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(14) C. U. Pittman, S. P. McManus, and J. W. Larsen, *Chem. Rev.*, **72**, 357 (1972).
(15) The formation of **1c** instead of diethyl acetal **9** (R = R′ = Et) could also result from the presence of water in the reaction medium. We do not favor this explanation because strictly anhydrous ethanol was used, because a high water content would be required to account for the high yield of **1c**, and because the hydrolysis reaction was not significant under similar conditions in methanol.
(16) The choice of pH is critical. Acidification of the solution to pH 2 results in complete conversion of **9** to **3b**, whereas at a pH of 5 the acetal–acid is not extracted into the organic phase.

Cyclization of Conjugated Azines. Synthesis and Thermal Rearrangements of 1-Oxo-3,4-diaza-2,4,6,7-octatetraenes (Allenyl Azines)

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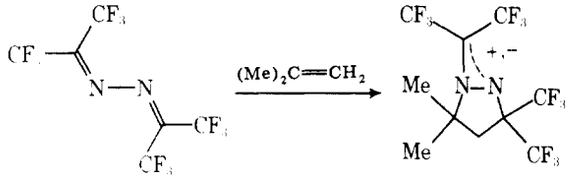
The Wittig reaction of certain 2-(alkylidenehydrazono)propylidenephosphoranes with ketenes provides a general route to 1-oxo-3,4-diaza-2,4,6,7-octatetraenes (allenyl azines). The allenyl azines undergo a facile intramolecular thermal cycloaddition reaction to yield pyrazolo[5,1-*c*]-1,4-oxazines and/or 4,9-dihydropyrazolo[1,5-*b*]isoquinolines depending on the nature of the substituents introduced via the ketene.

In contrast to all carbon,[2] monoaza,[3] and other diaza[4] dienes, the intra- and intermolecular cycloaddition reactions of acyclic azines (eg., **1** and **8**, Scheme I) or 2,3-diazabutadienes are characterized by the 1,3 reactivity of the C=N—N=C grouping. For example, simple aldehyde and ketone azines (**1**) react with the olefins to yield perhydropyrazolo[1,2-*a*]pyrazoles (**2**), a reaction known as "criss-cross" cycloaddition[5] (Scheme I, eq 1). The intermediacy of azomethinimine 1,3-dipoles has been confirmed by the isolation and characterization[6] of **13** in the reaction of hexafluoroacetone azine (**12**) with isobutylene.

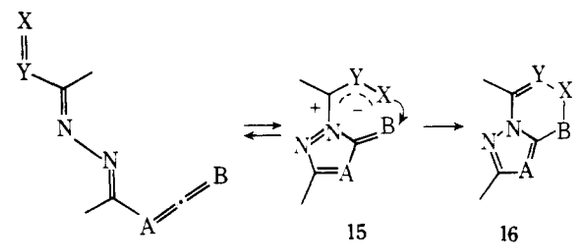


12 **13**

Analogous reactivity has been observed[7,8] with acetylenes, leading to 1,5-dihydropyrazolo[1,2-*a*]pyrazoles (**3**). These azine–acetylene criss-cross cycloadducts are thermally unstable, rearranging to either acyclic azines[7] (e.g., **7**) or N-substituted pyrazoles (e.g., **5** and **6**; Scheme I, eq 2). The key step in these reactions is the ring opening of **3** to a stabilized azomethinimine (**4**).[9] When R = H, **4** can proceed on to the N-substituted pyrazoles (**5**/**6**) by a simple intramolecular proton transfer to the 3-carbon side chain. When R is something other than hydrogen, this proton transfer is not possible and the dipolar intermediate (**4**) decomposes by a second ring opening reaction to yield the acyclic azines **7**.

An analogous intermediate (i.e., **9**) is presumably involved in the thermal rearrangement of certain conjugated azines (**8**) to N-substituted pyrazoles (**10** and **11**). Symmetrical azines derived from α,β-unsaturated aldehydes and ketones[10] (i.e., **8a**) and unsymmetrical azines formed from α-diketone monohydrazones and α,β-unsaturated aldehydes and ketones[11] (i.e., **8b**) rearrange to *N*-propenylpyrazoles (**10a**) and α-pyrazolyl ketones (**11**), respectively (Scheme I, eq 3).

It occurred to us that in a suitably designed system avenues of intramolecular reaction other than proton transfer might be observed in the reactions of azomethinimines such as **4** and **9**. One intriguing system, **14**, has the azine functional group



14 **15** **16**

in conjugation with a cumulene system. If these azines were to react in the same manner as other conjugated azines (**8a** and **8b**), one would expect stabilized azomethinimines such as **15** to be formed. One possible mode of reaction open to **15** would be an internal Michael-type addition to the exocyclic C=B bond, generating bicyclic heterocycles **16**. In theory, a wide variety of heterocyclic systems could be obtained by varying A, B, X, and Y. To establish the feasibility of this reaction concept, we have chosen to study the synthesis and thermal rearrangements of 1-oxo-3,4-diaza-2,4,6,7-octatetraenes (**14**; A = B = Y = carbon, X = oxygen).

Results and Discussion

The required allenyl azines (**14**; A = B = Y = C, X = O) are unknown in the literature. The ready availability[11] of the stabilized phosphorane **17** and the known[12] reaction of phosphonium ylides with ketenes to form allenes suggested the route to the allenyl azines (e.g., **18**) outlined in Scheme II.

As an initial test of the feasibility of this scheme, we investigated the reaction of **17** with diphenylketene (generated in situ by the action of triethylamine on diphenylacetyl chloride,[13] **19**). The reaction proceeds smoothly and rapidly at room temperature in benzene to produce a single product in addition to triphenylphosphine oxide. Although this material proved to be quite thermally labile, by rapidly chromatographing the reaction mixture we were able to isolate it in essentially quantitative yield as an orange solid. Examination of the infrared [1930 (allene) and 1680 cm^{-1} (PhC=O)]

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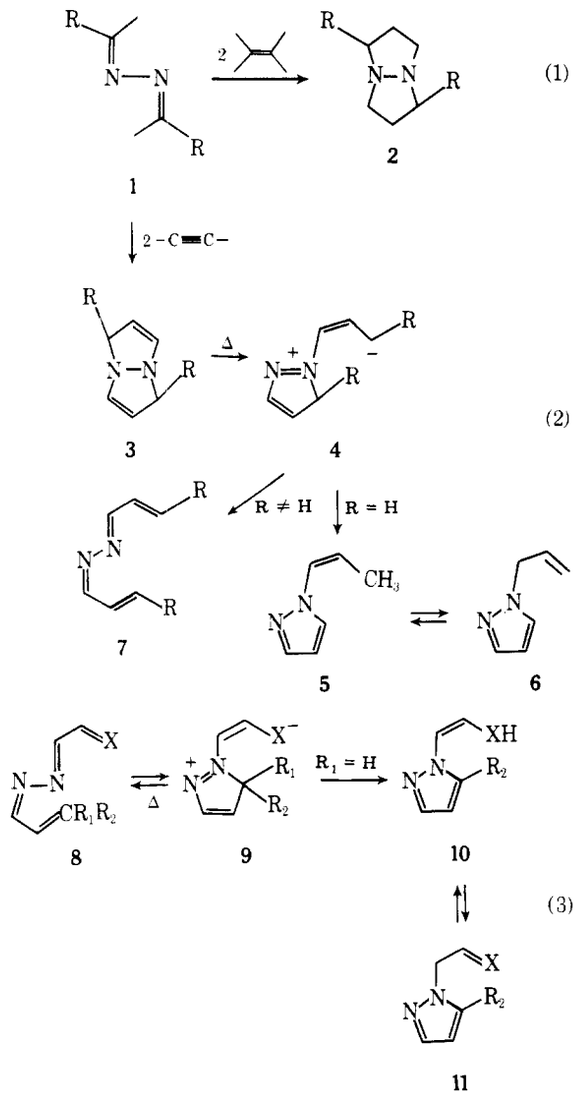
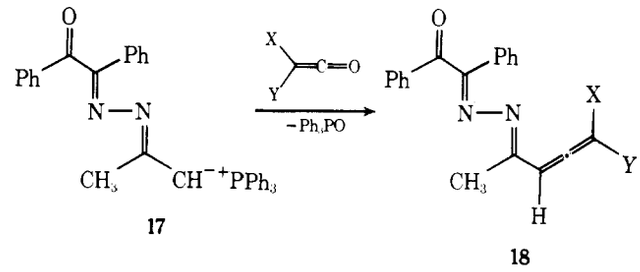
Scheme I

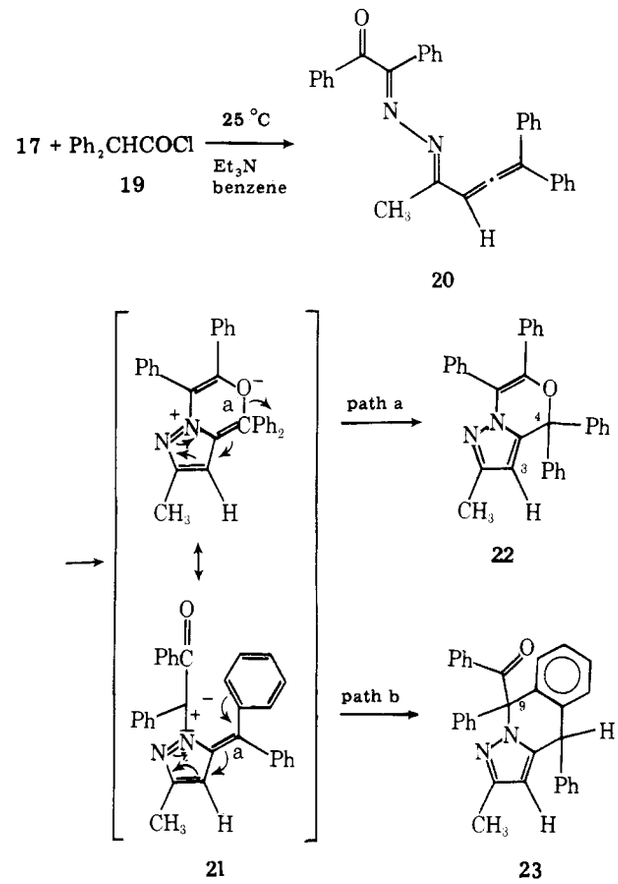


8–11: a, X = CR_1R_2; b, X = O

Scheme II



Scheme III



and ^{13}C NMR [δ 212.1 (C=C=C), 100.2 (C=C=CPh_2), and 197.9 (PhC=O)] spectra confirmed our identification of this orange solid as the allenyl azine **20** (Scheme III).

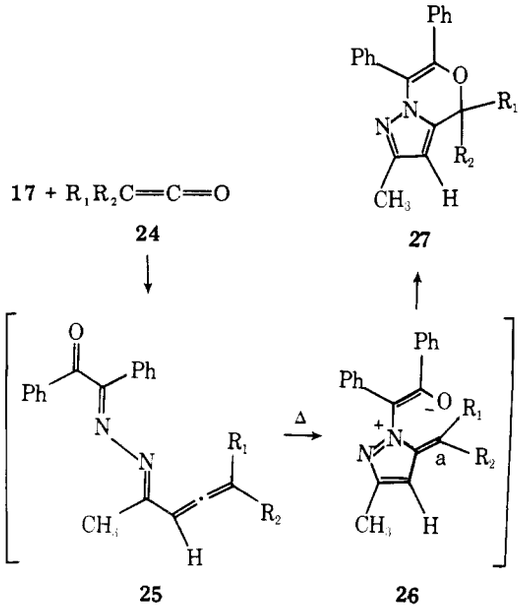
Thermolysis of a benzene solution of **20** (2 h at reflux) led to the formation of two products as determined by thin-layer chromatography (TLC) which were separated by column chromatography. The minor (39% isolated yield) product was a colorless solid isomeric with **20** but lacking a carbonyl in both the IR and ^{13}C NMR spectra. A 3-methylpyrazole ring was indicated by peaks at δ 104.5 (C-3) and 14.0 (CH_3) in the ^{13}C NMR spectrum and at δ 5.62 (s, 1 H, C-3 H)[11] and 2.19 (s, 3 H, CH_3) in the proton NMR spectrum. This data appeared consistent with the 4*H*-pyrazolo[5,1-*c*]-1,4-oxazine structure (**22**), and this was confirmed by a moderate IR band at 1640 cm^{-1} (vinyl ether) and a peak at δ 83.6 in the ^{13}C NMR spectrum[14] assignable to C-4 (Scheme III).

The major product of this thermolysis was also a colorless isomer of **20.** Again the ^{13}C and ^1H NMR spectra indicated a 1,3,5-trisubstituted pyrazole, but a strong band at 1680 cm^{-1} in the IR spectrum suggested a phenyl ketone. In addition to the ^{13}C NMR peak attributable to the 3-methyl carbon (δ 13.6), there were two other "saturated" carbon resonances (at δ 44.5 and 75.2). We assign these two signals to C-4 and C-9, respectively, of the 4,9-dihydropyrazolo[1,5-*b*]isoquinoline **23.** Apparently, **23** is isolated as a mixture of isomers about C-4 although appearing homogeneous by TLC. Two signals are observed for C-4 H (0.5 H each) in the ^1H NMR spectrum as well as for C-3 and the benzoyl carbonyl carbon in the ^{13}C NMR spectrum (Scheme III).

The propensity of conjugated azines to undergo intramolecular cycloaddition reactions via azomethinimines[10,11] (see Scheme I) suggests that the thermolysis of **20** involves a zwitterionic intermediate (**21**), and the products isolated are entirely consistent with this assumption. Intramolecular alkylation of the enolate oxygen by the activated exocyclic Michael acceptor (path a, Scheme III) would lead to the pyrazolooxazine **22,** while conjugate addition of the enolate carbon to one of the phenyl rings (path b, Scheme III) would yield, after rearomatization of the phenyl ring, the pyrazoloisoquinoline **23.**

This same phosphonium ylide (**17**) reacted equally well with phenylketene (**24a**), ketene[15] (**24b**), and vinylketene[16] (**24c**) as outlined in Scheme IV. In these cases, the allenyl azines **25a–c** proved too unstable to isolate, so the thermolyses were carried out directly by briefly heating the crude reaction mixtures. Single products were formed in each case which we isolated and identified (on the basis of spectral and analytical

Scheme IV



	R_1	R_2	yield of 27 (% isolated)
24–27a,	H	Ph	67
b,	H	H	65
c,	H	$-CH=CH_2$	35

analyses) as the pyrazolo[5,1-*c*]-1,4-oxazines **27a–c.** No other products could be detected or isolated.

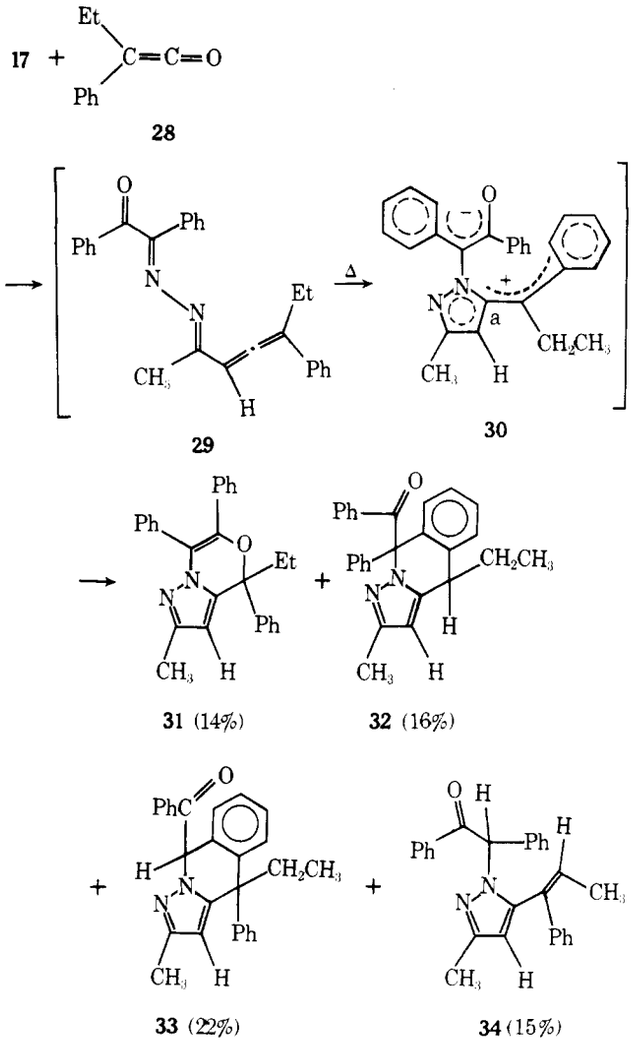
To further probe the effect of substituents at C_a on the course of these rearrangements, we allowed ethylphenylketene (generated in situ from α-phenylbutyryl chloride/Et_3N) to react with **17.** Thermolysis of the resulting allenyl azine (**29,** Scheme V) led to an extremely complex reaction mixture from which we were able to isolate four isomeric heterocycles, **31–34.** Two of the products were the "expected" pyrazolooxazine **31** and dihydropyrazoloisoquinoline **32.** In addition, significant amounts of the isomeric pyrazoloisoquinoline **33** and the monocyclic 5-(1-phenylpropenyl)pyrazole **34** were isolable. As above, all structural assignments were based on and are entirely consistent with spectral and analytical data.

All four products are consistent with a common intermediate, the azomethinimine **30** (Scheme V). Pyrazolooxazine **31** and pyrazoloisoquinoline **32** would result from O- and C-alkylation of the enolate portion of **30** as discussed above in the diphenylketene reaction (Scheme III). The other pyrazoloisoquinoline (**33**) would be the product of attack of the ortho carbon of the phenyl ring α to the pyrazole nucleus on position a. Monocyclic pyrazole **34** can be derived from **30** by a simple intramolecular proton transfer from the methylene group to the anionic portion of the molecule.

The mode of reactivity of these benzoyl stabilized azomethinimines (e.g., **21, 26,** and **30**) is dependent to a large extent on the nature of the substituents on the exocyclic carbon (a). In order to probe the effect of perturbing the anionic portion of these zwitterionic intermediates, we have investigated the reaction of carbethoxy stabilized ylide **35**[11] with several ketenes (summarized in Scheme VI.)

The reaction of **35** with diphenylketene proceeded smoothly to yield a single product after thermolysis of the allenyl azine. This material was isolated in good (80%) yield and identified as the pyrazolo[1,5-*b*]isoquinoline **38** on the basis of spectral and analytical data. No other products could be detected or isolated. However, although **35** reacted with phenyl- and vinylketene, as well as ketene itself, to form the corresponding allenyl azines **40a–c** (as determined by TLC), subsequent

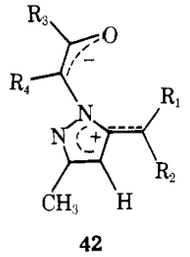
Scheme V



thermolysis led to complex tarry reaction mixtures from which no identifiable products could be isolated.

What was originally envisioned as a rather straightforward extension of known azine chemistry has proven to be another interesting and complex example of the unique cycloaddition chemistry of the azine system. The number and nature of substituents in the allenyl azine molecule have a great effect on the course of its thermal rearrangements. An analysis of the types of products formed as a function of the substituent patterns allows us to make some rational assumptions about both the nature of reactive intermediates and the factors important in determining the course of the rearrangements.

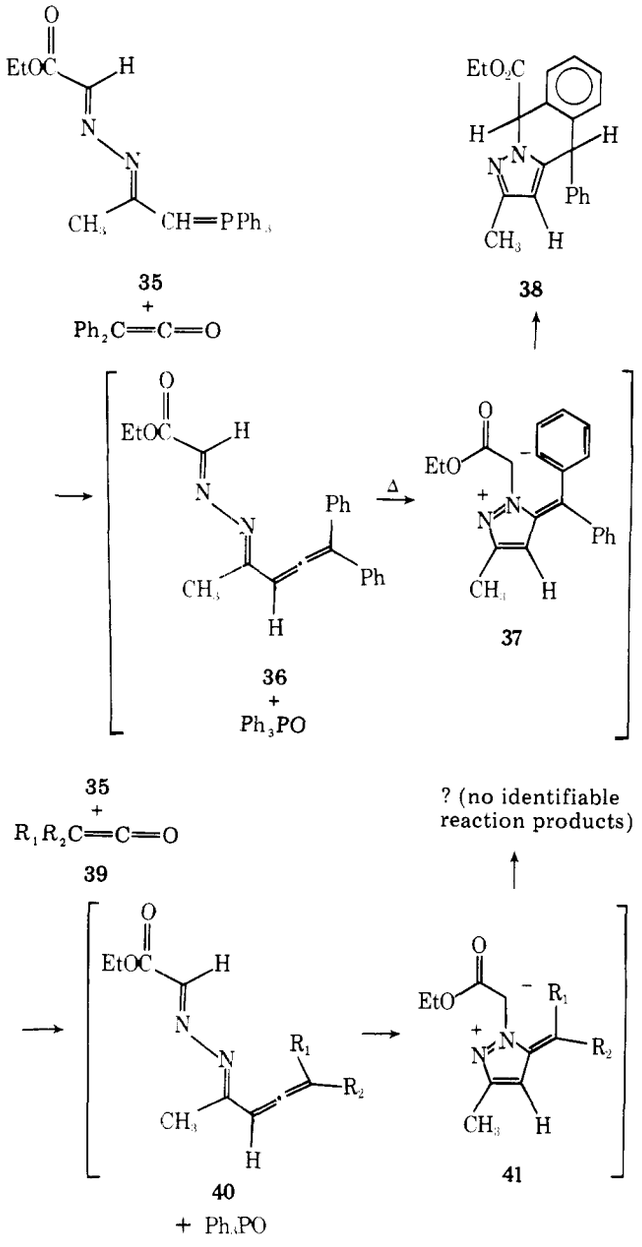
All of the products isolated are consistent with the intermediacy of resonance delocalized azomethinimines such as **42,** which are analogous to intermediates implicated and/or



42

isolated in a number of other azine cycloadditions (see Scheme I). Nearly all of the possible modes of intramolecular reactivity open to **42** have been observed.

Scheme VI

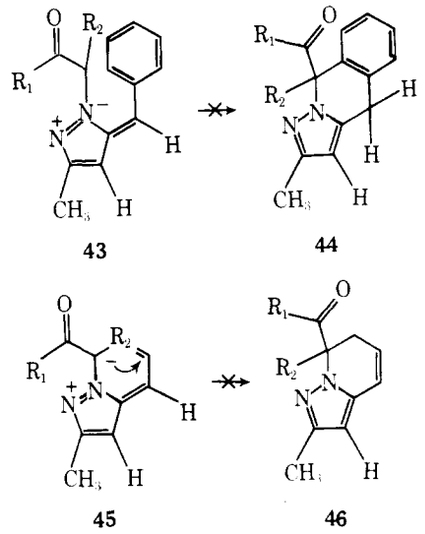


39–41: a, R_1 = H, R_2 = Ph; b, R_1 = H, R_2 = H; c, R_1 = H, R_2 = HC=CH_2

A comparison of the product composition in the thermolysis of the allenyl azine formed from diphenylketene and benzoyl stabilized ylide **17** (**20**, Scheme III) and the carbethoxy stabilized phosphorane **35** (**36**, Scheme VI) supports the intermediacy of dipoles such as **42** in these rearrangements as well as pointing up the effect on reactivity of substituents R_3 and R_4. Pyrazoloisoquinoline **38** is the only product formed when the cabethoxyallenyl azine **36** is thermolyzed (Scheme VI), while nearly equal amounts of the analogous pyrazoloisoquinoline **23** and pyrazolooxazine **22** arise from the benzoylallenyl azine **20** (Scheme III). One would expect a greater preference for C-alkylation (pyrazoloisoquinoline formation) with an ester stabilized carbanion (**42**; R_3 = OEt, R_4 = H) than with a ketone stabilized carbanion (**42**; R_3 = R_4 = Ph).

When R_1 or R_2 is a proton, subsequent reactions of dipole **42** depend on the nature of R_3 and R_4. The reaction of phenyl- and vinylketene with the benzoyl stabilized phosphorane **17** and thermolysis of the allenyl azines **25a** and **25c** (Scheme IV) led to exclusive formation of the pyrazolooxazine derivatives (**27a** and **27c**), that is, O-alkylation of the intermediate dipole. When the benzoyl group is replaced by a carbethoxy substituent, however, the same sequence of reactions leads to complex tarry mixtures, probably the result of intermolecular reactions (oligomerization/polymerization) of the azomethinimine intermediate (**41**, Scheme VI).

In neither of these systems were the products **44** and **46**,



a, R_1 = R_2 = Ph; b, R_1 = EtO, R_2 = H

expected from C-alkylation of the intermediate dipoles **43** and **45**, isolated or detected. This is somewhat surprising since in the systems derived from disubstituted ketenes C-alkylation is actually preferred (see Schemes III, V, and VI). One would certainly expect the pyrazolo[1,5-*a*]pyridine derivatives **46a** and **46b** to be formed readily since the conjugate addition of the anion to the vinyl group involves no loss of aromatic resonance energy. This seems to suggest that when R_1 is a proton in **42** the other substituent is unavailable for reaction with the anionic portion of the dipole. This forces the dipole (**42**) into an alternate mode of reactivity, either O-alkylation when R_3 = R_4 = Ph or unspecified intermolecular reactions when R_3 = EtO and R_4 = H.

When one substituent (R_1 or R_2) in **42** is considerably larger than the other, the prefered conformation of the ground state of the dipole will have the larger group (i.e., R_2) "trans" to the anionic center. This thermodynamically favorable orientation will be maintained as the anionic and cationic centers approach, and a significant amount of energy will be required to bring R_2 into a potentially reactive position. In the benzoyl stabilized systems [e.g., **42** (R_3 = R_4 = Ph)] the dipole has a reasonable alternative (O-alkylation) when faced with the barrier to reaction at R_2. However, since O-alkylation is also a relatively high energy process (see Scheme VI), the carbethoxy stabilized systems (**42**; R_3 = EtO, R_4 = H) have no reasonable intramolecular avenues of reaction available and decompose by complex intermolecular pathways. Further examination of the decomposition products of **41** or of the possible trapping of the azomethinimine **41** and its precursor **40** is underway.

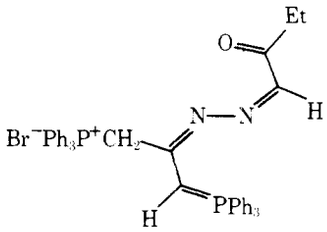
Experimental Section

General. Infrared spectra were recorded on a Perkin-Elmer Model 337 spectrophotometer and calibrated by comparison with a standard polystyrene film sample. Proton NMR spectra of approximately 10% (w/v) solutions in $CDCl_3$ were obtained on either a Varian A60-A or a Perkin-Elmer R12-b spectrometer. Chemical shifts are reported in parts per million (δ scale) vs. tetramethylsilane as an internal stan-

dard, and they were corrected for instrument drift/miscalibration by references to a standard solution containing approximately proton-equivalent amounts of Me_4Si, cyclohexane, acetone, 1,4-dioxane, methylene chloride, and chloroform in $CDCl_3$. In reporting the NMR data, the following abbreviations have been employed: coupling constant in hertz (J), singlet (s), doublet (d), doublet of doublets (dd), triplet (t), quartet (q), pentet (p), and multiplet (m). The ^{13}C NMR data were collected on a Brüker HFX-90 spectrometer equipped for Fourier transform pulsed NMR with a Nicolet 1085 data system. Electron impact mass spectra were recorded using a duPont CEC21-110D instrument with a resolution of 5000 (20% valley).

Dry (concentrated H_2SO_4 followed by sodium hydroxide and calcium chloride) nitrogen was routinely employed as the reaction atmosphere in all reactions. Eastman Chromagram precoated (silica gel on polyethylene) sheets impregnated with a fluorescent indicator were employed in thin-layer chromatographic operations. Melting points were obtained with a Thomas-Hoover apparatus, and boiling points are uncorrected. Elemental analyses were performed by Micro Analysis Inc. of Wilmington, Del.

Diphenylacetyl chloride,[17] crotonyl chloride,[18] and α-phenylbutyryl chloride[19] were prepared by known methods and distilled prior to use. Phenylacetyl choride was purchased from the Aldrich Chemical Co. and distilled prior to use. Ylide **35** was prepared[11] by mild hydrolysis of the ylide salt **47**, and the resulting mixture with Ph_3PO was used



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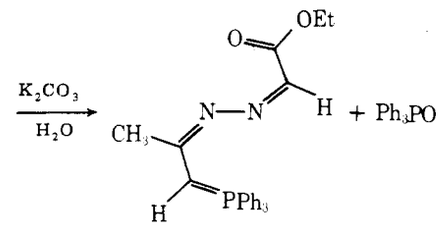

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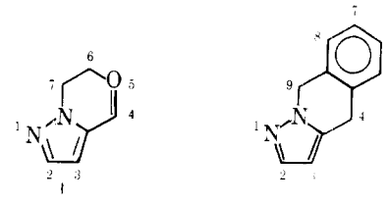
as is in further reactions. Both benzene and triethylamine were dried and distilled from sodium metal. In light of its toxicity, benzene should be replaced by toluene or some other suitable aprotic solvent in any attempts to repeat or extend this work. All glassware was baked at 110–120 °C for a minimum of 4 h before use. The numbering systems used in referring to the 4*H*-pyrazolo[5,1-*c*]-1,4-oxazine (**e.g., 48**) and 4,9-dihydropyrazolo[1,5-*b*]isoquinoline (e.g., **49**) systems are shown in Scheme VII.

Reaction of Ylide 17 with Diphenylketene. Isolation of the Allenyl Azine 20 (1-Diphenylvinylidene-2-benzoylbenzylidenehydrazonopropane). To an orange solution of 1.05 g (2.0 mmol) of ylide **17** in 20 mL of benzene was added 0.42 g (4.15 mmol) of triethylamine. The reaction mixture was cooled to ~5 °C with an ice bath (some **17** crystallized but did not hamper the reaction), and a solution of 0.58 g (2.5 mmol) of diphenylacetyl chloride in 5 mL of benzene was added dropwise over 15 min (cooling maintained throughout the addition). The resulting light orange hazy solution was then stirred at 10–15 °C (maintained by intermittent immersion in an ice bath) for 2 h. The solvent was removed in vacuo at less than 35 °C, and the residual orange oil was rapidly chromatographed on a 35 × 350 mm silica gel column eluting with methylene chloride. The mobile orange band was collected in three 125-mL fractions which were combined, and the solvent was evaporated (<35 °C) to yield 0.92 g (theory = 0.88 g) of **20** as an orange solid. Crystallization from warm MeOH afforded an analytical sample: mp 115–115.5 °C; IR (CCl_4) 1930 (C=C=C), 1685 (C=O), 1600, 1580, 1495 cm^{-1}; ^1H NMR δ 2.21 (s, 3 H, CH_3C=N–), 6.28 (br s, 1 H, HC=CCPh$_2$), 7.21 (s) and 7.11–7.48 (m) (total of 16 H, aromatic), 7.51–8.00 (m, 4 H, aromatic ortho to C=N/C=O); ^{13}C NMR δ 14.8 (CH_3), 100.2 (C=C=CPh$_2$), 162.9, 163.7 (C=N), 197.9 (C=O), 212.1 (C=C=C).

Anal. Calcd for $C_{31}H_{24}N_2O$: C, 84.52; H, 5.49. Found: C, 84.35; H, 5.41.

Scheme VII



48 **49**

Reaction of Ylide 17 with Diphenylketene. In Situ Thermolysis of the Allenyl Azine 20. Preparation of 2-Methyl-4,4,6,7-tetraphenyl-4*H*-pyrazolo[5,1-*c*]-1,4-oxazine (22) and 2-Methyl-4,9-dihydro-9-benzoylpyrazolo[1,5-*b*]isoquinoline (23). To an orange solution of 1.05 g (2.0 mmol) of ylide **17** and 0.23 g (2.28 mmol) of triethylamine in 20 mL of benzene was added 0.48 g (2.08 mmol) of diphenylacetyl chloride in 5 mL of benzene dropwise over 3 min. There was a slight exotherm, the color faded to a pale orange, and a very fine precipitate formed (presumably Et_3N·HCl). The hazy solution was stirred at ambient temperature for 1 h and at reflux (80 °C) for 2 h. Thin-layer chromatography (TLC; CH_2Cl_2, silica gel) showed the formation of two products (along with Ph_3PO). After removal of solvent in vacuo, the crude reaction mixture was chromatographed on a 35 × 350 mm silica gel column eluting with methylene chloride. This yielded the following in order of elution.

(a) **22** (0.34 g, 39%) as a tan solid. Recrystallization from CH_2Cl_2/heptane yielded a colorless analytical sample: mp 233.5–234.5 °C; IR (KBr) 1640, 1540, 1485, 1440 cm^{-1}; ^1H NMR δ 2.19 (s, 3 H, C-2 CH_3), 5.62 (s, 1 H, C-3 H), 6.93 (s, 5 H, C-6 or C-7 Ph), 7.11 (s, 5 H, C-7 or C-6 Ph), 7.18 (s, 10 H, C-4 Ph$_2$); ^{13}C NMR δ 14.0 (C-2 CH_3), 83.6 (C-4), 104.5 (C-3), 149.4 (C-6); mass spectrum, *m/e* (% base peak) 440 (2.9, M^+), 336 (30.8), 335 (100), 294 (19.5).

Anal. Calcd for $C_{31}H_{24}N_2O$: C, 84.52; H, 5.49. Found: C, 84.40; H, 5.26.

(b) **23** (0.43 g, 49%) as an amber resinous solid. Crystallization from 95% ethanol afforded a colorless analytical sample: mp 157–172 °C; IR ($CHCl_3$) 1680, 1595, 1540, 1480, 1435 cm^{-1}; ^1H NMR δ 1.98 (s) and 2.01 (s) (total of 3 H, C-2 CH_3), 4.84 (br s, 0.5 H, C-4 H), 5.49 (br s, 1 H, C-3 H), 5.94 (br s, 0.5 H, C-4′ H), 6.46–7.80 (m, 20 H, aromatic); ^{13}C NMR δ 13.6 (C-2 CH_3), 44.5 (C-4), 75.2 (C-9), 104.0 (C-3), 104.6 (C-3′), 193.5 (C=O), 194.2 (C=O′).

Anal. Calcd for $C_{31}H_{24}N_2O$: C, 84.52; H, 5.49. Found: C, 84.55; H, 5.33.

Reaction of Ylide 17 with Phenylketene. Preparation of 2-Methyl-4,6,7-triphenyl-4*H*-pyrazolo[5,1-*c*]-1,4-oxazine (27a). Ylide **17** (1.05 g, 2.0 mmol) was reacted as above with 0.64 g (6.35 mmol) of triethylamine and 0.66 g (4.27 mmol) of phenylacetyl chloride (Aldrich). Column chromatography (35 × 350 mm of silica gel, CH_2Cl_2) of the crude product yielded 0.49 g (67%) of **27a** as a tan solid. Recrystallization from ethanol afforded a colorless analytical sample: mp 211–213 °C; IR (KBr) 1640, 1550, 1495, 1440 cm^{-1}; ^1H NMR δ 2.21 (s, 3 H, C-2 CH_3), 5.78 (s, 1 H, C-3 H), 6.24 (s, 1 H, C-4 H), 7.01 (s, 5 H, C-4 Ph), 7.16–7.66 (m, 10 H, C-6 and C-7 Ph); ^{13}C NMR δ 14.0 (C-2 CH_3), 75.7 (C-4), 102.6 (C-3), 149.6 (C-6); mass spectrum, *m/e* (% base peak) 365 (16.8, $M^+ + 1$), 364 (56.7, M^+), 260 (21.0), 259 (100).

Anal. Calcd for $C_{25}H_{20}N_2O$: C, 82.39; H, 5.53. Found: C, 82.26; H, 5.34.

Reaction of Ylide 17 with Ketene. Preparation of 2-Methyl-6,7-diphenyl-4*H*-pyrazolo[5,1-*c*]-1,4-oxazine (27b). Ketene was generated by the pyrolysis of acetone according to the method of Williams and Hurd.[15] The apparatus was calibrated by passing the ketene stream (after running for 30 min to thoroughly purge the system) thru a sodium hydroxide solution of known concentration for a known period of time, followed by titration of the residual hydroxide to the phenolpthalein end point. The rate of ketene generation was calculated to be 2.7 mmol/min (average of two runs). The ketene stream was then bubbled through a solution of 1.05 g (2.0 mmol) of ylide **17** in 25 mL of benzene for 5 min (~13.5 mmol of ketene). The resulting solution was stirred for 5 min at ambient temperature and 2 h at reflux. After removal of the solvent in vacuo, crude **27b** (0.38 g, 65%) was isolated as a tan solid by trituration of the residue with cold ethanol. Recrystallization from ethanol afforded a colorless analytical sample: mp 168.5–169.0 °C; IR (KBr) 1645, 1555, 1495, 1450 cm^{-1}; ^1H NMR δ 2.23 (s, 3 H, C-2 CH_3), 5.25 (s, 2 H, C-4 H_2), 5.90 (s, 1 H, C-3 H), 7.10 (s, 5 H, aromatic), 7.30 (br s, 5 H, aromatic); ^{13}C NMR δ 14.0 (C-2 CH_3), 63.2 (C-4), 101.0 (C-3), 149.4 (C-6); mass spectrum, *m/e* (% base peak) 289 (20.8, $M^+ + 1$), 288 (100, M^+), 259 (23.1), 183 (46.0).

Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59. Found: C, 79.02; H, 5.44.

Reaction of Ylide 17 with Vinylketene. Preparation of 2-Methyl-4-vinyl-6,7-diphenyl-4*H*-pyrazolo[5,1-*c*]-1,4-oxazine (27c). Ylide **17** (1.05 g, 2.0 mmol) was reacted as above with 0.57 g (5.65 mmol) of triethylamine and 0.32 g (3.06 mmol) of crotonyl chloride. Column chromatography (35 × 350 mm of silica gel, CH_2Cl_2) of the crude reaction mixture yielded 0.22 g (35%) of **27c** as a slightly yellow solid, mp 113–116 °C. Recrystallization afforded a colorless analytical sample: mp 118–119 °C; IR (KBr) 1640, 1540, 1495, 1450 cm^{-1}; ^1H NMR δ 2.18 (s, 3 H, C-2 CH_3), 5.13–6.40 (m, 5 H, vinyl, C-4 H, and C-3 H), 7.00 (br s, 5 H, aromatic), 7.20 (br s, 5 H, aromatic); ^{13}C NMR δ 14.0 (C-2 CH_3), 74.2 (C-4), 101.6 (C-3), 119.5 (-CH=CH_2), 149.5 (C-6); mass spectrum, *m/e* (% base peak) 315 (7.1, $M^+ + 1$), 314 (26.4, M^+), 210 (31.3), 209 (100).

Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77. Found: C, 80.30; H, 5.92.

Reaction of Ylide 17 with Ethylphenylketene. A solution of 1.57 g (3.0 mmol) of ylide **17** in 25 mL of benzene was treated as above with 0.55 g (5.45 mmol) of Et_3N followed by 0.74 g (4.05 mmol) of α-phenylbutyryl chloride. After stirring for 1 h at room temperature and 2 h at reflux, the solvent was removed in vacuo and the residue chromatographed on silica gel (35 × 350 mm) eluting with CH_2Cl_2. This yielded the following in order of elution.

(a) 2-Methyl-4,6,7-triphenyl-4-ethyl-4*H*-pyrazolo[5,1-*c*]-1,4-oxazine (**31**; 0.16 g, 14%) as a white solid: mp 109–111 °C (ethanol); IR (KBr) 1640 (m), 1600 (w), 1550 (m), 1500 (s), 1460 (s), 1440 (s) cm^{-1}; ^1H NMR δ 1.06 (br t, $J \cong 7.5$ Hz, 3 H, -CH_2CH_3), 2.25 (s, 3 H, C-2 CH_3), 2.32 (br q, $J \cong 7.5$ Hz, 2 H, -CH_2CH_3), 6.01 (s, 1 H, C-3 H), 6.97, 7.05, and 7.12 (s, 5 H each, aromatic); ^{13}C NMR δ 8.6 (-CH_2CH_3), 14.1 (C-2 CH_3), 33.9 (-CH_2CH_3), 82.3 (C-4), 102.2 (C-3), 149.4 (C-6). Calcd for $C_{27}H_{24}N_2O$: *m/e* 392.188. Found: *m/e* 392.191.

(b) 2-Methyl-4-ethyl-9-phenyl-9-benzoyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (**32**; 0.19 g, 16%) as a white solid: mp 198–201 °C; IR 1690 (s), 1595, 1575, 1545, 1485, 1445 cm^{-1}; ^1H NMR δ 0.50–1.49 (m, 5 H, -CH_2CH_3), 2.02 (s, 3 H, C-2 CH_3), 3.89 (dd, J = 5.5 and 8.0 Hz, 1 H, C-4 H), 5.82 (s, 1 H, C-3 H), 6.49–7.39 (m, 14 H, aromatic); ^{13}C NMR δ 12.3 (-CH_2CH_3), 13.8 (C-2 CH_3), 31.6 (-CH_2CH_3), 41.6 (C-4), 75.9 (C-9), 104.1 (C-3), 193.3 (C=O).

Anal. Calcd for $C_{27}H_{24}N_2O$: C, 82.62; H, 6.16. Found: C, 82.63; H, 6.15.

(c) A mixture of 2-methyl-4-phenyl-4-ethyl-9-benzoyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (**33**) and 1-phenyl-1-[3-methyl-5-(1-phenylpropenyl)pyrazol-1-yl]acetophenone (**34**) (0.44 g, 37.5%) as an amber semisolid. Treatment of the mixture dissolved in 2.0 mL of ethanol with 2.5 mL of a saturated ethanol solution of picric acid yielded the picrate salt of **33** (0.41 g; 22% based on ylide **17**) as a yellow solid, mp 181.5–182 °C.

Anal. Calcd for $C_{33}H_{27}N_5O_8$: C, 63.76; H, 4.38. Found: C, 63.78; H, 4.29.

The free base (**33**) was liberated by treatment of the picrate salt with dilute sodium hydroxide, extracting with ether, drying the organic layer (Na_2SO_4), and evaporation of the solvent in vacuo. This yielded **33** as a colorless oil: IR 1700, 1600, 1580, 1544, 1500, 1450 cm^{-1}; ^1H NMR δ 0.46 (t, J = 7.7 Hz, 3 H, -CH_2CH_3), 2.10 (s, 3 H, C-2 CH_3), 2.43 (q, J = 7.7 Hz, 2 H, -CH_2CH_3), 5.60 (s, 1 H, C-3 H), 6.85 (s, 1 H, C-9 H), 6.89–7.52 (m, 12 H, aromatic), 7.78 (m, 2 H, aromatic ortho to C=O); ^{13}C NMR δ 8.8 (-CH_2CH_3), 13.8 (C-2 CH_3), 37.1 (-CH_2CH_3), 49.0 (C-4), 63.5 (C-9), 102.8 (C-3), 195.4 (C=O).

Neutralization of the filtrate from the picrate formation above with dilute NaOH, extraction with ether, drying of the organic phase (Na_2SO_4), and evaporation of solvent yielded **34** as an amorphous amber solid: IR 1705, 1595, 1580, 1545 cm^{-1}; ^1H NMR δ 1.67 (d, J = 6.6 Hz, 3 H, >C=CHC**H**$_3$), 2.03 (C-3 CH_3), 5.73 (q, J = 6.6 Hz, 1 H, >C=C**H**CH_3), 5.86 (s, 1 H, C-4 H), 6.17 (s, 1 H, PhCOC**H**Ph-), 6.52–7.30 (m, 15 H, aromatic); ^{13}C NMR δ 13.8 (C-3 CH_3), 15.3 (>C=CH**C**H$_3$), 67.0 (PhC**H**CHPh-), 107.4 (C-4), 193.1 (C=O). Calcd for $C_{27}H_{24}N_2O$: *m/e* 392.188. Found: *m/e* 392.184.

Reaction of Ylide 35 with Diphenylketene. Preparation of 2-Methyl-4-phenyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline-9-carboxylic Acid Ethyl Ester (38). The crude mixture of ylide **35** and Ph_3PO prepared from 3.97 mmol of ylide salt precursor **47** was charged to a 50-mL three-neck round-bottom flask and dissolved in 20 mL of benzene. Triethylamine (1.03 g, 10 mmol) was added, followed by the dropwise addition over 5 min of a solution of 1.39 g (6 mmol) of diphenylacetyl chloride in 10 mL of benzene, which caused a slight exotherm. The reaction was stirred at ambient temperature for 1 h and at reflux for 2 h, the solvent was removed in vacuo, and the crude residue was chromatographed as above to yield 1.05 g (80%) of **38** as a light orange solid. Recrystallization from ethanol afforded a colorless analytical sample: mp 134.5–135.5 °C; IR (KBr) 1750, 1545, 1500, 1455, 1295 cm^{-1}; ^1H NMR δ 1.12 (t, J = 7.0 Hz, 3 H, C**H**$_3$CH$_2$), 2.19 (s, 3 H, C-2 CH_3), 4.03 (q, J = 7.0 Hz, 2 H, CH_3C**H**$_2$), 5.20 (br s, 1 H, C-4 H), 5.75 (s, 1 H, C-3 H), 5.95 (br s, 1 H, C-9 H), 6.85–7.55 (m, 9 H, aromatic); ^{13}C NMR δ 13.8 (**C**H$_3$CH$_2$O- and C-2 CH_3), 44.1 (C-4), 62.1 (CH_3**C**H$_2$O- and C-9), 103.2 (C-3), 169.3 (EtO_2C-); mass spectrum, *m/e* (% base peak) 332 (12.0, M^+), 260 (33.8), 259 (100), 217 (10.6), 216 (16.8).

Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06. Found: C, 75.93; H, 5.98.

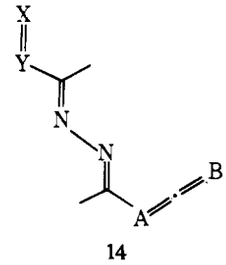
Reaction of Ylide 35 with Phenylketene. The crude mixture of **35** and Ph_3PO prepared from 2.0 mmol of **47** was allowed to react at ambient temperature in 20 mL of benzene with 0.52 g (5.15 mmol) of triethylamine and 0.62 g (4.0 mmol) of phenylacetyl chloride for 1 h. The formation of the allenyl azine **40a** was observed by TLC (CH_2Cl_2, silica gel). When the reaction was heated under reflux for 2 h, it turned very dark and TLC showed the disappearance of **40a** and the formation of a number of non-TLC "mobile" products. The reaction mixture was poured into 50 mL of H_2O, 30 mL of benzene was added, and the layers were thoroughly mixed and separated. The organic layer was extracted two times with 10 mL of 5% HCl and once with 10 mL of water. The organic layer was dried (Na_2SO_4) and the solvent removed in vacuo. The dark brown residue was heated with five 20-mL portions of ether (with decantation of the supernatant each time). The hot ether-insoluble portion (0.22 g) was dark brown glass containing at least nine products (by TLC) with similar R_f values. Concentration of the ether solutions (above) to ~20 mL and chilling in ice lead to the crystallization of 0.77 g (70%) of Ph_3PO. The filtrate from this contained at least five products (in addition to some residual Ph_3PO) which again had very similar R_f values. All attempts at separating these complex mixtures proved fruitless.

Reaction of Ylide 35 with Ketene. Ketene, generated as above in the preparation of **27b**, was bubbled through a benzene solution of the crude **35**/Ph_3PO mixture (from 2.0 mmol of **47**) for 3 min (~7.5 mmol of ketene). The reaction was stirred at ambient temperature for 1 h, at which time TLC (CH_2Cl_2, silica gel) indicated the formation of a single product, presumably allenyl azine **40b**. The reaction mixture was then heated under reflux for 2 h, during which time the solution turned extremely dark. Thin-layer chromatography (silica gel, CH_2Cl_2) showed the disappearance of the spot assigned to the allenyl azine **40b** and the formation of a number of (6–10) new spots with very low (<0.3) R_f values (R_f values of 0.5–0.75 would have been expected for the products of this reaction). Removal of the solvent in vacuo and trituration of the dark brown residue with ether allowed the isolation of 0.84 g (78% of theory) of Ph_3PO, identical in all respects with authentic material. The ether-soluble material was a nearly black viscous oil containing at least 6–10 products with very similar R_f values. Attempts at product isolation by crystallization (CH_2Cl_2/heptane, EtOH/water, ether/hexane) failed to give any solid material. Various solvent combinations ($CHCl_3$/MeOH, benzene, EtOAc) failed to improve the TLC separation.

Reaction of Ylide 35 with Vinylketene. The crude mixture of **35** and Ph_3PO prepared from **47** was allowed to react at ambient temperature in 20 mL of benzene with 0.52 g (5.15 mmol) of triethylamine and 0.42 g (4.0 mmol) of crotonyl chloride for 1 h. The formation of the allenyl azine **40c** was observed by TLC. Heating at reflux for 2 h and workup as above yielded 0.89 g (80%) of Ph_3PO and 0.25 g of a dark brown gum containing a number (5–10) of products with similar R_f values in a variety of solvents. All attempts at separation failed.

Conclusions

The thermal rearrangements of 1-oxo-3,4-diaza-2,4,6,7-octatetraenes (allenyl azines) provide another example of the unique cycloaddition behavior and potential synthetic utility of the azine functional group. Our results have confirmed, for the most part, our original hypothesis concerning the reactivity of azines conjugated with cumulene systems. This reaction concept should be readily extended to general azine–cumulene systems such as **14**. Work in these laboratories will



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continue to be directed toward the understanding and synthetic exploitation of the 1,3 reactivity of 2,3-diazabutadienes.

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Registry No.—**17** (charged), 63570-24-1; **17** (unchanged), 63570-25-2; **20**, 67478-68-6; **22**, 67478-69-7; **23**, 67478-70-0; **27a**, 67478-71-1; **27b**, 67478-72-2; **27c**, 67478-73-3; **31**, 67478-74-4; **32**, 67478-75-5; **33**, 67478-76-6; **33** picrate, 67478-77-7; **34**, 67478-78-8; **35**, 63570-22-9; **38**, 67478-79-9; **40a**, 67478-80-2; **40b**, 67478-81-3; **40c**, 67478-82-4; **47**, 63570-20-7; diphenylketene, 525-06-4; phenylketene, 3496-32-0; ketene, 463-51-4; vinylketene, 50888-73-8; ethylphenylketene, 20452-67-9; diphenylacetyl chloride, 1871-76-7; phenylacetyl chloride, 103-80-0; crotonyl chloride, 10487-71-5; α-phenylbutyryl chloride, 36854-57-6.

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Stereoselectivity in Photocycloaddition of Bicyclic Enones to Olefins

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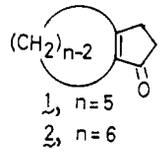
Stereoselectivity in photocycloaddition of bicyclic enones **1**, **2**, **5**, and **6** to 2-butene and cyclohexene is discussed. In the cases of **1** and **5**, having a five-membered ring fused to the double bond of monocyclic enones, from two to four kinds of cycloadducts were always obtained regardless of the ring size of the enone moieties, and, therefore, stereoselectivity is relatively low. On the other hand, in the cases of **2** and **6**, having a six-membered ring fused to the double bond of monocyclic enones, the formation of cis-anti-trans cycloadducts proceeded stereoselectively. This remarkable effect of fused ring size on stereoselectivity in photocycloaddition is ascribed to the degree of nonbonded hydrogen interaction in 1,4-diradical intermediates and can be associated with differing flexibility and rigidity of cyclohexane and cyclopentane rings.

While the stereochemistry of photocycloaddition and the factors controlling it are the most important and intriguing problems in the field of photocycloaddition of cyclic enones to olefins, relatively few studies have been made. Recently reports on the stereochemical assignment of photocycloadducts of cyclohexenone to cycloheptene,[1a] monocyclic cyclohexenone derivatives to cyclopentene,[1b] and bicyclic cyclohexenone **5** to 2-butene [1c]have appeared. In these reactions, photocycloaddition proceeded nonstereoselectively, and, therefore, two or three stereoisomers of cycloadducts were always formed. Subsequently, we reported that photocycloaddition of bicyclic cyclopentenone **2** to cyclohexene took place stereoselectively to afford cis-anti-trans adduct **15** as a sole cycloadduct, though enones **1**, **3**, and **4** gave mixtures of three or four stereoisomeric cycloadducts.[2] This marked distinction in stereoselectivity in photocycloaddition between these enones was interpreted in terms of differences in steric effects in the alicyclic rings fused to the double bond of cyclopentenone. To further clarify this concept, we have investigated the stereoselectivity in photocycloaddition of bicyclic



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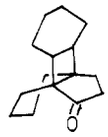
3, n=7
4, n=8



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enones **1**, **2**, **5**, and **6**, composed of five- and six-membered rings, to 2-butene and cyclohexene.

First, we examined the photoreaction with about a 20-fold excess of *cis*- or *trans*-2-butene in methylene chloride at −70 °C. In the case of bicyclic cyclopentenone **1**, four stereoisomeric cycloadducts (**7a–d**)[3] were obtained. With bicyclic cyclohexenone **5**, as also reported by Cargill et al.,[1c] three isomeric cycloadducts (**10a–c**)[3] and keto olefin **11** were given. On the other hand, with enones **2** or **6** one of two kinds of cycloadducts (**8a** or **12a**)[3] was obtained in quantity, respectively, along with small amounts of another cycloadduct (**8b** or **12b**)[3]

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