H), 1.19 (d, $J = 6.2$ Hz, 6H), 1.54 (m, 2H), 1.86 (s, 3H), 3.13 (pseudo q, 2H), 4.37 (s, 1H), 4.95 (septet, $J = 6.2$ Hz, 1H), 8.55 (br s, 1H); ¹³C NMR δ 11.36, 19.34, 22.22, 28.64, 44.71, 64.90, 82.19, 161.81, 170.23.

3-(Propylamino)-2-butenic acid, butyl ester (9c): ¹H NMR δ 0.89 (m, 6H), 1.32 (m, 2H), 1.55 (m, 4H), 1.85 (s, 3H), 3.10 (pseudo q, 2H), 4.37 (s, 1H), 8.52 (br s, 1H); ¹³C NMR δ 11.26, 13.68, 19.15, 19.26, 23.54, 31.04, 44.61, 62.11, 81.61, 161.81, 170.67.

3-(Propylamino)-2-butenic acid, methyl ester (9d): ¹H NMR δ 0.93 (t, $J = 7.4$ Hz, 3H), 1.54 (m, 2H), 1.88 (s, 3H), 3.13 (pseudo q, 2H), 3.58 (s, 3H), 4.39 (s, 1H), 8.53 (br s, 1H); ¹³C NMR δ 11.31, 19.33, 23.60, 44.70, 49.82, 81.29, 162.07, 170.93.

3-(Propylamino)-2-butenic acid, 2,2,2-trifluoroethyl ester (9e): ¹H NMR δ 0.95 (t, $J = 7.2$ Hz, 3H), 1.59 (m, 2H), 1.92 (s, 3H), 3.17 (pseudo q, 2H), 4.40 (q, $J = 8.7$ Hz, 2H), 4.48 (s, 1H), 8.49 (br s, 1H); ¹³C NMR δ 11.28, 19.42, 23.49, 44.86, 58.56 (q, $J = 10.4$ Hz), 80.00, 123.63 (q, $J = 138.8$ Hz), 163.93, 168.08.

3-Oxo-2-butenic acid, propylamide (10): ¹H NMR δ 0.89 (t, 3H, $J = 7.36$ Hz), 1.47 (hexet, 2H, $J = 7.14$ Hz), 2.23 (s, 3H), 3.19 (q, 2H, $J = 5.9$ Hz), 3.38 (s, 2H), 7.04 (br s, 1H); ¹³C NMR δ 11.3, 22.6, 31.0, 41.2, 49.5, 165.4, 204.3.

3-(Propylamino)-2-butenic acid, propylamide (11): ¹H NMR δ 0.90 (m, 6H), 1.50 (hexet, 4H, $J = 7.36$ Hz), 1.83 (s, 3H), 3.11 (m, 4H), 4.21 (s, 1H), 4.82 (br s, 1H), 9.04 (br s, 1H); ¹³C NMR δ 11.3, 19.2, 23.2, 23.7, 40.4, 44.5, 62.3, 84.2, 158.3, 170.9.

Ab Initio Calculations. The *ab initio* molecular orbital calculations were carried out using Gaussian 92.³⁷ Geometry optimizations were performed at the MP2(FC)/6-31G* level. MP2 optimizations give reasonable agreement with MCSCF-geometries for orbital symmetry allowed pericyclic reactions.³⁸ Frequency calculations verified the identity of each stationary point as a minimum or transition state. Full geometries and vibrational frequencies are available in the Supporting Information. Single-point energies of each structure were obtained at the MP4(FC, SDQ)/6-31G* level. The zero-point vibrational energy (ZPE) corrections were obtained by scaling the MP2/

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(36) Inconsistent results were obtained with larger dead space, presumably due to selective vaporization of the more volatile of the traps.

6-31G* ZPE by 0.9646, as recommended by Pople *et al.*¹⁹ Absolute energies are reported in the supporting information; relative energies are reported in Table 3.

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Supporting Information Available: Optimized geometries, vibrational frequencies, and a table of absolute energies for all MP2/6-31G*-optimized structures are available (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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