

Amination of Ketene: A Theoretical Study

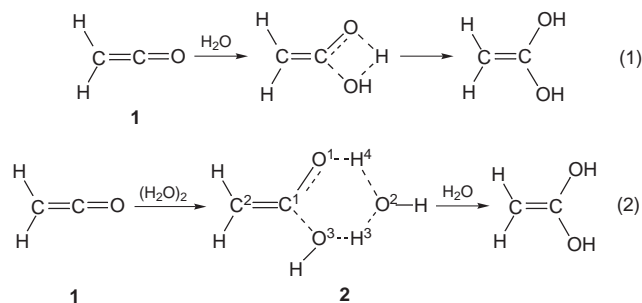
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Abstract: The reactions of NH_3 , $(\text{NH}_3)_2$, and $(\text{H}_3\text{N}\cdot\text{H}_2\text{O})$ with ketene have been studied by *ab initio* calculations. Attack by the dimer $(\text{NH}_3)_2$ or by $(\text{H}_3\text{N}\cdot\text{H}_2\text{O})$ through six-membered cyclic transition states is found to be favored, with a preference of 12.8 kcal/mol for initial addition of $(\text{NH}_3)_2$ to the C=O bond of the ketene giving the enol amide, as compared to initial addition to the C=C bond to give the more stable amide directly. These results are in contrast to previous theoretical studies for the reaction of monomeric NH_3 with ketene, in which direct addition to the C=C bond was reported to be favored, and for the reaction of ketene with $(\text{H}_2\text{O})_2$, in which addition to the C=O bond is calculated to be only 1.9 kcal/mol more favorable than addition to the C=C bond. The barrier via $\mathbf{10}_{\text{ts}}$ for the NH_3 -catalyzed rearrangement of the enol amide/ NH_3 complex $\mathbf{6}$ to the amide is 16.5 kcal/mol above that of $\mathbf{6}$, consistent with the experimental observation of an intermediate in ketene amination, and the barrier for reversion of $\mathbf{6}$ to the reactant complex $\mathbf{5a}$ is 4.0 kcal/mol lower than that for amide formation via $\mathbf{10}_{\text{ts}}$, suggesting the initial amination may be reversible. These results demonstrate that previous theoretical calculations of ketene amination used inadequate levels of theory. The structure of the zwitterion $\text{CH}_2=\text{C}(\text{O}^-)\text{NMe}_3^+$ ($\mathbf{14}$) from reaction of ketene with NMe_3 has also been calculated, and in the gas phase this reaction is calculated to be exothermic by only 0.6 kcal/mol.

The hydration of ketene and the microscopic reverse of the dehydration of acetic acid are prototypical reactions of these species that have been the subject of intensive theoretical¹ and experimental study.^{1a,2} After prolonged controversy there is now agreement that in solution the hydration is driven by in-plane nucleophilic attack by H_2O on the carbonyl carbon of the ketene leading to a carboxylic acid enol or enolate, with the participation of other H_2O molecules in hydrogen bonding to the carbonyl oxygen and the attacking H_2O molecule (eqs 1 and 2). The most thorough calculations^{1c} of transition states involving ketene and one or two H_2O molecules indicate that structure $\mathbf{2}$ involving addition of $(\text{H}_2\text{O})_2$ to the carbonyl oxygen is lowest in energy (eq 2), but that the structure involving addition of $(\text{H}_2\text{O})_2$ to the C=C bond with proton transfer perpendicular to the ketene plane to C_β is only 1.9 kcal/mol higher in energy.



The reaction of ketenes with amines has long been of preparative use, but early kinetic^{3a,b} and theoretical^{3b,c} studies of this process were interpreted as involving direct addition to the C=C bond, and have been subjected to detailed criticism.⁴ The reactions of ketenes with chiral amines have been extensively studied,⁵ and the high stereoselectivities that have sometimes been observed have been explained^{5a} as arising during the proton transfer to the β -carbon from nitrogen in a zwitterion formed by attack of the amine on the carbonyl carbon of the ketene. More recent kinetic studies have utilized laser flash photolysis generation of ketenes and UV^{6a,b} or IR^{6b,c} detection for reactions in H_2O ^{6a} or CH_3CN ,^{6b,c} and have been interpreted by a mechanism in which the amine attacks in the ketene plane on the carbonyl carbon giving an intermediate enol

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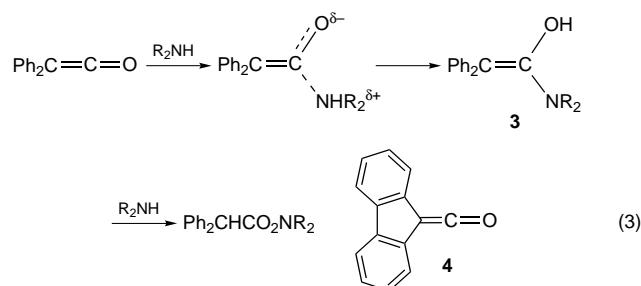
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amide (or zwitterion) which then isomerizes to the amide (eq 3). An enol amide that subsequently rearranged to the amide was observed long ago by Quinkert and co-workers^{6d,e} by photolysis of a 2,4-cyclohexadienone at $-189\text{ }^{\circ}\text{C}$ in the presence of cyclohexylamine, in which a UV absorption maximum at 465 nm was attributed to the enol amide, which on warming formed the amide. More recently an enol amide has been directly observed by ^1H NMR in the reaction of bis(2,4,6-triisopropylphenyl)acetic acid with Me_2NH .^{6f,g} Formation of a species identified as a zwitterion or enol amide analogous to **3** from $\text{PhCH}=\text{C}=\text{O}$ and Et_2NH concomitant with the disappearance of the ketene was observed by IR,^{6c} while fluorenylidene ketene (**4**) also reacted with amines to give intermediates identified as zwitterions observed by both IR and UV detection.^{6b}



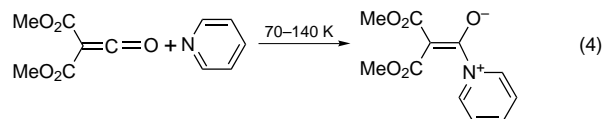
In a competition study the reaction of a dienyketene with a 1/5 mixture of *n*-BuNH₂ and *n*-BuOH gave amide and ester products in a ratio of 9.5, suggesting a 50-fold greater reactivity of the amine.^{6h,i} In aqueous solution the observed rate constant for $\text{Ph}_2\text{C}=\text{C}=\text{O}$ hydration is 275 s^{-1} ,^{6a} and this divided by $[\text{H}_2\text{O}]$ gives a formal second-order hydration rate constant of $4.95\text{ M}^{-1}\text{ s}^{-1}$. The second-order rate constant for amination of $\text{Ph}_2\text{C}=\text{C}=\text{O}$ by *n*-BuNH₂ in H₂O is $3.52 \times 10^5\text{ M}^{-1}\text{ s}^{-1}$,^{6a} and this leads to an estimated rate ratio of $k(n\text{-BuNH}_2)/k(\text{H}_2\text{O}) = 7.1 \times 10^4$ for $\text{Ph}_2\text{C}=\text{C}=\text{O}$ in H₂O.

The reaction of ketenes with tertiary amines leads to zwitterions (eq 4), and the IR spectra of these have been observed in matrixes at low temperatures,^{7a,b} and by UV and IR with use of time-resolved laser flash photolysis.^{6b,7c} The IR spectra of these zwitterions were calculated by using the BLYP/6-31G* method.^{7a} Similar zwitterions have been implicated in numerous reactions of ketenes catalyzed by tertiary amines,^{1a} and the X-ray structure of such a species has been reported, and the structure calculated by AM1.^{7d} Zwitterionic structures have also been observed by IR in ketene reactions

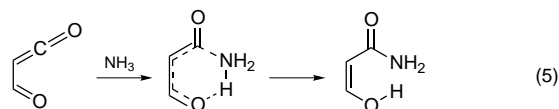
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with imines^{8a,b} and imidazoles,^{8b} and have been examined by calculations.^{8c,d}



A recent theoretical study of the reaction of NH₃ with formylketene (eq 5) revealed formation of an initial complex, which gave a cyclic transition state with no enthalpic barrier at the highest level of calculation (MP4(sdq)/6-31G*+ZPVE//MP2/6-31G*^{9j}). However, there was still a significant entropic barrier ($T\Delta S = -16.4\text{ kcal/mol}$). Competition experiments indicated that *n*-BuNH₂ was only 2.3 times more reactive than *n*-BuOH toward $\text{CH}_3\text{COCH}=\text{C}=\text{O}$ in this reaction.^{6j}



The amination of ketenes promises to be the subject of increasing attention in coming years, and we have undertaken a synthetic and mechanistic study of ketene and bisketene reactions with amines, comparable to our previous studies of hydration and alcohol additions.^{2a–d} Reported here is an ab initio theoretical study of the reaction of ketene with NH₃ and NMe₃.

Results

Stationary structures were calculated with Gaussian 94^{9a} for the reaction of $\text{CH}_2=\text{C}=\text{O}$ with both NH₃ and the dimer (NH₃)₂, adding to the C=C and to the C=O bonds. Structures located at the HF/6-31G* and MP2/6-31G* levels included prereaction complexes **5**_{cmplx}, transition structures **5**_{ts}, enol amide complex with NH₃ **6**, enol amide **7**, and amide **8**. For NH₃ and ketene only a single complex **5b**_{cmplx} was found, while for (NH₃)₂ there are two distinct complexes **5a**_{cmplx} and **5c**_{cmplx}, involving association with the C=O and C=C bonds, respectively. Transition structure **9** for the uncatalyzed conversion of **7** to **8** was also calculated, as were the complex and transition structure **10** for the NH₃-catalyzed conversion of **7** to **8**. For addition of the complex H₃N---H₂O to the C=O bond of $\text{CH}_2=\text{C}=\text{O}$ the structures of the complex and transition structure **11** were calculated, as well as that of the resulting complex **12** of the enol amide with H₂O.

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Table 1. Calculated Relative Energies (kcal/mol) of Stationary Points for Amination of Ketene

process	level ^a	reactant	complex	TS	products	
1 + (NH ₃) ₂ (C=O addition)	HF/6-31G*	1 + (NH ₃) ₂ 0.00	5a _{cmplx} -3.71	5a _{ts} 11.77	6 -9.31	7 + NH ₃ -4.07
	MP2/6-31G*	0.00	-5.21	0.36	-12.10	-2.97
	MP2/6-31+G**	0.00	-4.70	1.73		-5.70
	MP2/6-31+G** ^b	0.00		2.11		-5.64
	MP3/6-31G*	0.00	-5.18	2.42		-7.18
	MP4(sdtq)/6-31G*	0.00	-5.28	1.05		-0.90
1 + NH ₃ (C=O addition)	HF/6-31G*	1 + NH ₃ 0.00	5b _{cmplx} -2.14	5b _{ts} 45.90		7 + NH ₃ -5.80
	MP2/6-31G*	0.00	-3.04	30.03		-5.90
	MP2/6-31+G**	0.00	-2.55	28.46		-7.69
	MP3/6-31G*	0.00	-3.02	31.33		-9.84
	MP4(sdtq)/6-31G*	0.00	-3.05	32.50		-3.68
1 + H ₃ N·H ₂ O	MP2/6-31G*	1 + (H ₃ N·H ₂ O) 0.00	11 _{cmplx} -2.61	11 _{ts} 2.86	12 -8.23	7 + H ₂ O 0.27
1 + (NH ₃) ₂ (C=C addition)	HF/6-31G*	1 + (NH ₃) ₂ 0.00	5c _{cmplx} -2.88	5c _{ts} 31.36		8 + NH ₃ -35.85
	MP2/6-31G*	0.00	-4.66	13.14		-34.67
	MP2/6-31+G**	0.00	-4.17	13.45		-33.21
	MP3/6-31G*	0.00	-4.22	16.70		-35.87
	MP4(sdtq)/6-31G*	0.00	-4.57	16.89		-32.92
1 + NH ₃ C=C addition	HF/6-31G*	1 + NH ₃ 0.00	5b _{cmplx} -2.14	5d _{ts} 57.14		8 -37.58
	MP2/6-31G*	0.00	-3.04	39.80		-37.60
	MP2/6-31+G**	0.00	-2.55	39.61		-35.20
	MP3/6-31G*	0.00	-3.02	43.37		-38.53
	MP4(sdtq)/6-31G*	0.00	-3.05	41.98		-35.70
enol → amide (NH ₃ catalyzed)	HF/6-31G*	7 + NH ₃ 0.00	10 _{cmplx} -7.14	10 _{ts} 21.90		8 + NH ₃ -31.78
	MP2/6-31G*	0.00	-9.91	7.33		-31.70
	MP2/6-31+G**	0.00	-8.69	9.34		-27.51
	MP3/6-31G*	0.00	-9.12	13.21		-28.69
	MP4(sdtq)/6-31G*	0.00	-9.49	9.20		-32.02
enol → amide (uncatalyzed)	HF/6-31G*	7 0.00		9 50.21		8 -31.78
	MP2/6-31G*	0.00		39.07		-31.70
	MP2/6-31+G**	0.00		38.91		-27.51
	MP3/6-31G*	0.00		44.46		-28.69
	MP4(sdtq)/6-31G*	0.00		39.78		-32.02
1 + NMe ₃	HF/6-31+G*	1 + N(CH ₃) ₃ 0.00	13 _{cmplx} -1.66	13 _{ts} 15.69		14 16.28
	MP2/6-31+G*	0.00				-0.85
	MP2/6-31+G* ^c	0.00	-4.56	2.71		-2.05

^a HF/6-31G* (including 0.9135 ZPVE) energies using HF/6-31G* geometries; all MP2, MP3, and MP4 energies using MP2/6-31G* optimized geometry and 0.9646 MP2/6-31G* ZPVE except as noted. ^b MP2/6-31+G**/MP2/6-31+G** with 0.9135 HF/6-31G* ZPVE. ^c MP2/6-31+G**/HF/6-31+G* with 0.9135 ZPVE (HF/6-31+G*).

Energies (including zero-point vibrational energy, ZPVE) were calculated at the HF/6-31G*/HF/6-31G* level, and for the MP2/6-31G* geometry at the MP2, MP3, and MP4(sdtq) levels. These levels were chosen for direct comparison to similar calculations for the addition of H₂O and (H₂O)₂ to ketene.^{1c} To examine the possible polar nature of these species calculations at the MP2/6-31+G**/MP2/6-31G* level were also carried out, with the diffuse (+) and hydrogen polarization function.^{9b} For the key structure **5a**_{ts}, calculations were also carried out at the MP2/6-31+G**/MP2/6-31+G** level. At this level, the (NH₃)₂ dimer was no longer cyclic but was linear.^{9c,d} As expected on the basis of previous experience,^{9f} the MP2/6-31G* barriers were significantly lower than those at the HF/6-31G* level, while the differences in the energy changes to form the complexes and products were much less. As discussed below, the energies at the various MP levels do not appear strongly dependent on the particular level, lending confidence that even higher levels of theory will not change the essential conclusions. Entropies and free energies were also calculated, as described by Jorgensen et al.^{9e} The calculated

relative energies are given in Table 1, and complete energy details, dipole moments, and geometries are given in Tables 2–6 (Supporting Information). For comparative purposes the transition structure **2** for addition of (H₂O)₂ to the C=O bond of ketene at the HF/6-31G* level was recalculated^{1c} and is shown in Figure 1 together with the structures for **5a**_{ts}, **6**, **10**_{ts}, and **11**.

Dimerization of 2 NH₃ molecules to form (NH₃)₂ is calculated to be exothermic by 2.93 kcal/mol,^{9c} while formation of the complex H₃N·H₂O from NH₃ + H₂O is exothermic by 6.17 kcal/mol. For addition of NH₃ to ketene by the H₃N·H₂O complex the hydrogen bond between nitrogen and the H₂O proton must be broken. The complex H₂O·H₃N with hydrogen bonding of the NH₃ proton to oxygen is not an energy minimum structure, but a calculated structure for the latter using a fixed O---H---N bond angle of 180° has an energy 3.52 kcal/mol higher than that of the former complex.

For examination of zwitterions formed from ketene reactions with tertiary amines the structures and energies of the products from the reaction of CH₂=C=O with NMe₃ were also calcu-

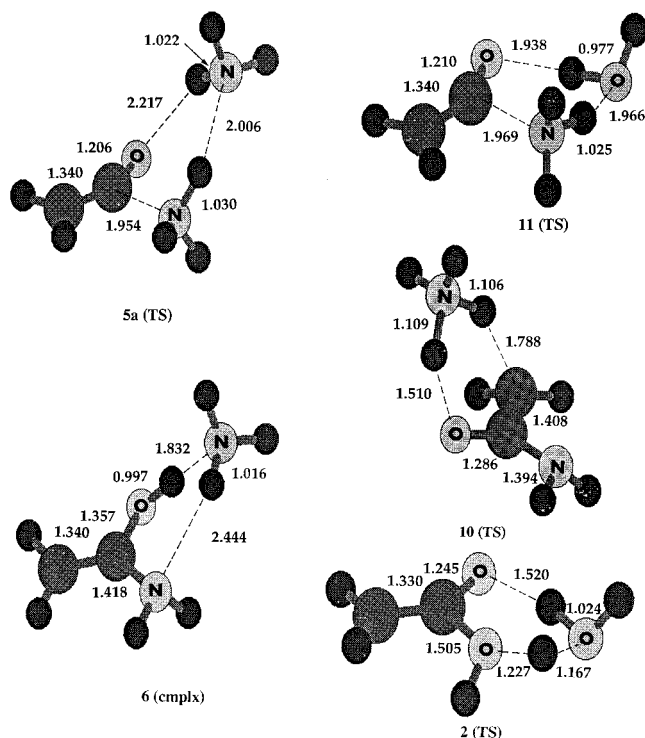
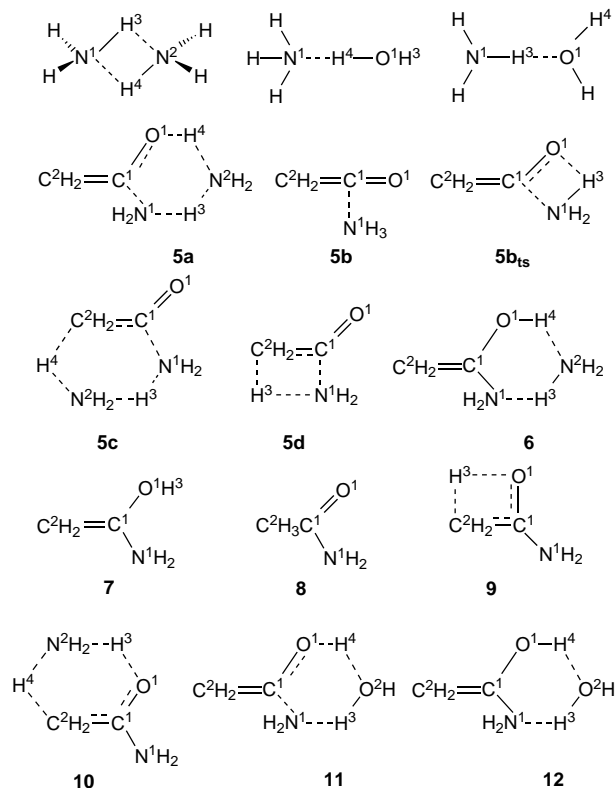


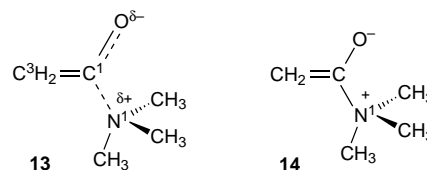
Figure 1. Calculated transition structures for addition of (NH₃)₂ (**5a**) and (H₃N·H₂O) (**11**) to C=O bonds of ketene, the NH₃ complex with CH₂=C(OH)NH₂ (**6**), the transition structure for NH₃-catalyzed isomerization of CH₂=C(OH)NH₂ to CH₃CONH₂ (**10**), and the HF/6-31G* transition structure for (H₂O)₂ addition to the C=O bond of ketene (**2**). Bond distances in Å (MP2/6-31G* except HF/6-31G* for **2**_{ts}).

Chart 1



lated. For these zwitterionic structures a diffuse function was added to the basis set, and a prereaction complex **13**_{cmplx}, a transition state **13**_{ts}, and a zwitterionic adduct **14** were calculated at the HF/6-31+G**//HF/6-31+G* level. Single-point energies

were also calculated at the MP2/6-31+G**//HF/6-31+G* level, and gave a barrier of 2.7 kcal/mol for forming **13**_{ts}. At the MP2/6-31+G* level no barrier or transition state could be found for the formation of **14**. For the addition of NH₃ to ketene only enol amide and no energy minimum zwitterionic structures could be found.



In previous studies of ketene reactions energies calculated at the MP2/6-31G* level have given good quantitative agreement with reaction barriers and overall energy changes and are better than HF/6-31G* energies.^{1c,9f} In the present study the transition state energies calculated at the MP2/6-31G* level are significantly lower than those calculated at HF/6-31G**//HF/6-31G*, but the energy changes calculated at various levels for the MP2/6-31G* geometries are quite similar. Thus for the transition states **5a–d** and **10** the barriers relative to the reactants vary by average values of $\pm(1.0$ to $3.4)$ kcal/mol. Similarly the MP2/6-31+G**//MP2/6-31+G** and MP2/6-31G**//MP2/6-31G* barriers to form **5a**_{ts} were very similar, indicating diffuse and polarization hydrogen functions do not significantly affect the results. A consistent set of energies was obtained at the MP2/6-31G**//MP2/6-31G* level and so the discussion below will refer to calculations at this level, unless otherwise noted.

Discussion

The results show that the most favorable processes for ketene amination involve initial attack at the C=O bond of ketene by either (NH₃)₂ or (H₃N·H₂O). At the MP2/6-31G* level the initial complexes **5a** or **11** are 5.2 and 2.6 kcal/mol, respectively, more stable than the reactants, while for the separated reagents 2 NH₃ and NH₃ + H₂O formation of these complexes is exothermic by 8.1 and 8.8 kcal/mol, respectively (Figures 2 and 3). The barriers for conversion of these complexes are 5.6 and 5.5 kcal/mol to give the hydrogen bonded enol amide complexes with NH₃ (**6**) or H₂O (**12**) that are 12.1 and 8.2 kcal/mol, respectively, more stable than the reactants. Dissociation of the complexes to enol amide **7** and NH₃ or H₂O is endothermic by 9.1 and 8.5 kcal/mol, respectively, while isomerization of **7** to the amide **8** is exothermic by 35.2 kcal/mol.

By contrast the complex **5c** of (NH₃)₂ with the C=C bond of ketene is 4.7 kcal/mol more stable than the reactants, but there is a barrier of 17.8 kcal/mol via **5c**_{ts} for conversion of this to the product amide, and this barrier is 12.8 kcal/mol greater than that via **5a**_{ts} for the addition to the C=O bond to give the enol amide complex **6**. However, there is a further barrier via **10**_{ts} for conversion of **6** to the amide, and the 8.8 kcal/mol lower energy of **10**_{ts} compared to **5c**_{ts} measures the preference for amide formation by C=O compared to C=C addition. Thus there is a strong kinetic preference for amination to proceed via a complexed intermediate enol amide **6** or **12**, even though direct formation of the amide **8** is thermodynamically much more favorable. This kinetic preference may arise from hydrogen bonding to the ketenyl oxygen by the assisting NH₃ or H₂O molecules leading to the enol in the transition states **5a** and **11**, respectively. This calculated kinetic preference for enol amide formation is in agreement with the experimental results

cited above, in which transient enol amides (or zwitterions) have been observed in ketene amination by both UV^{6b,d,e} and IR^{6b,c} detection.

Addition of monomeric NH₃ is much less favorable than reaction with either (NH₃)₂ or H₃N·H₂O. There is only one complex **5b** of NH₃ with ketene, but the barriers for conversion of this to amide or enol amide are 42.8 and 33.1 kcal/mol, respectively.

By comparison, in the hydration of ketene the reaction of dimeric species (H₂O)₂ is also strongly favored, but there is a preference of only 1.9 kcal/mol for addition to the C=O as compared to the C=C bond, and the product CH₃CO₂H is 34.9 kcal/mol more stable than CH₂=C(OH)₂.^{1c}

The energetics of the reaction of (NH₃)₂ and of (H₃N·H₂O) with ketene are rather similar, with complexes 5.2 and 2.6 kcal/mol below the reactants, and with barriers of 5.6 and 5.5 kcal/mol for conversion of the complexes to the enol amide complexes **6** and **12**, respectively. The reported kinetics of amination of Ph₂C=C=O in H₂O show only a first-order dependence on [amine],^{6a} but the absence of a dependence on [amine]² in H₂O may be understood as resulting from strong hydrogen bonding of H₂O to the amine. Thus based on the calculated energies of the individual species the reaction of eq 6 is exothermic by 4.3 kcal/mol, and particularly in completely aqueous medium no detectable amine dimer will be present. Assistance by H₂O in the amination transition structures analogous to **11** could also occur.



Another interesting feature of the experimental studies of amination in H₂O is the very small observed difference in the rate constants for reaction of different amines with Ph₂C=C=O.^{6a} Thus for a series of simple primary amines in which the pK_b values of the amines varied by 5.3 log units the relative reactivities changed by only a factor of 5.6. This also arises because of the strong tendency for the amines to hydrogen bond to H₂O (eq 6), as this hydrogen bond must be broken in order for the amine to act as a nucleophile toward the ketene. McClelland et al., have pointed out the importance of amine hydration in the reactivity of amines with carbocations,^{10a} and conversion of the complex HOH---NH₃ to H₂NH---OH₂ so the nitrogen may act as a nucleophile is endothermic by 3.5 kcal/mol. The strength of the hydrogen bonds would increase with increasing basicity of the amines, and as a result the net reactivities are very similar.

A further striking aspect of amination reactivity is the comparison of the rate constants for reaction of Ph₂C=C=O with *n*-BuNH₂ in H₂O^{6a} and in CH₃CN,^{6c} which are 3.52 × 10⁵ and 1.1 × 10⁷ M⁻¹ s⁻¹, respectively. Thus the reaction is 31 times faster in CH₃CN, although it might have been supposed that this reaction forming a rather polar transition state would be accelerated by the greater polarity of the H₂O solvent, as has been observed for ketene hydration in H₂O/CH₃CN mixtures.^{2a-c} Evidently strong hydrogen bonding of *n*-BuNH₂ to H₂O diminishes the nucleophilicity of the amine, and the

reaction in CH₃CN, which can hydrogen bond only to the amine protons, is faster.

Experimentally reactions of amines with ketenes in CH₃CN have also been found to follow a first-order dependence on [amine],^{6b,c} as has the aminolysis of phenyl dithioacetates in CH₃CN.^{10b} However, studies of association processes of amines in CH₃CN by IR^{10c} and ¹H NMR^{10d} suggest that while the nitrogen of CH₃CN forms hydrogen bonds with amines, these interactions may not be so strong as to break up all amine dimers. In studies of amination of ketenes by 3-chloroaniline in diethyl ether kinetic terms in both [ArNH₂] and [ArNH₂]² were found,^{3a,b} and in weakly hydrogen bonding nonprotic solvents such second-order terms in [amine] are not unexpected. However, a rate dependence on [amine]² does not necessarily imply reaction involving an amine dimer, as the aminolysis of esters has long been known to involve two molecules of the amine, one acting as a nucleophile and the second as a general base.^{10e} In ketene amination such a process could involve initial formation of an enol amide (**6**, **7**, or **12**) which is then converted to the amide through a transition state such as **10**. The first-order dependence on [amine] in ketene addition in CH₃CN could involve assistance by the solvent.

The favored calculated pathway for amination of ketene by (NH₃)₂ thus involves first the formation of the complex **5a** in which the nucleophilic N is in the ketene plane with a C¹N¹ bond length of 2.961 Å, while the second NH₃ molecule is above the plane, with N²H³ and O¹H⁴ bond lengths of 2.201 and 2.308 Å, respectively. In the transition state these shorten to 1.954, 2.006, and 2.217 Å, respectively. Upon conversion to the NH₃ bonded enol amide **6** these bonds are fully formed (1.418, 1.016, and 0.997 Å, respectively), and N² lies above the ketene plane hydrogen bonded to the enol OH (N²H⁴ 1.832 Å). The energetic changes for conversion of CH₂=C=O to CH₃CONH₂ are illustrated in Figure 2.

There are significant differences between the amination of ketene by (NH₃)₂ as compared to the hydration by (H₂O)₂. In the best calculations for the latter reaction^{1c} the transition state was reported to be nonplanar, but as shown in **2** (Figure 1) the two water oxygens are not far from the ketene plane. The hydration process has a significant barrier (19.9 kcal/mol),^{1c} and enediol formation is calculated to be exothermic by 5.4 kcal/mol.^{1c} However, for (NH₃)₂ addition in the transition state **5a** the nucleophilic nitrogen is in the ketenyl plane but the nitrogen acting as a general base is above the ketene plane (Figure 1). A measure of the degree of nonplanarity of a ring is the total of the ring torsional angles,^{11a} which is 60.3° for TS **2** with (H₂O)₂, but is 155.8° and 105.0° for the TS with (NH₃)₃ (**5a**) and with NH₃·OH₂ (**11**) (for comparison the value for cyclohexane is 336.0°). Thus replacement of one or both of the H₂O molecules in TS **2** causes a significant deviation from coplanarity, and as pointed out by a referee this evidently arises from the longer bonds and H bonds in the structures for NH₃ addition compared to H₂O addition. Formation of **5a** has a very low barrier relative to the reactants of 0.4 kcal/mol, and the overall process to form enol amide from ketene and NH₃ is exothermic by 3.0 kcal/mol (Table 1). The much lower barrier for ketene reaction with (NH₃)₂ compared to (H₂O)₂ agrees with the experimental observations,^{6a,h} and the shorter C=O bond length in the transition state for (NH₃)₂ compared to (H₂O)₂ attack (1.206 versus 1.245 Å, respectively) is consistent with an earlier transition state in the former process. In the product enol amide

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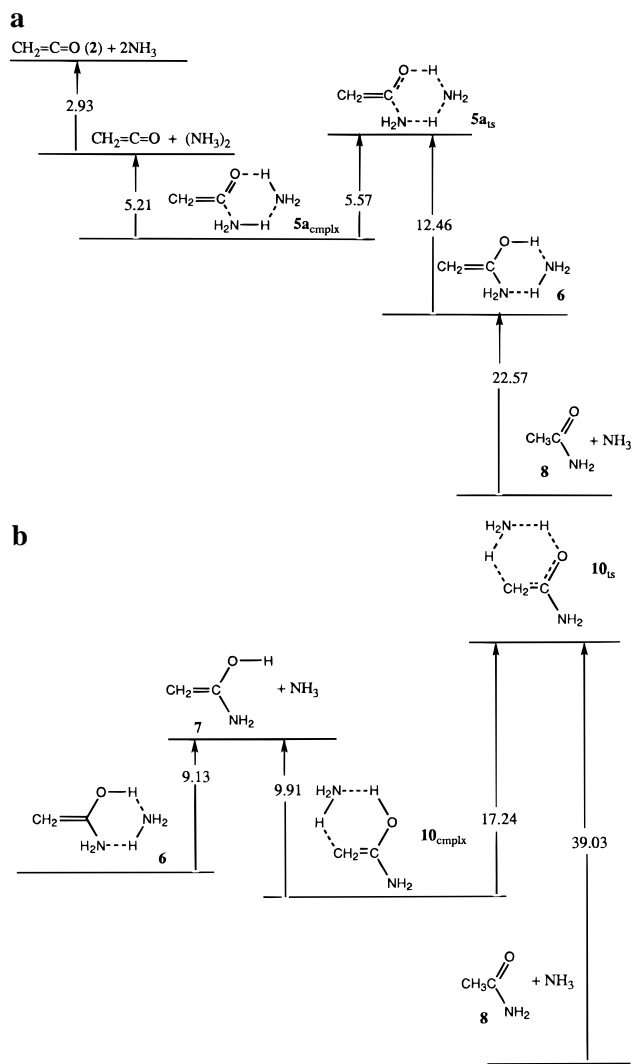


Figure 2. MP2/6-31G* energetic changes (kcal/mol) for (a) reaction of $\text{CH}_2=\text{C}=\text{O}$ with $(\text{NH}_3)_2$ to give amide enol **6** and (b) conversion of **6** to amide **8**.

coordination with NH_3 gives a complex **6** with hydrogen bonding of NH_3 to the hydroxyl proton and amido nitrogen (Figure 1). For hydration the MP4 calculated preference for $\text{C}=\text{O}$ compared to $\text{C}=\text{C}$ addition by $(\text{H}_2\text{O})_2$ was only 1.9 kcal/mol,^{1c} as contrasted to the 12.8 kcal/mol preference (MP2) found here for addition of $(\text{NH}_3)_2$.

The calculated ΔS values for addition of $(\text{NH}_3)_2$ to $\text{CH}_2=\text{C}=\text{O}$ to form **7** or **8** and NH_3 are -15.8 and -10.9 eu, while ΔS^\ddagger to form $5a_{\text{ts}}$ or $5c_{\text{ts}}$ are -45.2 and -55.2 eu, respectively (Table 3, Supporting Information). The resulting calculated ΔG^\ddagger of 16.3 kcal/mol for reaction of $\text{CH}_2=\text{C}=\text{O}$ with $(\text{NH}_3)_2$ is comparable to that reported by Birney et al.^{6j} for the reaction of formylketene with NH_3 (16.7 kcal/mol, eq 5).

The course of the reaction of $\text{H}_3\text{N}\cdot\text{H}_2\text{O}$ with ketene resembles that of $(\text{NH}_3)_2$, with the initial difference that in 11_{cmplx} the hydrogen bond of the proton to the carbonyl oxygen is from H_2O , with C^1N^1 , O^2H^2 , and O^1H^4 distances of 2.954, 2.168, and 2.099 Å, respectively. In the transition state these become 1.969, 1.966, and 1.938 Å, respectively. The geometry of this transition structure 11_{ts} is flatter than that for the $(\text{NH}_3)_2$ addition, with a total ring torsional angle of 105.0° , the nucleophilic nitrogen in the plane, and the general base, H_2O , above the ketene plane. The energetic changes for this process are illustrated in Figure 3.

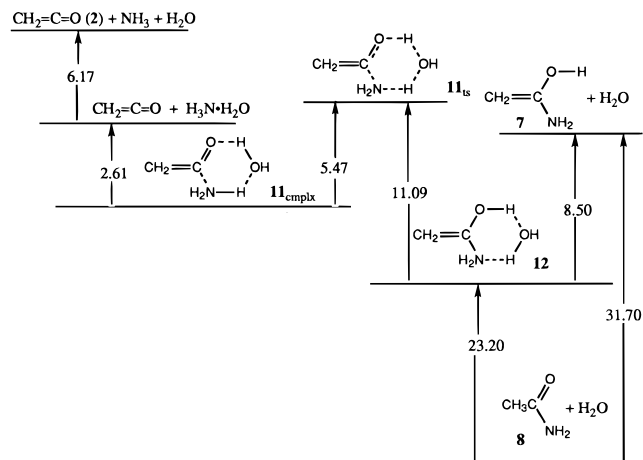


Figure 3. MP2/6-31G* energetic changes (kcal/mol) for reaction of $\text{CH}_2=\text{C}=\text{O}$ with $\text{H}_3\text{N}\cdot\text{H}_2\text{O}$ to form amide **8**.

For conversion of the intermediate enol amide **7** to the amide **8** the pathway catalyzed by NH_3 through transition state 10 is much more favorable than the uncatalyzed process, with a barrier relative to the reactants that is lower by 31.7 kcal/mol. The tautomerization proceeds from the complex **6** of the enol amide, which is stabilized by 9.1 kcal/mol, and 10_{ts} is 16.5 kcal/mol above **6**. This high barrier explains why there have been several recorded observations of enol amides,^{6b-e} even though the conversion of **7** to CH_3CONH_2 is highly exothermic by 31.7 kcal/mol. By contrast in the amination of ketenes in H_2O ^{6a} no enol intermediates were detected. This may be due to a more facile pathway for tautomerization involving assistance by H_2O molecules, analogous to the NH_3 assisted pathway shown by 10 .

Previous calculations^{3b,c} predicted NH_3 would prefer to add to the $\text{C}=\text{C}$ rather than the $\text{C}=\text{O}$ bond of ketene, in contrast to this study, and to the experimental results.^{6a-e} This discrepancy may be attributed to the low levels of theory utilized in the previous studies, namely simple Hückel^{3b} and MNDO^{3c} methods.

The NH_3 complex **6** may return to the reactants by $5a_{\text{ts}}$, which is 4.0 kcal/mol lower in energy than 10_{ts} , which leads to the amide. This result suggests that the initial addition of NH_3 to $\text{CH}_2=\text{C}=\text{O}$ is reversible, as has already been found for hydration of certain ketenes by ^{18}O labeling.^{11b}

In summary, the calculated pathway for amination of ketene is shown to prefer initial attack on the $\text{C}=\text{O}$ bond to give an enol amide, in agreement with experiment but in contrast to previous theoretical studies. Reaction with NH_3 is less favorable than with $(\text{NH}_3)_2$ or with $(\text{H}_3\text{N}\cdot\text{H}_2\text{O})$, and reaction with the second species explains the experimental observation^{6a} that aminations in H_2O are first order in $[\text{RNH}_2]$. Transition structures for conversion of the enol amide to the amide have been calculated, in which catalysis by NH_3 is favored over the uncatalyzed process, in agreement with experiment.

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Supporting Information Available: Calculated structures, energies, and geometries (17 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.