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Ketene Reactions with Tertiary Amines

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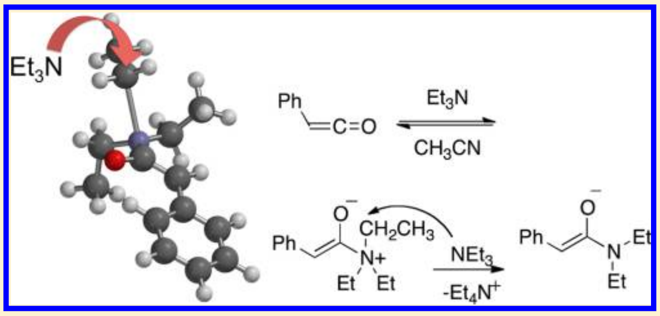
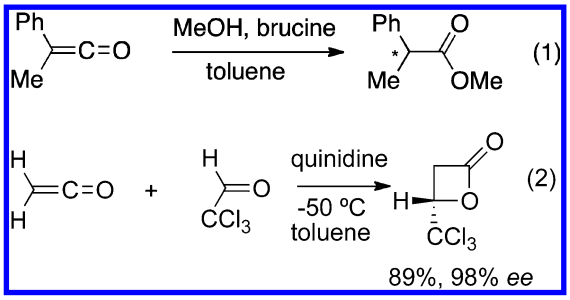
Supporting Information

ABSTRACT: Tertiary amines react rapidly and reversibly with arylketenes in acetonitrile forming observable zwitterions, and these undergo amine catalyzed dealkylation forming *N,N*-disubstituted amides. Reactions of *N*-methyldialkylamines show a strong preference for methyl group loss by displacement, as predicted by computational studies. Loss of ethyl groups in reactions with triethylamine also occur by displacement, but preferential loss of isopropyl groups in the phenylketene reaction with diisopropylethylamine evidently involves elimination. Quinuclidine rapidly forms long-lived zwitterions with arylketenes, providing a model for catalysis by cinchona and related alkaloids in stereoselective additions to ketenes.



INTRODUCTION

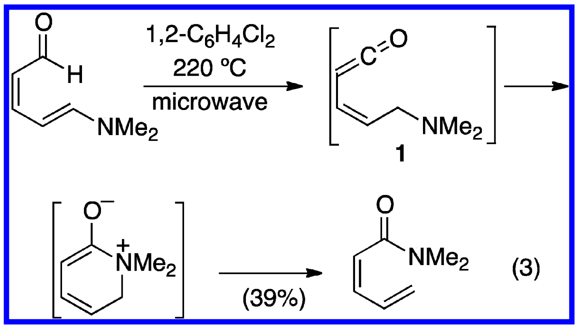
Additions to ketenes catalyzed by chiral tertiary amines are useful in asymmetric synthesis[1] and continue to find new applications,[2] which have been recently reviewed.[2e,f] Early examples include brucine catalyzed ketene esterification over a range of temperatures (eq 1)[1a] and quinidine catalyzed



β-lactone formation (eq 2),[1b] in which reactions of ketene/tertiary amine complexes with methanol and chloral, respectively, were proposed. Recent studies include asymmetric synthesis of β-lactams[2a,c] and of α-fluoroacyl chlorides.[2d]

Dehydrochlorination of acyl chlorides with tertiary amines is one of the first[3] and most widely used methods for ketene generation,[2] but ketenes are also known to react with tertiary amines, forming observable transients assigned as zwitterionic intermediates.[4,5] Aminations of ketenes by primary and secondary amines have been the object of mechanistic study,[6a−d] and a ketene−benzoylquinine complex has been identified using IR spectroscopy.[2c] In a recent report asymmetric ketene esterification with *R*-pantolactone in the preparation of a glucokinase activator proceeded with catalysis by the dimethylethylamine used in the generation of the ketene.[6e]

Examples of tertiary amine reactions with ketenes include intramolecular reaction of the tertiary amine substituted vinylketene **1** generated by thermal rearrangement of a dienyl aldehyde and proposed to cyclize to a zwitterionic intermediate which ring opens to an amide product (eq 3).[7] Allylic tertiary amines had



previously been found to react with ketenes to give similar rearrangements of zwitterionic intermediates to amides.[8a]

Intramolecular [4 + 2] electrocyclization of vinylketene **2** generated by cyclobutenone ring opening occurs with attack of the pyridyl nitrogen on the ketene to give a substituted quinolizinone (eq 4).[8b]

Ketene **3** generated by diazo ketone flash photolysis in acetonitrile was observed by IR and UV and reported to react with triethylamine producing a transient zwitterion, which formed the amide **4** with removal of an ethyl group (eq 5).[5a−c] It was concluded that "In the case of tertiary amines product formation involves alkene loss, for example, diethylamine and triethylamine give the same product, but in the latter case ethylene is lost."[5c] Identification of ethylene as a product has however not been described, and the mechanism by which the

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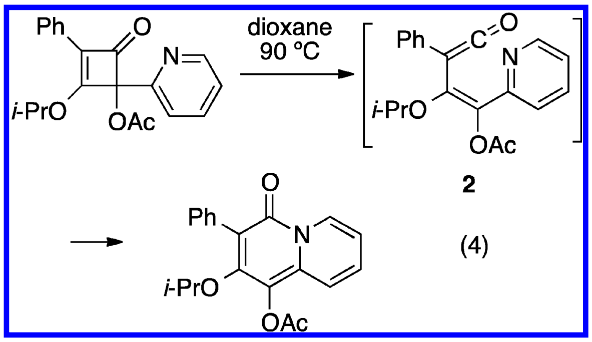
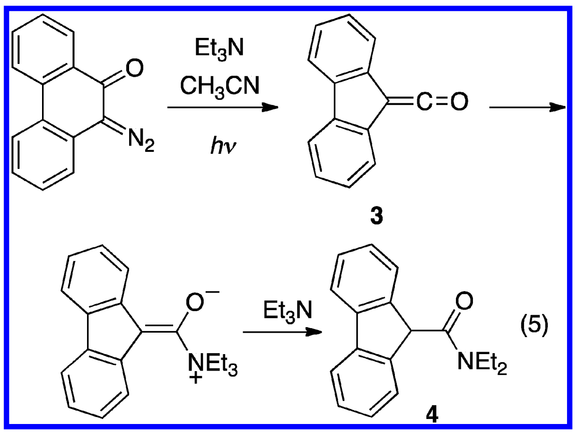


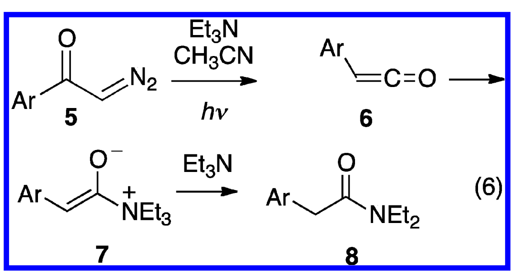


alkyl group is removed has apparently not been confirmed, or even discussed further.

■ RESULTS AND DISCUSSION

In view of the great utility of tertiary amines in ketene generation and catalysis, and the seemingly unexplained occurrence of degradation of tertiary amines in diarylketene reactions (eq 5),[5b,c] we have now carried out systematic experimental and computational studies of the reaction of arylketenes with tertiary amines.

Photolysis of diazo ketones **5**[9] was carried out as in previous studies,[6c,9] with 308 nm light in CH_3CN containing Et_3N, and subsequent reactions were monitored using UV spectroscopy (eq 6). Products from amine reactions with arylketenes formed



by preparative photolysis in a Rayonet reactor were isolated and identified and, in some cases, were confirmed to be the same for ketene generation by diazo ketone photolysis followed by amine addition, showing the products were not formed during the photolysis step.

Rate constants for ketene reactions with triethylamine forming transient zwitterions and subsequent amine catalyzed dealkylation forming amides (eq 6) were measured by UV spectroscopy (Table 1). Previously arylketene intermediates **6** formed similarly in acetonitrile[5a] or hexane[9] had also been identified by their characteristic IR spectra. The kinetic

Table 1. Rate Constants for Reactions of Ketenes 6 ($4\text{-RC}_6H_4CH{=}C{=}O$) with Et_3N and Quinuclidine (9) in CH_3CN, 25 °C

ketene, amine	k (M^{-1} s^{-1}) ketene decay[a]	k (M^{-1} s^{-1}) amide formation[c]
6a (R = MeO), Et_3N	2.57×10^6	1.40×10^5
6b (R = H), Et_3N	9.6×10^{5b}	1.30×10^5
6c (R = NO_2), Et_3N	3.81×10^8	6.62×10^2
6a (R = MeO), **9**	1.42×10^9	not formed
6b (R = H), **9**	1.66×10^9	not formed
6c (R = NO_2), **9**	2.44×10^9	not formed

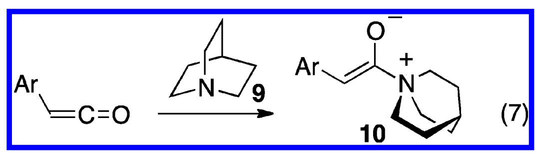
[a]Measured by UV spectroscopy. [b]Previously[5a] measured using IR spectroscopy as 2.3×10^5 M^{-1} s^{-1} at 23 °C. [c]Decay of transient, product formation not monitored.

measurements show higher reactivity for the p-NO_2 substituted ketene **6c**, consistent with stabilization of the intermediate enolate **7c**, and similarly a slower decay of this intermediate.

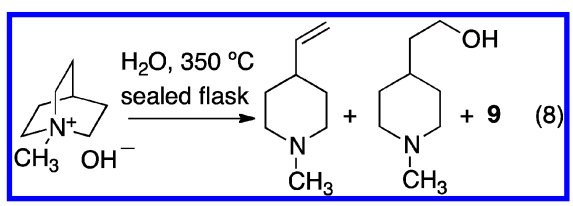
Reactions of quinuclidine (**9**) with arylketenes **6** were also studied and gave high rate constants, near the diffusion controlled limit (Table 1). The intermediates from these reactions were long-lived but did not form observable products.

The measured rate constants show that 4-nitrophenylketene is the most reactive with both amines, as expected for the formation of zwitterionic intermediates **7** and **10**, while the 4-methoxy and unsubstituted derivatives have similar but lower reactivity. Correlation of the rate constants for the ketene–quinuclidine reactions with σ^- values gives a ρ value of 0.15, showing a very small dependence on the substituents, characteristic of reactions near diffusion control.

The high reactivity of quinuclidine **9** in forming zwitterions **10** (eq 7) has been observed previously,[5c] and this and the slow

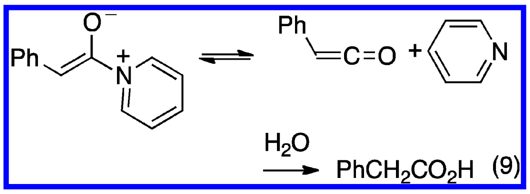


decay of these transients are as expected for the unencumbered facade of the amino nitrogen. Isolable products from quinuclidine reactions with arylketenes incorporating quinuclidine have not been reported, but N-methylquinuclidinium hydroxide upon heating is converted to **9**, 4-vinyl-N-methylpiperidine, and 4-(2-hydroxylethyl) N-methylpiperidine (eq 8).[10a] Also a sample of the hydroxide heated at 65 °C under high

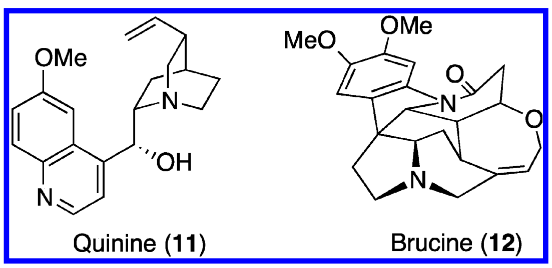


vacuum to dehydrate the sample resulted in the formation of **9** and CH_3OH.[10b] Extreme conditions are required for alkene formation by proton abstraction from the bridging groups because of the almost orthogonal arrangement of the breaking C–H and C–N bonds.

Tertiary amines are present in considerable excess relative to the diazo ketones in our reactions (eq 6), but the final absorbance of the zwitterion from 4-methoxyphenylketene and quinuclidine increases with quinuclidine concentration, indicating that the reactions are reversible. Similar results are found for the phenylketene reaction with triethylamine. Our calculations[11] show the reaction of phenylketene with triethylamine in acetonitrile forming the zwitterion is exothermic by 4.6 kcal/mol (B3LYP/6-31+G(d)) or 13.0 kcal/mol (RI-MP2/6-31G(d)), with free energy barriers of 2.6 or 0.5 kcal/mol, respectively. Consistent with this interpretation the reaction of phenylketene with pyridine in water has been reported to form an observable zwitterion, which decays with formation of phenylacetic acid, in a process interpreted as involving the reversible dissociation of the zwitterion to the ketene and capture by water (eq 9).[4d]



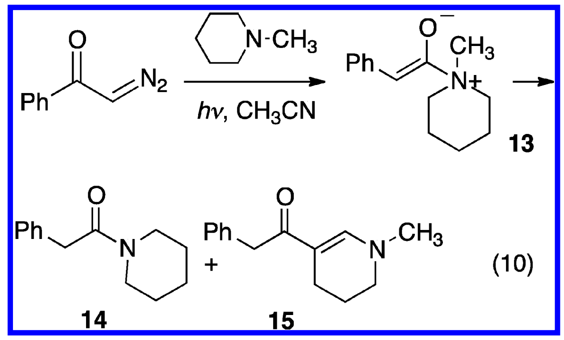
The high reactivity of quinuclidine with ketenes and the long lifetime of the quinuclidine zwitterion explain the ability of the structurally related alkaloids such as quinine (**11**) and brucine (**12**) to form chiral zwitterions with long lifetimes that can be converted stereoselectively to the final products. These compete effectively in ketene capture with acyclic trialkylamines used in ketene generation. Comparative nucleophilicity *N* values have been reported as Et_3N (17.1),[12a] *N*-methylpiperidine (18.72),[12a] and quinuclidine (20.54).[12b]

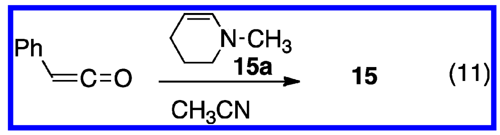


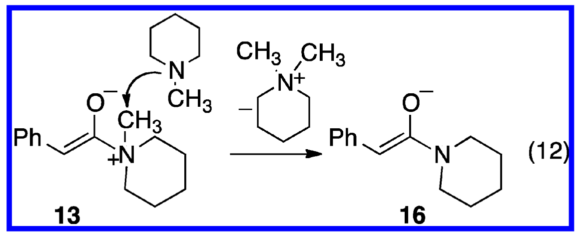
To test for alkene formation by elimination from intermediate zwitterions, we examined the reaction of tri-*n*-octylamine with phenylketene, since ethylene formed from the reaction with triethylamine[5c] would be difficult to detect, but the less volatile 1-octene is expected to be easily observable. However an elimination reaction was not confirmed, as while *N*,*N*-di-*n*-octyl phenylacetamide was isolated, no trace of 1-octene was detected by ^{1}H NMR in the reaction product.

Similarly no elimination product was detected upon generation of phenylketene in the presence of *N*-methylpiperidine, but *N*-piperidinyl phenylacetamide (**14**)[13] was isolated in 34% yield, with CH_3 group loss from the expected intermediate **13** (eq 10). The enone **15** was also isolated and evidently results from ketene addition[14a,b] to the enamine **15a**[14c] derived[14d,e] by oxidative hydrogen abstraction from *N*-methylpiperidine (eq 11).

The decays of the zwitterionic intermediates are amine catalyzed, and in the absence of evidence for alkene formation a displacement reaction by a further amine provides a plausible explanation of these results (eq 12). Displacement of alkyl groups from tertiary amines with nucleophiles occurs by the von Braun reaction,[15a,b] and preparative reactions by alkyl group displacement from quaternary ammonium ions by tertiary amines were developed by Hünig and Baron.[15c,d] These studies

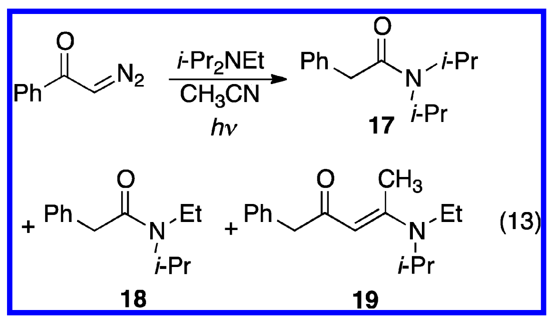






found that methyl and ethyl groups are displaced much more readily than the attack on pyrrolidinyl or piperidinyl rings.[15c,d]

Product studies of the reactions of other tertiary amines with ketenes were undertaken, and phenylketene generated in the presence of diisopropylethylamine (DIPEA, Hünig's base) gave the diisopropyl amide **17**,[13b] the ethyl isopropyl amide **18**, and the ketone **19** (eq 13), in a ratio of 1:5:4. The loss of the ethyl



group is consistent with the loss of ethyl groups shown above (eqs 5, 6) by a displacement reaction, and formation of **19** may be explained by the reaction of phenylketene with the enamine $CH_2{=}CMeNEt$-*i*-Pr, as in the formation of **15**. However the preferential formation of **18** with the loss of an isopropyl group indicates that in this case an elimination reaction is involved, as originally proposed for ethyl group loss.[5c]

Although tertiary amines are frequently used in ketene preparations by dehydrohalogenation for in situ reactions with other substrates, such dealkylations have not been observed under these conditions. This is evidently due to rapid reactions of the ketenes and zwitterions with the intended substrates such as imines or alkenes, and also because the amine concentrations are typically much lower than in the experiments reported here.

Diarylketenes react similarly,[16] as photolysis of azibenzil in an aqueous solution containing *N*-methylmorpholine gives diphenylacetic acid by diphenylketene hydration, as well the corresponding *N*-morpholinyl amide **20**,[16a] in a ratio of 1:5 as

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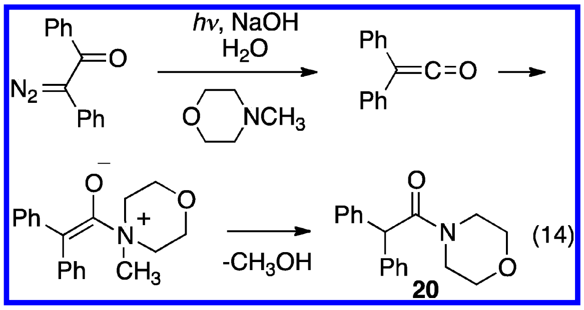
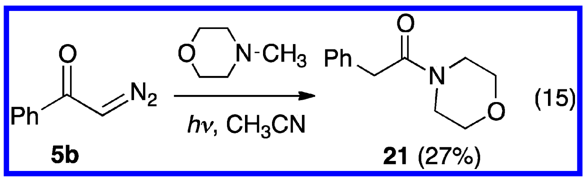
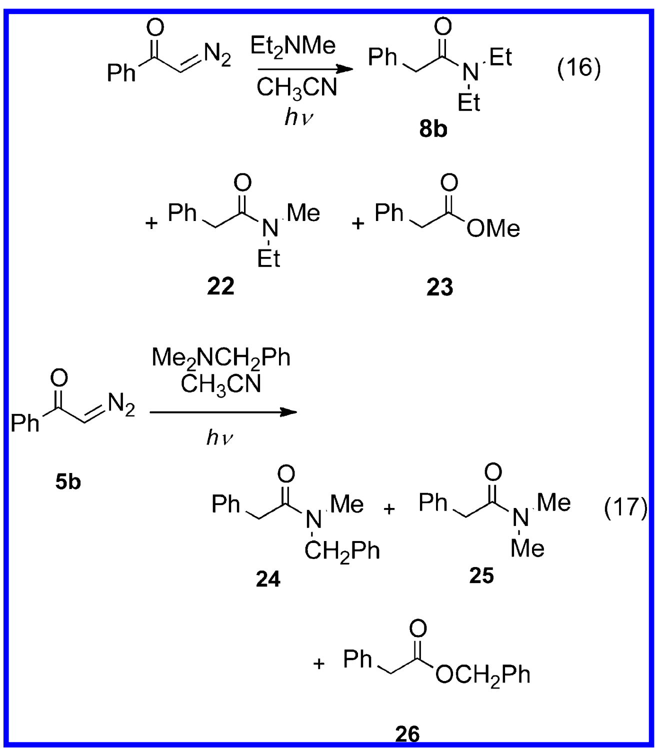
determined by HPLC, indicating competitive nucleophilic addition of water and the amine to the ketene and demethylation of an initial zwitterion by water, hydroxide, or the amine (eq 14).[16b]



N-Methylmorpholine also reacts with phenylketene in CH_3CN by demethylation, giving the analogous morpholinyl phenylacetamide (**21**),[13a] in 27% isolated yield (eq 15).



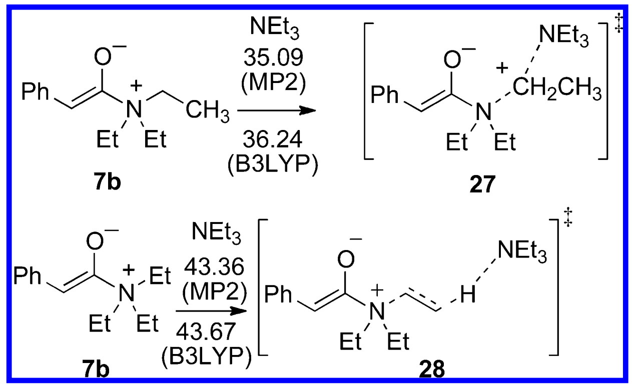
Phenylketene with diethylmethylamine gave three products, dialkylamides **8b**[17a] and **22**[17b] resulting from the loss of methyl or ethyl groups, respectively, together with the methyl ester **23**, in the ratio **8b**:**22**:**23** = 3:1:2.5, again with preferential methyl loss by zwitterion dealkylation (eq 16). Similarly the reaction of phenylketene with $PhCH_2NMe_2$ gave the amide **24**[17] by demethylation and **25** by the loss of benzyl, as well as the ester **26** (eq 17). The formation of esters **23** and **26**, evidently by net



transfer of methyl or benzyl to oxygen with loss of the amino group, is apparently unprecedented, and the origin of these products remains a matter of conjecture that requires further study.[19]

Computations at both the MP2 and B3LYP/6-31G+d levels are in agreement with the conclusion from the experimental results that triethylamine catalyzed dealkylation of the zwitterion **7b** from phenylketene and triethylamine occurs preferentially by displacement (Scheme 1).[11] Thus the free energy of elimination

Scheme 1. Comparative Free Energies (MP2 and B3LYP/6-31G+d) (kcal/mol) for Dealkylation of the Zwitterion 7b by Et_3N in CH_3CN by Displacement and Elimination Routes[11]



with alkene loss is found to be 8.3 (MP2) or 7.4 (B3LYP) kcal/mol higher than for the displacement pathway.

■ CONCLUSION

The dealkylation of zwitterions obtained from tertiary amine additions to ketenes occurs with preferential loss of methyl groups, and displacement reactions by amines offer a plausible mechanism for this process. Computational studies and the failure to detect elimination products from dealkylation of tri-*n*-octylamine adducts with phenylketene indicate displacement is also the preferred route for the loss of *n*-alkyl groups. However for the diisopropylethylamine reaction with phenylketene, loss of an isopropyl group is favored, evidently by an elimination route. Ketene reactions with tertiary amines are found to be reversible, and the fast reaction of quinuclidine with ketenes and the long lifetimes of the resulting zwitterions provide a rationale for how the structurally related cinchona alkaloids can effect addition to ketenes with zwitterion formation and promote subsequent stereoselective additions even in the presence of triethylamine. The dealkylation reaction is remarkable due to its occurrence with the stable diphenylketene as well as the much more reactive phenylketene. We can envision many extensions of this work to other ketenes and amines, as well as investigations to elucidate the formation of the esters **23** and **26**, but can no longer pursue such studies, and welcome others to these tasks.

■ EXPERIMENTAL SECTION

General Procedure: *N,N*-Diethyl-2-phenylacetamide (8b) [CAS 2431-96-1][17a] from Phenylketene and Triethylamine. To a glass tube (20 cm × 3.5 cm) equipped with a septum cap was added acetonitrile (130 mL, HPLC grade, dried and kept over molecular sieve 3A), 2-diazo-1-phenylethanone (**5b**, 6.5 mg, 0.044 mmol), and triethylamine (1.8 mL, 12.9 mmol). The solution was purged with argon for 30 min and then irradiated 5 min in a Rayonet reactor at 300 nm while purging with argon. The UV spectrum of the irradiated solution showed that all starting diazo ketone had been consumed. The solution was evaporated to give the

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crude product (7.2 mg, 85%), and the ^{1}H NMR spectrum showed **8b** as the major product. Column chromatography (silica gel, $CHCl_3$ followed by $CHCl_3$/MeOH 9:1 v/v) gave **8b** (3.1 mg, 36%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.25 (m, 5H), 3.70 (s, 2H), 3.39 (q, *J* = 7.24 Hz, 2H), 3.30 (q, *J* = 7.04 Hz, 2H), 1.18−1.08 (m, 6H).

***N,N*-Diethyl-2-(4-methoxyphenyl)acetamide (8a) CAS [115348-15-7].**[18] By the general procedure, 2-diazo-1-(4-methoxyphenyl)ethanone (**5a**, 9 mg, 0.051 mmol) and triethylamine (1.9 mL, 13.6 mmol) in CH_3CN gave a crude product (6.2 mg) found by ^{1}H NMR to contain **8a** and 4-methoxyacetophenone in a ratio of 76:24. Column chromatography (silica gel CH_2Cl_2/EtOAc 8:2 v/v) gave **8a** (2.6 mg, 24%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.80 Hz, 2H), 6.85 (d, *J* = 8.61 Hz, 2H), 3.79 (s, 3H), 3.63 (s, 2H), 3.38 (q, *J* = 7.04 Hz, 2H), 3.30 (q, *J* = 7.04 Hz, 2H), 1.18−1.08 (m, 6H) and 4-methoxyacetophenone ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 9.00 Hz, 2H), 6.94 (d, *J* = 9.00 Hz, 2.6 H), 3.87 (s, 3 H), 2.56 (s, 3H). The latter product is evidently a byproduct from the photo-Wolff rearrangement.

***N,N*-Diethyl-2-(4-nitrophenyl)acetamide (8c) CAS [50507-86-3].**[18] By the general procedure, 2-diazo-1-(4-nitrophenyl)ethanone (9.2 mg, 0.048 mmol) and triethylamine (1.8 mL, 12.9 mmol) in CH_3CN gave the crude product which after column chromatography (silica gel EtOAc/hexanes 7:3 v/v) gave **8c** (3 mg, 27%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.80 Hz, 2H), 7.47 (d, *J* = 8.80 Hz, 2H), 3.79 (s, 3H), 3.41 (q, *J* = 7.24 Hz, 2H), 3.34 (q, *J* = 7.24 Hz, 2H), 1.18−1.08 (m, 6H).

Product Study for Phenylketene Reaction with Tri-*n*-octylamine: *N,N*-Di-*n*-octyl-4-phenylacetamide (8d). To a septum capped NMR tube was added 850 μL of $CDCl_3$, 2-diazo-1-phenylethanone (5.8 mg, 0.044 mmol), and tri-*n*-octylamine (28 μL, 0.064 mmol), and the solution was purged with argon for 5 min and then irradiated in a Rayonet reactor for 5 min while being purged with argon. The ^{1}H NMR spectrum of the irradiated solution showed some starting material remained which upon further irradiation for 21 min disappeared. ^{1}H NMR showed the presence of **8d**, but no absorption attributable to the vinyl H of 1-octene was observed (estimated detection limit 5% relative to **8d**). The solution was evaporated (0.029 g, crude), and *N,N*-di-*n*-octyl phenylacetamide (**8d**, CAS [514808-21-0], a previously unreported compound) was obtained after 3-fold column chromatographic separation (CH_2Cl_2/hexanes 8:2 v/v), (CH_2Cl_2/EtOAc 8:2 v/v) and (CH_2Cl_2/EtOAc 98:2 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.3−7.2 (m, 5H), 3.69 (s, 2 H), 3.30 (t, *J* = 7.63 Hz, 2H), 3.19 (t, *J* = 7.82 Hz, 2H), 1.4−1.6 (m, 4H), 1.2−1.3 (m, 20 H), 0.9−0.8 (m, 6H).

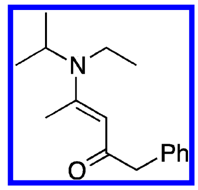
Phenylketene *N*-Methylpiperidine Reaction. By the general procedure, the product from 2-diazo-1-phenylethanone (7.8 mg, 0.053 mmol) and *N*-methylpiperidine (1.5 mL, 12.3 mmol) in acetonitrile upon chromatography (silica gel, CH_2Cl_2/EtOAc 8:2 v/v) gave amide **14** (3.7 mg, 34%) and a later fraction gave ketone **15**, evidently derived from the corresponding enamine, 1,2,3,4-tetrahydro-1-methylpyridine CAS [57005-69-3].[10] Another column chromatography (silica gel, EtOAc/CH_2Cl_2, 8:2 v/v) gave pure **15**.

2-Phenyl-1-(1-piperidinyl)ethanone (14) [CAS: 3626-62-8].[13] ^{1}H NMR (400 MHz, $CDCl_3$) **14** δ 7.31−7.25 (m, 5H), 3.73 (s, 2H), 3.57 (t, $^3J_{H,H}$ = 5.7 Hz, 2H), 3.37 (t, $^3J_{H,H}$ = 5.7 Hz, 2H), 1.59−1.52 (m, 4H), 1.37−1.33 (m, 2H). EIMS *m*/*z* 203 (51, M^+), 112 (100, [M^+ − CH_2Ph]). HREIMS *m*/*z* calcd for $C_{13}H_{17}NO$ 203.1315, found 203.1310.

Phenylketene Diisopropylethylamine Reaction. By the general procedure, photolysis of 2-diazo-1-phenylethanone (**5b**, 7.1 mg, 0.049 mmol) and DIPEA (2.0 mL, 11.5 mmol) in CH_3CN and purification by 3-fold chromatography on silica gel {(CH_2Cl_2/EtOAc 8:2 v/v), (hexanes/EtOAc 6:4 v/v), (CH_2Cl_2/EtOAc 6:4 v/v)} gave three isolated products identified as (*N,N*-diisopropyl-2-phenylacetamide, **17**, CAS: [34251-46-310 2])[13b,15e] **18**, and **19**, which from the ^{1}H NMR spectra of three separate preparations were present in the crude product in a ratio of 11:51:38.

***N*-Ethyl-*N*-isopropyl-2-phenylacetamide (18) CAS: [125576-07-0].**[13c] Pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.20 (m, 10H), 4.69 (sept, *J* = 6.6 Hz, 1H), 4.05 (sept, *J* = 6.6 Hz, 1H), 3.74 (s, 2H), 3.69 (s, 2H), 3.26 (q, *J* = 7.04 Hz, 2H), 3.23 (q, *J* = 7.04 Hz, 2H), 1.19 [(t, *J* = 7.04 Hz, 3H), 1.17 (t, *J* = 7.04 Hz, 3H), 1.16 (d, *J* = 6.6 Hz, 6H), 1.03 (d, *J* = 6.6 Hz) (6H)]. ESIMS (AIMS AccuTOF-DART-MS) *m*/*z* ([M•H]$^+$) 206. HRESIMS *m*/*z* calcd for $C_{13}H_{20}N_1O_1$ 206.15449, found 206.15485.

1-Phenyl-4-(ethylisopropylamino)-pent-2-one-3-ene (19). Previously unreported (**19**), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (m, 5H), 5.02 (s, 1H), 4.11 (sept, *J* = 6.6 Hz, 1H), 3.58 (s, 2H), 3.11 (q, *J* = 7.0 Hz, 2H), 2.55 (s, 3H), 1.13 (d, *J* = 6.6 Hz, 2 × CH_3), 1.05 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 161.1, 138.2, 129.4, 128.3, 126.0, 94.6, 52.0, 48.4, 37.9, 20.6, 15.7. UV λ_{max} = 313 nm (CH_3CN), IR ($CDCl_3$) ν_{max} 1600, 1525 cm^{-1}. ESIMS



(AIMS Accu TOF-DART-MS) *m*/*z* ([M•H]$^+$) 246; HRESIMS *m*/*z* calcd for $C_{16}H_{24}N_1O_1$ 246.18579, found 246.18748.

The UV spectrum may be compared to that reported for *trans*-MeCOCH=C(Me)NMe_2: (MeOH) λ_{max} 310 nm (28 700).[20]

Diphenylketene *N*-Methylmorpholine Reaction.[16] Flash photolysis of azibenzil in aqueous *N*-methylmorpholine afforded *N*-morpholinyldiphenylacetamide (**20**)[16a] and diphenylacetic acid at a buffer ratio of 0.993. The amide−acid product ratio at this buffer concentration is 0.16, in good agreement with the value from kinetic experiments.[16c]

Phenylketene *N*-Methylmorpholine Reaction. By the general procedure, the product from 2-diazo-1-phenylethanone (7.8 mg, 0.053 mmol) and *N*-methylmorpholine (1.4 mL, 12.7 mmol) upon column chromatography (silica gel, CH_2Cl_2/EtOAc 8:2 v/v) gave the known[13] amide 1-(4-morpholinyl)-2-phenyl ethanone (**21**). CAS: 17123-83-0 (3 mg, $C_{12}H_{15}NO_2$, MW 205.25, 15 mmol, 27%). Further chromatography gave the sample for ^{1}H NMR measurement. ^{1}H NMR (400 MHz, $CDCl_3$) **21** δ 7.33−7.23 (m, 5H), 3.74 (s, 2H), 3.65 (bd s, 4H), 3.5−3.4 (m, 4H).

Phenylketene Diethylmethylamine Reaction with in Situ Ketene Generation and Amine Reaction. By the general procedure, 2-diazo-1-phenylethanone (**5b**, 7.4 mg, 0.051 mmol) and *N,N*-diethylmethylamine (1.4 mL, 11.6 mmol) in 130 mL of acetonitrile were purged for 40 min with argon, and the solution was then irradiated for 5 min in a Rayonet reactor with 300 nm lamps while purging with argon. The solvent was evaporated, and the ^{1}H NMR spectrum showed a mixture of products. Column chromatography (silica gel, CH_2Cl_2/EtOAc 9:1 v/v) gave in fractions 1−5 $PhCH_2CO_2Me$ (**23**)[11] and fractions 11−17 $PhCH_2CONEt_2$ (**8b**). Further elution with EtOAc gave $PhCH_2$CONMeEt (**22**). Relative yields by ^{1}H NMR intergration are $PhCH_2CONEt_2$ (**8b**) (47%); $PhCH_2$CONMeEt (**22**) (11%); $PhCH_2CO_2Me$ (**23**) (42%).

***N,N*-Diethyl-2-phenylacetamide (8b). CAS: [2431-96-1].** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.26 (m, 5H), 3.70 (s, 3H), 3.63 (s, 2H), 3.39 (q, *J* = 7.04 Hz, 2H), 3.30 (q, *J* = 7.04 Hz, 2H), 1.14−1.07 (m, 6H).

Identification of $PhCH_2$CONMeEt (22). *N*-Methyl-*N*-ethyl-2-phenylacetamide [CAS: 105879-33-2]. ^{1}H NMR (400 MHz, $CDCl_3$) **22** mixture of rotamers, 1:1.2 (average 2.8 to 3.8 ppm) (major rotamer) δ 7.38−7.20 (m, 5H), 3.70 (s, 3H), 3.34 (q, *J* = 7.04 Hz, 2H), 2.94 (s, *J* = 7.04, 2H), 1.08−1.26 (rotamers overlapping t, 3H); (minor rotamer) δ 7.38−7.20 (m, 5H), 3.72 (s, 3H), 3.44 (q, *J* = 7.43 Hz, 2H), 2.93 (s, *J* = 7.04, 2H), 1.08−1.26 (rotamers overlapping *t*, 3H).

Identification of $PhCH_2CO_2Me$ (23).[21] ^{1}H NMR (400 MHz, $CDCl_3$) **25** δ 7.31−7.26 (m, 5H), 3.70 (s, 3H), 3.63 (s, 2H).

Modified Phenylketene Diethylmethylamine Reaction. A solution of **5b** (3.8 mg, 0.026 mmol) in 35 mL of acetonitrile was purged for 40 min with argon, and the solution was then irradiated in a Rayonet reactor for 3 min with 16 lamps at 300 nm while purging with argon. Immediately after irradiation diethylmethylamine (0.7 mL, 5.8 mmol) was added, and the solution turned bright yellow. After 10 min, the purging was stopped and the solvent evaporated under reduced pressure giving a residue of 5.7 mg, which by ^{1}H NMR showed the presence of $PhCH_2CONEt_2$ (**8b**), $PhCH_2CO_2NMeEt$ (**22**), and $PhCH_2CO_2Me$ (**23**), in a similar ratio to that observed previously.

Phenylketene Reaction with *N,N*-Dimethylbenzylamine. By the general procedure, **5b** (2-diazo-1-phenylethanone, 7.7 mg, 0.053 mmol) and *N,N*-dimethylbenzylamine (1.75 mL, 11.6 mmol) in 130 mL of acetonitrile were purged with argon for 30 min. The solution was then irradiated in a Rayonet reactor for 5 min at 300 nm while purging with argon. The reaction was monitored by UV, which showed the depletion of all starting material. The solvent was evaporated, and the ^{1}H NMR spectrum of the residue showed unreacted amine and a mixture of products. Characteristic peaks for $PhCH_2CO_2CH_2Ph$ (**26**) at 5.12 and 3.66 ppm were observed in the crude ^{1}NMR and in the early CH_2Cl_2 chromatography fraction. Gradient column chromatography on silica gel from CH_2Cl_2 to CH_2Cl_2/EtOAc 9:1 to CH_2Cl_2/EtOAc 8:2 to EtOAC and MeOH was performed, and by further column chromatography on silica gel hexanes/EtOAc 9:1, pure $PhCH_2CO_2CH_2Ph$ (**26**) and $PhCH_2CONMeCH_2Ph$ (**24**)[17] were isolated from CH_2Cl_2/EtOAc 8:2 fractions and $PhCH_2CONMe_2$ (**25**) was isolated in the EtOAc fraction.

Identification of $PhCH_2CONMeCH_2Ph$ (24).[17] *N*-Benzyl-*N*-methyl-2-phenylacetamide CAS: [105879-33-2]. ^{1}H NMR (400 MHz, $CDCl_3$) **24** 1:1.4 (average 2.8 to 4.8 ppm) mixture of rotamers: (major rotamer) δ 7.38−7.21 (m, 9H), 7.11−7.09 (m, 1H), 4.61 (s, 2H), 3.79 (s, 2H), 2.90 (s, 3H); (minor rotamer) δ 7.38−7.21 (m, 9H), 7.11−7.09 (m, 1H), 4.53 (s, 2H), 3.76 (s, 2H), 2.96 (s, 3H).

Identification of $PhCH_2CONMe_2$ (25).[22a] *N,N*-Dimethyl-2-phenylacetamide CAS: [135339-78-5]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.5−7.22 (m, 5H), 3.72 (s, 2H), 3.00 (s, 3H), 2.97 (s, 3H).

Identification of $PhCH_2CO_2CH_2Ph$ ($C_{15}H_{14}O_2$) (26).[22b] Phenylacetic acid benzyl ester CAS: [102-16-9]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4−7.3 (m, 5H), 5.14 (s, 2H), 3.67 (s, 2H). HRESIMS *m/z* calcd for M + H$^+$ $C_{15}H_{15}O_2$ 227.10720, found 227.10765; calcd for M + NH_4^+ $C_{15}H_{18}NO_2$ 244.13375, found 244.13390.

■ ASSOCIATED CONTENT

Supporting Information

NMR, UV, and IR spectra, computational results. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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