Tetrahedron Vol. 34, pp. 2617–2626
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0040-4020/78/0501-2617/$02.00/0

# THE DIELS–ALDER CHEMISTRY OF 1-VINYL-2-PYRIDONES†

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(*Received in the USA* 16 *November* 1977; *Received in the UK for publication* 26 *January* 1978)

**Abstract**—The Diels–Alder chemistry of a series of 1-vinyl-2-pyridones using a variety of dienophilic species including dimethyl acetylenedicarboxylate, benzyne, maleic anhydride and methyl vinyl ketone has been explored in order to determine the generality of this method for generation of *N*-vinylisoquinuclidines. In general, the cycloaddition reactions lead to modestly high yeilds of the azabicyclooctane products. In the course of these studies, we noted that retro-Diels–Alder reactions of *N*-vinylisoquinuclidienones lead to generation of *N*-vinylisocyanates and a benzene fragment while the corresponding mono-unsaturated isoquinuclidenones form the corresponding pyridones by elimination of an ethylene unit. Lastly, the regio- and stereochemical courses for the $\pi 2 + \pi 4$ addition reactions of methyl vinyl ketone and 1-vinyl-2-pyridones were investigated. The major products from these reactions appear to result from reaction pathways predicted to be of low energy using first-order molecular orbital methods.

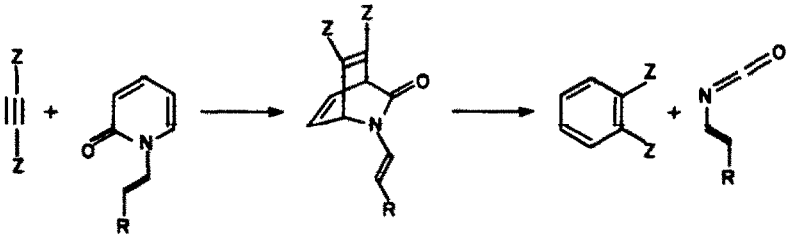
The Diels–Alder chemistry of compounds containing the dienamine or dienamide grouping has been used advantageously for the construction of interesting heterocyclic compounds and nitrogen containing natural products.[2] A preliminary phase of our current studies, concerning the development of novel methods for hydroisoquinoline synthesis utilizing aza-Claisen rearrangements of properly functionalized *N*-vinylisoquinuclidenes,[1,3] was devoted to an exploratory investigation of the Diels–Alder chemistry of a series of 1-vinyl-2-pyridones. Although the literature holds isolated reports describing this and related methods for generation of isoquinuclidenes,[4,5] information relating to the employment of this strategy to prepare the *N*-vinyl substituted systems is minimal. Indeed, we have found that efficiencies of $\pi 2 + \pi 4$ cycloaddition reactions of *N*-vinylpyridones with a series of dienophiles are dependent upon the nature of the dienophilic species and the substituents on the exocyclic *N*-vinyl moieties. Both of these factors strongly influence the rates of Michael addition reactions involving the exocyclic vinylamide residue, and retro Diels–Alder fragmentations and hydrolysis of the enamide functions in products, all of which combine to lead to diminished yields of the desired *N*-vinylisoquinuclidene products. The results of this exploratory study are summarized below using an outline that is based upon the types of dienophiles investigated.

*Cycloaddition reactions using dimethyl acetylenedicarboxylate*

In order to determine if the methodology developed by Heep[4a] to synthesize *N*-substituted isoquinuclidienones, exemplified by the cycloaddition reactions of 1 - substituted - 4,6 - dimethyl - 2 - pyridone with dimethyl acetylenedicarboxylate **1**, is applicable to the preparation of *N*-vinyl-substituted systems, the Diels–Alder chemistry of **1** with a series of 1-vinyl-2-pyridones was explored. The acetylenic dienophile was found to undergo smooth cycloaddition to 1-β-styryl-2-pyridone **2**[6] at elevated temperatures to furnish the *N*-styrylisoquinuclidienone **4** (22%). Purification of **4** by silica gel TLC yielded material which was easily characterized as the product of Diels–Alder addition using spectroscopic methods (UV max 293 nm (18,000); $^1$H NMR characteristic vinyl and bridghead proton resonances at $\delta$ 6.98, 4.76 and 6.01). The *N-trans*-propenylisoquinuclidienone **5** can be obtained in an analogous fashion by reaction of **1** with 1-*trans*-propenyl-2-pyridone **3**.[7]

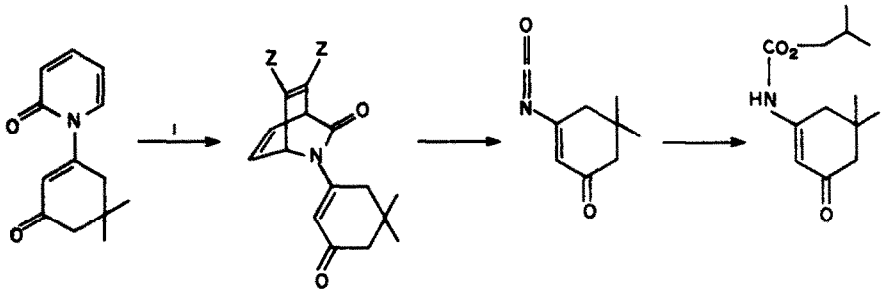
†A preliminary report of the results of these studies has been presented.[1]

‡Camille and Henry Dreyfus Foundation Teacher–Scholar grantee 1975–80.



**1**: (Z = $CO_2CH_3$) **2**: (R = Ph) **3**: (R = $CH_3$) **4**: (R = Ph) **5**: (R = $CH_3$) **6** **7**

The surprisingly low yields associated with these Diels–Alder reactions appear to be directly attributable to two factors. First, under the high temperature reaction conditions (*ca.* 100°C) required to produce both **4** and **5**, retro Diels–Alder fragmentations of the isoquinuclidienone systems occur to produce dimethyl phthalate **6** and most probably the *N*-vinylisocyanates **7** (R = Ph or R).[4a,8] The deleterious effect of this process on reactions used to produce isoquinuclidienones is dramatized by observation made during attempts to prepare the cyclohexenonylazabicyclic system **9**. Reaction of the dimethylcyclohexenonyl - 2 - pyridone **8**[7] with **1** failed to produce detectable quantities of the isoquinuclidienone **9** using a variety of conditions. In each case, dimethyl phthalate was formed along with the interesting vinylisocyanate **10**, which could be trapped as the *iso*-butyl carbamate **11** when *iso*-butyl alcohol was used as solvent for the cycloaddition reaction. These observations appear to highlight a positive feature of the retro Diels–Alder processes concerning its utilization as a general method to prepare highly reactive substances containing the carbon nitrogen double bond. This aspect has been briefly explored using the closely related *N*-ethoxycarbonyl isoquinuclidiene **12**, prepared previously in our laboratory by the reaction of **1** with 1 - ethoxycarbonyl - 1,2 - dihydropyridine.[9] Thermally induced $\pi 2 + \pi 4$ fragmentation of this substance would generate the *N*-ethoxycarbonyl formaldimine **13**, a reactive intermediate used previously in the synthesis of interesting heterocyclic compounds.[10] As expected, thermolysis of **12** in refluxing carbon tetrachloride led to quantitative production of dimethyl phthalate. The two-carbon formaldimine fragment produced in this reaction could be isolated as its crystalline trimer **14**[11] using slightly different reaction conditions in which boron trifluoride etherate serves to Lewis acid catalyze the retro Diels–Alder reaction and stabilize the aldimine. Alternatively, the short-lived aldimine **13** can be used in ensuing reactions to generate interesting azabicyclic systems. This is exemplified by the preparation of the amido ether **16** from reaction of **12** with boron trifluoride etherate in the presence of 2,3-benzofuran **15**.



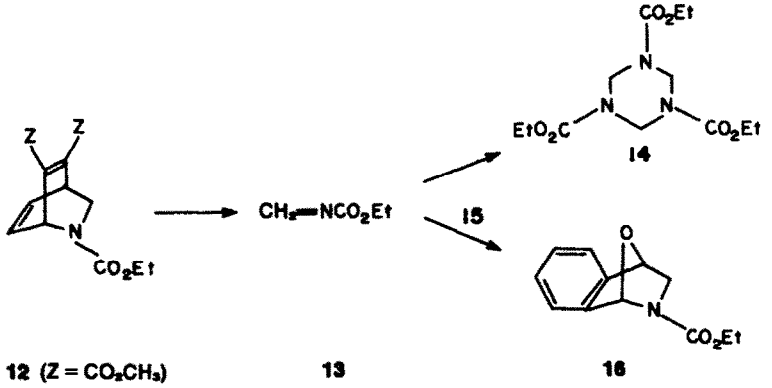

**8** **9** ($Z = CO_2CH_3$) **10** **11**

Alternate processes, resulting from addition of the acetylenic ester to the exocyclic *N*-vinyl moiety, are responsible for the reduced yields of isoquinuclidienone products when 1-vinyl-2-pyridones lacking phenyl or carbonyl substitution on the vinyl group are used. For example, the parent 1-vinyl-2-pyridone **17**[12] undergoes reaction with dimethyl acetylenedicarboxylate by these pathways exclusively, resulting in production of the benzene-tetracarboxylic acid ester **19** and **20**. The reaction modes followed in this case appear to be directly analogous to those noted in reactions of simple enamines[13] and closely related 1-vinyl-1,2-dihydropyridine[9] with **1**. Accordingly, Michael addition of the enamide function in **17** to the acetylenic ester would result in formation of the dipolar intermediate **18**, which is capable of proceeding to the tetracarboxylic acid esters by the two pathways shown.

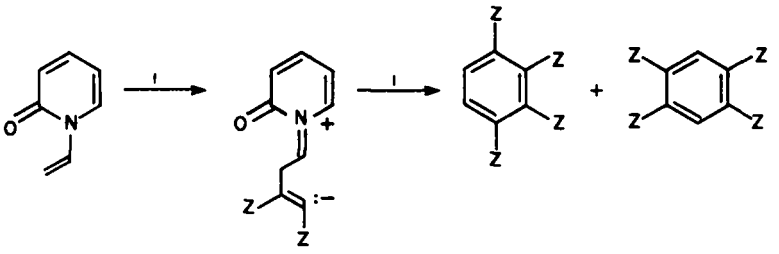
Thus, it appears that despite the simplicity of the synthetic design, Diels–Alder routes to *N*-vinylisoquinuclidienones are somewhat limited in terms of the range of substituents that are required on the *N*-vinyl moiety to minimize competitive additions to the exocyclic vinyl groups of the 1-vinyl-2-pyridone substrates or ensuing retro Diels–Alder fragmentations of the generated azabicyclic systems.

*Cycloaddition reactions using benzyne*

Diels–Alder addition reactions of benzyne with 1-vinyl-2-pyridones appear to be potentially useful for generation of *N*-vinylisoquinuclidienones containing



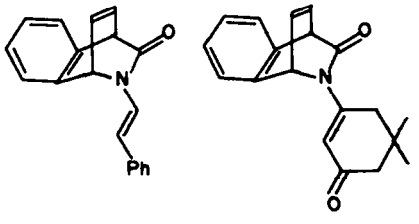

**12** ($Z = CO_2CH_3$) **13** **16**



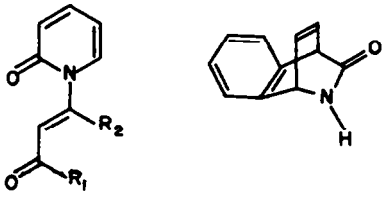
17 18 (Z = $CO_2CH_3$) 19 20

benzoetheno bridges. Although precedent for this procedure is found in an earlier study by Bauer and his collaborators[4b] of the simple 1-methyl-2-pyridone system, the possibility did exist that the presence of exocyclic vinyl moieties in 1-vinyl-2-pyridones would disrupt the $\pi 2 + \pi 4$ reaction pathway in favor of documented $\pi 2 + \pi 2$ modes leading to benzocyclobutenes.[14]

In order to gain insight into these questions, reactions of benzyne, generated by *iso*-amylnitrite diazotization of anthranilic acid, with a number of 1-vinyl-2-pyridones were explored. Accordingly, we have found that the crystalline *N*-styryl benzoisoquinuclidienone **21** can be prepared (40%) in this way starting with the *N*-styrylpyridone **2** and excess anthranilic acid. Similarly, addition of benzyne to the dimedonylpyridone **8**[7] proceeds in high yield (42%) to furnish the corresponding benzoisoquinuclidienone **22** containing the *N*-vinyl group as part of a 5,5-dimethylcyclohex-2-en-1-onyl ring system.



21 22



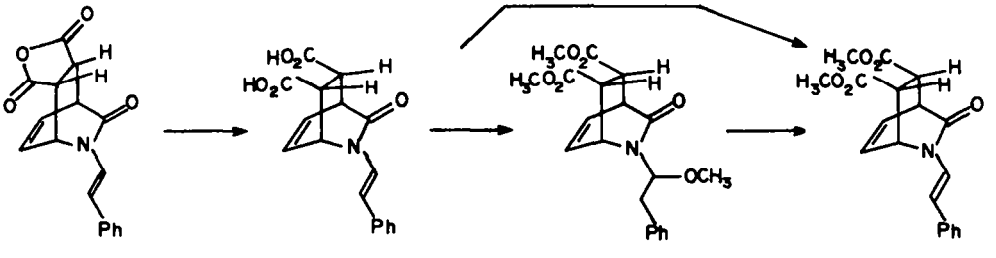
23: ($R_1$, $R_2$ = $(CH_2)_3$)
24: ($R_1$ = $R_2$ = $CH_3$) 25

Surprisingly different results were obtained from attempted Diels–Alder addition reactions to the related 1-cyclohexenonyl- and 1-pentenonyl-2-pyridones **23** and **24**.[7] Under reaction conditions which were known to lead to maximum yields of the analogous Diels–Alder adduct **22**, the pyridones **23** and **24** failed to produce isolable quantities of benzoisoquinuclidienone products. Low yields (*ca.* 13%) of a substance, tentatively identified as the parent azabicyclic system **25**, were obtained in both cases. It is not clear at this time why reactions of **23** and **24** are unsuccessful. The nature of the isoquinuclidenone product obtained, however, appears to suggest that cycloaddition is proceeding normally but that the products are exceptionally susceptible to hydrolytic or oxidative fragmentation.

*Cycloadditions using olefinic dienophiles*

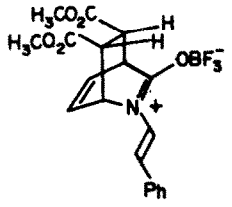
We have found that Diels–Alder reactions of 1-vinyl-2-pyridones with activated olefinic dienophiles are ideally suited for the preparation of *N*-vinylisoquinuclidienes. These reactions, which occur in modest yields, display interesting regio- and stereochemical outcomes which are readily predictable using first-order molecular orbital methods.

The first reaction explored was that of the 1-styryl-2-pyridone **2** with maleic anhydride resulting in the production (92%) of the anhydride **26**. Purification of **26** was easily accomplished by repeated trituration of the crude solid obtained directly for the reaction mixture with hot benzene followed by recrystallization from carbon tetrachloride. The stereochemistry of the single diastereomer obtained from this reaction is assumed to be *cis–endo* on the basis of earlier detailed studies conducted by Tomisawa *et al.*[4c] using the more simple *N*-methyl system. In order to test the thermal stability of this substance, the anhydride function was first transformed into a diester **29** using the reaction sequence outlined below. When **29** is subjected to thermolysis conditions (refluxing decalins) in the presence or absence of the Lewis acid catalyst, aluminum trichloride, efficient retro Diels–Alder reaction occurs liberating the *N*-styrylpyridone **3** in yields ranging from 95 to 97%.



26 27 28 29

As this observation points out, the chemoselectivity of thermal retro $\pi 2+\pi 4$ fragmentation reactions of isoquinuclidone systems appears to be controlled by the nature of the diene product liberated. When both two-carbon bridges in these substances are unsaturated, reaction occurs to generate a benzene and C=N containing fragment. However, retro Diels–Alder cleavage apparently leads to pyridones by extrusion of an olefinic residue in cases where one of the bridges is saturated, as would be expected due to the greater thermodynamic driving force associated with formation of the partially aromatic pyridone ring system. In addition, Lewis acid catalysts appear to accelerate the latter process most probably as a result of prior complexation at the amide carbonyl-oxygen. This would generate the intermediate **30** which is isoelectronic with a bicyclo[2.2.2]-octa-2,5-diene system and activated for cleavage to dimethyl maleate and the pyridium salt.

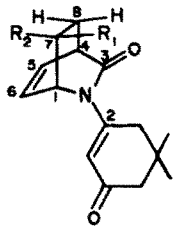


**30**

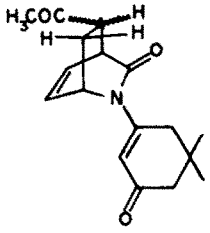
Methyl vinyl ketone was also found to serve as a good dienophile in Diels–Alder reactions with 1-vinyl-2-pyridone systems. Although these reactions lead to mixtures of regio- and stereoisomeric products, the *N*-vinylacetylisoquinuclienones can be obtained in acceptable yields under carefully controlled reaction conditions. For example, addition of methyl vinyl ketone to 1-*trans*-propenyl-2-pyridone **3**[7] results in the production of the regioisomeric 7- and 8-acetylisoquinuclidenones **31** and **32** as mixtures of *endo* and *exo* epimers. The ratio of **31**-*endo*, **31**-*exo*, and **32** obtained in this fashion is 1.8:1.0:1.5 as determined by NMR-analysis. Purification of this mixture by column and preparative layer chromatography afforded the pure 7-*exo* and 7-*endo*-acetyl isomers. Characterization of the regio- and stereochemistries of these materials was made principally using proton-NMR spectroscopic techniques.† The proton at H-7 in the *exo*-isomer, **31**-*exo*, should resonate at high field due to its location in the shielding region of the C-5–C-6 $\pi$-bond. The observed chemical shifts for the H-7 protons in **31**-*exo* and **31**-*endo* (Table 1) are in excellent accord with this expectation. Similarly, the acetyl methyl proton resonances for the *exo* and *endo* isomers ($\delta$ 2.20 and 2.15) are controlled to a lesser extent by the same magnetic anisotropic effect. The multiplicities for the H-1 bridgehead proton resonances ($\delta$ 5.02 and 4.96) in spectra of **31**-*exo* and **31**-*endo* aid in assignment of C-7 as the location for the acetyl substituent in these substances. Accordingly, both resonances appear as doublets of triplets due to vincinal and allylic couplings (Table 1) to the H-5 and H-6 vinyl protons and to vicinal couplings to the methine protons in the *exo* and *endo* isomers. The observed multiplicity would result only in the case where the 7-position possesses a single proton. This is further substantiated by the fact that the H-4 proton resonances in spectra of **31** and the H-1 resonances for **32** appear as doublets of quartets due to the presence of methylene units adjacent to these positions.

Table 1. Partial $^1$H NMR spectroscopic data for the methyl vinyl ketone, *N*-propenylpyridone and *N*-dimedonylpyridone adducts

| Isoquinuclidenone | H-7 (ppm) | $J_{7,1}$ (Hz) | $J_{7,8\text{-}exo}$ (Hz) | $J_{7,8\text{-}endo}$ (Hz) |
|---|---|---|---|---|
| **31**-*endo* | 3.13 | 2.8 | 10.0 | 6.0 |
| **31**-*exo* | 2.78 | 2.0 | 5.0 | 11.0 |
| **33**-*endo* | 3.27 | 3.0 | 10.0 | 6.0 |
| **33**-*exo* | 2.85 | 2.0 | 5.0 | 10.5 |



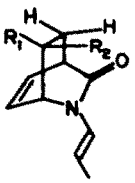
**33** *exo*: ($R_1$ = $CH_3CO$, $R_2$ = H)
**33** *endo*: ($R_1$ = H, $R_2$ = $CH_3CO$)



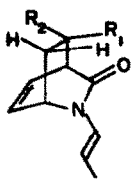
**34**

Cycloaddition of methyl vinyl ketone to the dimedonylpyridone **8**[7] follows a similar course leading to a mixture of the 7-acetylisoquinuclidenones epimers, **33**-*exo* and **33**-*endo*, and the regioisomeric 8-acetylisoquinuclidenones **34** in a ratio of 3:1. A mixture containing only the 7-acetyl-isomers in an *endo*:*exo* ratio of 4:1 can be isolated in a 41% yield by careful column chromatographic purification of the crude reaction mixture. Stereochemical assignments were easily made in this case using chemical shift and coupling data similar to that employed above (Table 1).

†$^1$H NMR analyses were made easy by comparison of the spectroscopic data given with that recorded for related *N*-methyl-7,8-diethoxycarbonyl isoquinuclidenes, prepared earlier by Tomisawa *et al.*[4c]

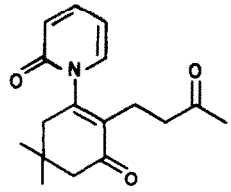


**31** *exo*: ($R_1$ = $CH_3CO$, $R_2$ = H)
**31** *endo*: ($R_1$ = H, $R_2$ = $CH_3CO$)



**32** *exo*: ($R_1$ = $CH_3CO$, $R_2$ = H)
**32** *endo*: ($R_1$ = H, $R_2$ = $CH_3CO$)

One of the major problems associated with the synthesis of the isoquinuclidenones **34** results from the observation that the efficiencies of Diels–Alder cycloaddition of methyl vinyl ketone to the dimedonylpyridone **8** are greatly dependent upon the purity of the starting pyridone. In cases where only repeatedly recrystallized **8** was employed for this reaction, significant quantities of enamine addition product **35** are generated. We have found that the best yields of **33** can be obtained when **8** is first subjected to a basic wash, using methylene chloride solutions and 10% potassium hydroxide, followed by evaporative distillation. Thus, it seems reasonable that trace quantities of acid present in recrystallized dimedonylpyridone serve to catalyze the enamine addition pathway.



**35**

*Theoretical treatment of the methyl vinyl ketone cycloaddition regiochemistry and stereochemistry*

The regiochemical and stereochemical outcomes of the methyl vinyl ketone Diels–Alder cycloaddition reactions with the propenyl- and dimedonyl-2-pyridones, **3** and **8**, summarized in Table 2 appear interesting since moderate degrees of selectivities are observed.

Table 2. Product ratios for the MVK-vinylpyridone, **3** and **8**, cycloaddition reactions

| 2-Pyridone reactant | Relative product ratios 7-acetyl-isomer *endo* | 7-acetyl-isomer *exo* | 8-acetyl-isomer |
|---|---|---|---|
| **3** | 1.8 | 1.0 | 1.5 |
| **8** | 2.4 | 0.6 | 1.0 |

Although a liberal application of valence bond reasoning can be used in developing predictions about the preferred regiochemistries for these reactions, the chemical basis for this is not sound. In addition, attempts to predict the stereochemical course of each of these reactions using the familiar Alder-rule are complicated by the presence of two $\pi$-chromophores in the heterocyclic portions of the developing isoquinuclidenes. As a result of these features, PMO methods[15,16] have been employed in developing regiochemical and stereochemical predictions.

PMO calculations were conducted using Hückel molecular orbitals, calculated using the parameters suggested by Streitweiser[17] and a computer program to solve the secular determinant. Relative stabilization energies ($\Delta E$) were calculated using the equation shown,[18] assuming that the interaction integrals, $\gamma$, are equal and that, as suggested by Fukui,[16] changes in energy associated with interactions at the primary and secondary centers are controlled mainly by properties of the highest filled (HOMO) and lowest vacant (LUMO) orbitals of the diene and dienophile. The Hückel MO-coefficients and energies used in the calculations of stabilization energies are given in Table 3. The 1 - alkoxycarbonyl - 1,2 - dihydropyridine data is also provided for comparison, since this diene has been shown to yield predominantly the 7-acetylisoquinuclidene from reaction with methyl vinyl ketone.[3] The stabilization energies and pictorial diagrams representing HOMO-LUMO interaction are given in Table 4.

$$\Delta E = 2\left[\sum_{m}^{occ}\sum_{n}^{vac} - \sum_{m}^{vac}\sum_{n}^{occ}\right](a_{mr}b_{ns} + a_{ns}b_{nr})^2\gamma^2/E_m - E_n$$

As can be seen by inspection of the results presented in Table 4, introduction of the carbonyl functionality as in the pyridone system lowers the energies of both the HOMO and LUMO with respect to those of the analogous dihydropyridine. The effect of this is to bring the energy difference between the diene-dienophile HOMO-LUMO pair closer to that of the diene-LUMO and dienophile-HOMO. It is this interaction which leads to the prediction that formation of the 7-acetyl-

Table 3. MO-Coefficients and energies for 1-vinyl-2-pyridone, 1-alkoxycarbonyl-1,2-dihydropyridine and methyl vinyl ketone

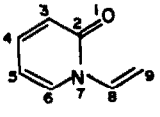
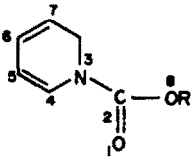
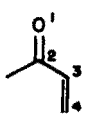
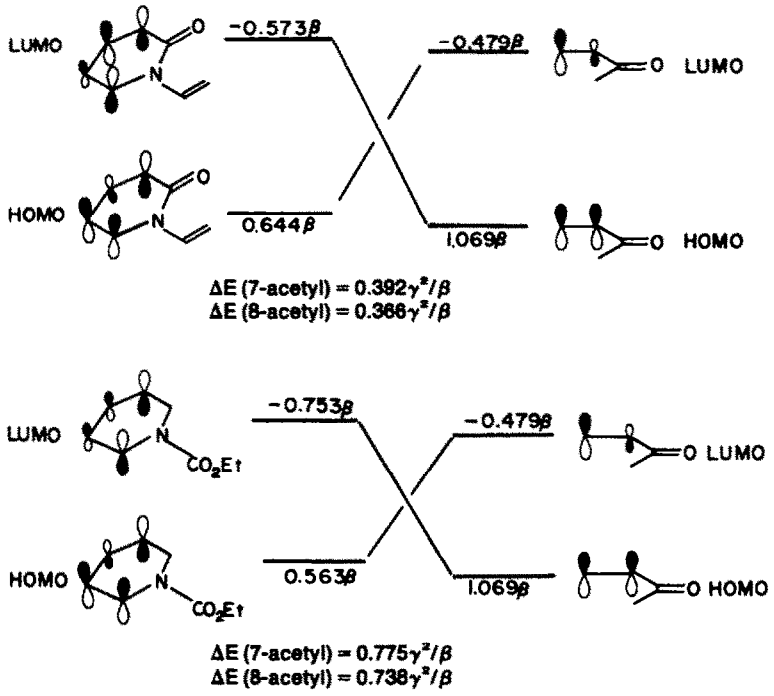
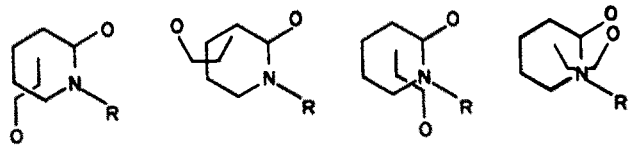
| Compound | MO | Energy ($\beta$) | $C_1$ | $C_2$ | $C_3$ | $C_4$ | $C_5$ | $C_6$ | $C_7$ | $C_8$ | $C_9$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
|  | HOMO | 0.644 | −0.500 | 0.178 | 0.394 | 0.085 | −0.421 | −0.316 | 0.325 | −2.10 | −0.35 |
| | LUMO | −0.573 | −0.286 | 0.450 | 0.284 | −0.516 | −0.019 | 0.432 | −0.284 | −0.147 | 0.28 |
|  | HOMO | 0.563 | −0.188 | 0.082 | 0.543 | 0.278 | −0.490 | −0.478 | 0.338 | −0.046 | — |
| | LUMO | −0.753 | 0.246 | −0.431 | 0.504 | −0.345 | −0.327 | 0.506 | −0.027 | 0.125 | — |
|  | HOMO | 1.069 | −0.575 | −0.040 | 0.569 | 0.585 | — | — | — | — | — |
| | LUMO | −0.479 | 0.408 | −0.603 | −0.265 | 0.609 | — | — | — | — | — |

Table 4. HOMO–LUMO Interactions for methyl vinyl ketone cycloadditions




isoquinuclidenes would be preferred. Interestingly the diene-LUMO dienophile-HOMO interaction in the 2-pyridone cycloaddition is significant and leads to stabilization of the pathway leading to the 8-acetyl isomer. Thus, the simple PMO-methods appear to nicely rationalize the regiochemistries observed for these reactions.

Qualitative predictions[19] about the stereochemistry for reaction of the 1-vinyl-2-pyridones with methyl vinyl ketone leading to the 7-acetylisoquinuclidenes can be obtained by inspection of secondary orbital interactions in the four possible transition states listed below. Accordingly, the *endo-s-trans* and *endo-s-cis* transition states possess a favorable (bonding) interaction between $C_5$ and $C_{2'}$ and $C_{1'}$ and $C_4$ in both HOMO–LUMO pairs. The opposite is true for the *exo*-transition states in which symmetry disallowed secondary orbital interactions are present.†




†Complimentary results and predictions are found in studies of the methyl vinyl ketone - 6,6 - dichloro - 2,4 - cyclohexadienone Diels–Alder reaction.[20] In this case, PMO calculations led to predictions that the *exo*-8-acetyl isomer should predominate, contrary to observation. However, inspection of the MO-coefficients given in the paper[20] summarizing these results appears to show preferences for the *endo*-stereochemistry, in accord with the results presented above.

## EXPERIMENTAL

Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn. Preparative absorption chromatographic separations were accomplished using, Baker silica gel 7GF or Baker aluminum oxide 9F for TLC and Grace silica gel (Davison grade 923, 100–200 mesh), MCB activated alumina Type F-20 or Fisher Florisil (100–200 mesh) for column chromatography. Analytical GLC measurements were made using a Varian-940 chromatograph and preparative GLC separations were performed using a Varian 2400 chromatograph. M.ps were measured on a Griffin Mel-Temp apparatus and are reported uncorrected.

$^1$H NMR spectra were recorded using a Varian T-60 or HA-100 spectrometer using $(CH_3)_6Si$ as an internal standard. Chemical shifts are recorded in ppm relative to $(CH_3)_4Si$. $^{13}$C NMR spectra were obtained from a JEOL PS-100 NMR with dedicated probe using a Nicolet pulsed FT data collection system at an operating frequency of 25.0345 MHz with $(CH_3)_6Si$ as an internal standard. Chemical shifts are reported in ppm relative to $(CH_3)_4Si$. Mass spectra were recorded at 70 eV using a DuPont CEC21-110B high resolution spectrometer. IR spectra were measured on a Perkin–Elmer 237B or Beckman IR-8 spectrophotometer. UV data were obtained from a Beckman ACTA-III spectrophotometer.

*Dimethyl* 2 - (trans - 2 - *phenylethen* - 1 - *yl*) - 2 - *azabicyclo*[2.2.2]*octa* - 5,7 - *diene* - 3 - *one* - 5,6 - *dicarboxylate* 4

A mixture of 0.51 g (2.6 mmol) of 1 - (*trans* - 2 - phenylethen - 1 - yl) - 2 - pyridone and 0.7 ml (5.7 mmol) of dimethyl acetylenedicarboxylate was heated at 105°C for 72 h under a $N_2$

atmosphere. The crude reaction mixture was subjected to preparative TLC on silica gel; elution was with 1:1 chloroform–benzene. The desired isoquinuclidienone **4** was obtained as an oil, 0.19 g (22%). IR ($CHCl_3$) 3047, 3000, 2973, 2928, 1720, 1686, 1645, 1598 $cm^{-1}$; UV (ethanol) $\lambda_{max}$ 293 nm ($\epsilon$ 18,000); $^1H$ NMR ($CDCl_3$) $\delta$ 3.81 (s, 6H, $OCH_3$), 4.76 (m, 1H, H-4), 6.01 (m, 1H, H-1), 6.25 (d, 1H, J = 14.8 Hz, *N*-vinyl), 6.98 (m, 2H, H-7 and H-8 vinyl), 7.24 (m, 6H, aromatic and *N*-vinyl); $^{13}C$ NMR ($CDCl_3$) ppm 52.8 (q, $OCH_3$), 54.9 and 55.3 (d, C-1 and C-4), 110.7 (d, =CHPh), 123.7 (d, N–CH=), 125.7, 126.7 and 128.6 (d, aromatic methylene), 135.2 and 136.4 (d, C-7 and C-8), 135.9 (s, aromatic quarternary), 140.4 and 145.7 (s, C-5 and C-6), 163.2 and 164.6 (s, ester C=O), 167.0 (s, amide C=O); MS *m/e* (rel intens) 339 P (9), 194 (7), 163 (72), 145 (100), 117 (25), 90 (35), 77 (27); High resol MS *m/e* 339.10962 ($C_{19}H_{17}NO_5$ required: 339.11064).

*Dimethyl* 2 - (trans - 1 - *propenyl*) - 2 - *azabicyclo*[2.2.2]*octa* - 5,7 - *dien* - 3 - *one* - 5,6 - *dicarboxylate* **5**

A mixture containing 41.59 g (0.31 mol) of 1 - (*trans* - 1 - propenyl) - 2 - pyridone and 75.7 ml (0.62 mol) of dimethyl acetylenedicarboxylate was heated at 100°C for 72 h under a $N_2$ atmosphere. The crude reaction mixture was subjected to column chromatographic separation on Florisil; elution was with 2 l hexane, 2 l 5% ether–hexane. One-liter fractions were collected. Fractions 10–22 contained a mixture of the starting pyridone and derived isoquinuclidienone. This mixture was dissolved in 200 ml of ether and extracted with water and saturated sodium chloride. The ethereal layer was concentrated *in vacuo* yielding 5.40 g (6.3%) of the desired isoquinuclidienone **5** as a red oil. IR ($CHCl_3$) 2985, 2933, 2899, 2833, 1721, 1689, 1669 $cm^{-1}$; UV (EtOH) $\lambda_{max}$ 247 nm ($\epsilon$ 5200); $^1H$ NMR ($CDCl_3$) $\delta$ 1.70 (m, 3H, allylic $CH_3$), 3.81 (s, 6H, $OCH_3$), 4.69 (m, 1H, H-4), 5.30 (m, 1H, =CH–$CH_3$), 5.79 (M, 1H, H-1), 6.49 (m, 1H, =CH–N), 6.95 (m, 2H, H-7 and H-8 vinyl); $^{13}C$ NMR ($CDCl_3$) ppm 15.1 (q, allylic $CH_3$), 52.7 (q, $OCH_3$), 55.2 and 55.6 (d, C-1 and C-4), 106.3 (d, =$CHCH_3$), 124.4 (d, =CHN), 135.2 and 136.5 (d, C-7 and C-8), 140.6 and 145.0 (s, C-5 and C-6), 163.3 and 164.7 (s, ester C=O), 166.9 (s, amide C=O); MS *m/e* (rel intens) 277 P (6), 194 (5), 164 (10), 163 (100), 82 (8), 83 (13), 77 (16); High resol MS *m/e* 277.09585 ($C_{14}H_{15}NO_5$ requires: 227.09500).

*N* - (5,5 - *Dimethyl* - 3 - *cyclohex* - 2 - *en* - 1 - *onyl*) - 0 - *isobutylcarbamate* **11**

A mixture of 0.506 g (2.33 mmol) of 1 - (5,5 - dimethyl - 3 - cyclohex - 2 - en - 1 - onyl) - 2 - pyridone and 0.6 ml (4.0 mmol) of dimethyl acetylenedicarboxylate were heated to reflux in 5 ml of isobutyl alcohol for 105 h under an $N_2$ atmosphere. The resulting reaction mixture was concentrated *in vacuo* giving 2.254 g of material. From this mixture 502 mg of material was subjected to preparative TLC on silica gel, eluting with 1:1 ether–hexane. A yellow oil was obtained from a band with an $R_f$ value of 0.09 containing 26 mg (21.5% conversion) of the desired carbamate: IR ($CHCl_3$) 3425, 2985, 2950, 2865, 1754, 1623 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.95 (d, 6H, J = 6.8 Hz, isobutyl-$C(CH_3)_2$), 2.25 (s, 2H, –$COCH_2$–), 2.40 (d, 2H, J = 1 Hz, –C=$CCH_2$–), 3.94 (d, 2H, J = 6.8 Hz, –$OCH_2$–), 6.40 (t, 1H, –NC=CH–), 6.84 (broad s, 1H, NH); MS *m/e* (rel intens) 239 P (14), 224 (16), 168 (18), 127 (39), 109 (16), 83 (18), 57 (55), 41 (36), 32 (23), 29 (25), 28 (100); High resol MS *m/e* 239.15294 ($C_{13}H_{21}NO_3$ requires: 239.15213).

*Attempted Diels–Alder reaction of* 1-*vinyl-2-pyridone with dimethyl acetylenedicarboxylate*

A mixture containing 1.462 g (0.012 mol) of 1-vinyl-2-pyridone and 3.0 ml (0.024 mol) of dimethyl acetylenedicarboxylate was stirred under a $N_2$ atmosphere at 105°C for 42 h. After cooling to room temperature, unreacted dimethyl acetylenedicarboxylate was removed by concentration *in vacuo* (90°C, 0.05 mm) giving 3.690 g of an oil. A 0.665 g portion of this material was subjected to preparative TLC on silica gel; elution was with 1:1 chloroform–benzene. Dimethyl phthalate, 29 mg (7%) was isolated from a band with an $R_f$ of 0.52. The remaining 3.025 g of the crude reaction mixture was subjected to column chromatographic purification on silica gel (73 × 2.2 cm); elution was with 3:2 ether–hexane; 20 ml fractions were collected. Fractions 46–69 were shown to contain 79 mg (3%) of pure tetramethyl 1,2,4,5-benzenetetracarboxylate, m.p. 140–141.5°C (from ethanol). IR ($CHCl_3$) 3003, 2923, 2824, 1727 $cm^{-1}$; UV (EtOH) $\lambda_{max}$ 290 nm ($\epsilon$ 2570); $^1H$ NMR ($CDCl_3$) $\delta$ 4.00 (s, 12H, $OCH_3$), 8.08 (s, 2H, aromatic); MS *m/e* (rel intens) 310 P (8) 279 (100), 251 (1), 233 (2), 177 (2), 162 (5), 161 (4), 124 (3), 75 (3); High resol MS *m/e* 310.06785 ($C_{14}H_{14}O_8$ requires: 310.06883).

Fractions 71–145 were shown to contain 240 mg (8%) of pure tetramethyl 1,2,3,4-benzenetetracarboxylate, m.p. 126–128°C (from ethanol). IR ($CHCl_3$) 3012, 2923, 1736, 1433 $cm^{-1}$; UV (EtOH) $\lambda_{max}$ 285 nm ($\epsilon$ 1230); $^1H$ NMR ($CDCl_3$) $\delta$ 4.00 (s, 12H, $OCH_3$), 8.13 (s, 2H, aromatic); MS *m/e* (rel intens) 310 P (1), 279 (100), 233 (2), 163 (9), 104 (5), 75 (3); High resol MS *m/e* 310.06815 ($C_{14}H_{14}O_8$ requires: 310.06883).

*Thermolysis of* 2 - *carboethoxy* - 5,6 - *dicarbomethoxy* - 2 - *azabicyclo*[2.2.2]*octa* - 5,7 - *diene*

A soln containing 0.5 g of the isoquinuclidiene **12** in 5 ml of carbon tetrachloride was refluxed under Ar for 18 h. $^1H$ NMR analysis of the resulting soln indicated the presence of dimethyl phthalate and other unidentifiable products. Identification of the major component in this mixture as dimethyl phthalate was confirmed by a comparison of the $^1H$ NMR chemical shifts with those of the known material.

1,3,5-*Tricarboethoxyl*-1,3,5-*triazine* **14**

To 1.01 g (3.4 mmol) of 2 - carboethoxy - 5,6 - dicarbomethoxy - 2 - azabicyclo[2.2.2]octa - 5,7 - diene[9] in 15 ml of anhydrous benzene was added 0.5 ml of freshly distilled boron trifluoride etherate. The solution was stirred under Ar for 2 h at room temp. then poured into 75 ml of saturated sodium bicarbonate. The soln was extracted with chloroform. The chloroform extracts were dried and concentrated *in vacuo* to give 1.01 g of a yellow oil. $^1H$ NMR analysis of this oil indicated that it consisted of dimethyl phthalate and the triazine **14** in a ratio of 3:1. The triazine **14** was crystallized from this oil, m.p. 100–101°C (lit.[11] 102–103°C). IR ($CCl_4$) 2950, 1720, 1475, 1420 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.27 (t, 3H, $CH_3$), 4.17 (q, 2H, $OCH_2$), 5.10 (s, 2H, $CH_2$); MS *m/e* (rel intens) 302 P-1 (6), 274 (22), 230 (100), 157 (25), 124 (100), 115 (26), 102 (62), 74 (22).

*Trapping of* N-*ethoxycarbonylformaldimine using isobenzofuran*

To 1.0 g (3.4 mmol) of 2 - carboethoxy - 5,6 - dicarbomethoxy - 2 - azabicyclo[2.2.2]octa - 5,7 - diene **12** in 15 ml of anhydrous benzene was added 0.5 ml of freshly distilled borontrifluoride etherate. After stirring the resulting soln at room temp. for 2 h, 0.52 g (4.4 mmol) of 2,3-benzofuran was added. Stirring was continued for 5 days. The reaction mixture was poured into 75 ml of saturated sodium bicarbonate and chloroform extracted. The chloroform extracts were dried and concentrated *in vacuo* giving a yellow oil which was purified by preparative TLC on silica gel (20% ether–hexane elution) followed by crystallization from pentane yielding 0.18 g (25%) of pure **16**, m.p. 75.5–77.5°C. No attempt was made to recover the remaining 0.08 g of **16** (11%) present in the mother liquors. IR ($CCl_4$) 3430, 3080, 3020, 1725, 1505, 1425, 1275 $cm^{-1}$; UV ($CH_3CN$) $\lambda_{max}$ 246 nm ($\epsilon$ 14,700); $^1H$ NMR ($CDCl_3$) $\delta$ 1.20 (t, 3H, J = 8 Hz, $CH_3$), 4.12 (q, 2H, J = 8 Hz, $OCH_2$), 4.42 (d, 2H, J = 6Hz, $NCH_2$), 5.42 (m, 1H, H-4), 6.52 (s, 1H, H-1), 7.26 (m, 4H, benzo CH); $^{13}C$ NMR ($CDCl_3$) ppm 14.6 (q, $CH_3$), 38.5 (t, $OCH_2$), 61.1 (t, $NCH_2$), 103.7 (d, C-4), 111.0 (d, C-1), 120.9, 122.7 and 124.0 (d, aromatic methine), 128.2, 154.5 (s, aromatic quarternary), 156.4 (s, C=O); MS *m/e* (rel intens) 219 P (83), 190 (53), 146 (100), 131 (80), 91 (40); High resol MS *m/e* 219.09006 ($C_{12}H_{13}NO_3$ requires: 219.08953).

2 - (trans - 2 - *Phenylethen* - 1 - *yl*) - 5,6 - *benzo* - 2 - *azabicyclo*[2.2.2]*octa* - 5,7 - *dien* - 3 - *one* **21**

To a soln containing 10.0 g (50.8 mmol) of 1 - (*trans* - 2 - phenylethen - 1 - yl) - 2 - pyridone and 12.5 g (107 mmol) of 3*iso*-amylnitrite in 200 ml of 1,2-dichloroethane under an $N_2$ atmosphere at reflux was added, an additional 12.5 g (107 mmol) of *iso*-amynitrite was added to the reaction flask. After addition was complete, the reaction mixture was refluxed for 2 h and poured into a water-chloroform mixture. The chloroform layer was

separated, washed with 10% hydrochloric acid, dried, and concentrated *in vacuo* giving a black oil which was further concentrated by vacuum distillative removal of volatile components (100°C, 0.05 mm). The black non-viscous residue was chromatographed on silica gel using a 76 cm × 6 cm column and 20% ether–hexane as eluant; 500 ml fractions were collected. Fractions 15–40 contained the desired isoquinuclidiene which was recrystallized from *n*-butyl alcohol yielding 4.64 g (40%) of **21** as a crystalline solid, m.p. 208–210°C. IR ($CHCl_3$) 3095, 3030, 1678, 1404 $cm^{-1}$; UV ($CH_3CN$) $\lambda_{max}$ 297 nm ($\epsilon$ 21,500); $^1H$ NMR ($CDCl_3$) $\delta$ 4.75 (dd, 1H, J = 4 and 1 Hz, H-4), 5.84 (dd, 1H, J = 4 and 1 Hz; dd, 1H, J = 3 and 1 Hz, H-7 and H-8), 7.41 (d, 1H, J = 16 Hz, *N*-vinyl), 7.1–7.3 (m, 9H, aromatic); $^{13}C$ NMR ($CDCl_3$) ppm 169.5 (s, C=O), 140.4 (s), 139.8 (s), 137.2 (d), 136.4 (s), 135.4 (d), 128.6 (d), 127.0 (d), 126.4 (d), 126.2 (d), 125.5 (d), 124.3 (d), 124.0 (d), 122.4 (d), 109.4 (d), 56.6 (d), 55.1 (d); MS *m/e* (rel intens) 273 P (10), 145 (25), 128 (100), 89 (10); High resol MS *m/e* 273.11397 ($C_{19}H_{15}NO$ requires: 273.11536).

2 - (5,5 - *Dimethylcyclohex* - 2 - *en* - 1 - *on* - 3 - *yl*) - 5,6 - *benzo* - 2 - *azabicyclo*[2.2.2]*octa* - 5,7 - *dien* - 3 - *one* **22**

The procedure used for this reaction was identical to that employed for the preparation of **21**. The quantities used were as follows: 14.5 g (67 mmol) of 1 - (5,5 - dimethylcyclo - hex - 2 - en - 1 - on - 3 - yl) - 2 - pyridone, 28.2 g (0.241 mol) of *iso*-anylnitrite, 28.2 g (2.41 mmol) of anthranilic acid and 400 ml of 1,2-dichloroethane. Purification of the product was performed using Florisil column chromatography with a 5 cm × 60 cm column, ether–hexane as eluant and 250 ml fractions being collected. Fraction 15–23 contained the desired material which was recrystallized from carbontetrachloride to yield 6.76 g (42%) of pure **22**, m.p. 170–171°C. IR ($CHCl_3$) 2975, 2895, 1695, 1655, 1600 $cm^{-1}$; UV (abs ethanol) $\lambda_{max}$ 298 nm ($\epsilon$ 13,700); $^1H$ NMR ($CDCl_3$) $\delta$ 1.00 (s, 3H, $CH_3$), 1.02 (s, 3H, $CH_3$), 2.19 (s, 2H, H-6 cyclohexenone), 270 (d, 2H, J = 1 Hz, H-4 cyclohexenone), 4.67 (dd, 1H, J = 6 Hz and 2 Hz, H-4), 5.70 (dd, 1H, J = 6 Hz and 2 Hz, H-1), 5.91 (q, 1H, J = 1 Hz, cyclohexenone vinyl), 6.8–7.4 (m, 6H, aromatic and vinyl); $^{13}C$ NMR ($CDCl_3$) ppm 199.2 (s, cyclohexenone C=O), 170.9 (s, C=O), 158.6 (s), 139.9 (s), 139.2 (s), 137.1 (d), 135.6 (d), 126.8 (d), 126.6 (d), 124.6 (d), 122.5 (d), 111.5 (d), 60.4 (d), 56.5 (d), 50.5 (t), 42.0 (t), 33.6 (s), 28.4 (q), 27.9 (q); MS *m/e* (rel intens) 293 P (w), 128 (100), 109 (8); High resol MS *m/e* 293.14120 ($C_{19}H_{19}NO_2$ requires: 293.14157).

*Attempt to prepare* 2 - (*pent* - 3 - *en* - 2 - *on* - 1 - *yl*) - 5,6 - *benzo* - 2 - *azabicyclo*[2.2.2]*octa* - 5,7 - *dien* - 3 - *one. Isolation of* 5,6 - *benzo* - 2 - *azabicyclo*[2.2.2]*octa* - 5,7 - *dien* - 3 - *one* **25**

The procedure used in this case was identical to that employed for preparation of **21**. The quantities used were as follows: 5.00 g (0.028 mol) of 1 - (pent - 3 - en - 2 - on 1 - yl) - 2 - pyridone, 6.66 g (0.057 mol) of *iso*-amylnitrite, 7.75 g (0.057 mol) of anthranilic acid and 200 ml of 1,2-dichloroethane. Silica gel chromatographic purification of the product mixture using a 90 × 2.5 cm column and ether–hexane as eluant, and collecting 250 ml fractions gave in fractions 34–39 1.56 g of the impure benzoisoquinuclidenone **25**. Recrystallization from ethanol yielded 0.35 g (13%) of the pure material, m.p. 215–218°C. IR (KBr) 3195, 3096, 1669, 758 $cm^{-1}$; UV (abs ethanol) $\lambda_{max}$ 254 nm ($\epsilon$ 7620); $^1H$ NMR ($CDCl_3$) $\delta$ 4.21 (m, 1H, H-1), 5.12 (m, 1H, H-4), 6.8–7.4 (m, 6H, aromatic and H-7 and H-8 vinyl), 8.45 (m, 1H, N–H); $^{13}C$ NMR ($d_6$-DMSO) ppm 174.9 (s, C-3), 143.7 and 141.2 (s, C-5 and C-6), 137.7, 136.4, 125.2 and 124.9 (d, aromatic), 123.7 and 121.7 (d, C-7 and C-8), 55.3 (d, C-1), 53.9 (d, C-4); MS *m/e* (rel intens) 171 P (1), 128 (100), 43 (1); High resol MS *m/e* 171.06905 ($C_{11}H_9NO$ requires: 171.06841).

2 - (trans - 2 - *Phenylethen* - 1 - *yl*) - 2 - *azabicyclo*[2.2.2]*oct* - 7 - *en* - 3 - *one* - 5,6 - *dicarboxylic acid anhydride* **26**

A mixture of 10.02 g (51 mmol) of 1 - (*trans* - 2 - phenylethen - 1 - yl) - 2 - pyridone and 19.99 g (204 mmol) of maleic anhydride was heated at 150°C under a $N_2$ atmosphere for 3 h. The resulting tar-like material was cooled, pulverized and continuously extracted with hot benzene in a Soxhlet extractor. Concentration of the benzene extracts gave a solid which was recrystallized from carbon tetrachloride yielding 13.8 g (92%) of **26**, m.p. 209–210°C. IR ($CHCl_3$) 3003, 1792, 1701, 1406, 1076, 931 $cm^{-1}$; UV ($CH_3CN$) $\lambda_{max}$ 288 nm ($\epsilon$ 22,000); $^1H$ NMR ($CDCl_3$) $\delta$ 4.0–4.2 (m, 3H, H-4, H-5 and H-6), 5.6 (m, 1H, H-1), 6.7 (d, 1H, J = 14 Hz, *N*-vinyl), 6.8 (m, 2H, H-7 and H-8 vinyl), 7.2–7.5 (m, 5H, aromatic), 7.4 (d, 1H, J = 14 Hz, *N*-vinyl); $^{13}C$ NMR ($CDCl_3$) ppm 168.6, 168.1 and 167.2 (s, C=O), 135.2 (s, aromatic C-1), 133.0 (d), 132.2 (d), 128.8 (d), 127.3 (d), 125.8 (d), 122.2 (d), 112.0 (d), 50.6 (d), 46.9 (d), 45.1 (d), 41.8 (d). Anal. Calc. for $C_{17}H_{13}NO_4$: C, 69.15; H, 4.44; N, 4.74. Found: C, 69.33; H, 4.33; N, 4.81%.

2 - (trans - 2 - *Phenylethen* - 1 - *yl*) - 2 - *azabicyclo*[2.2.2]*oct* - 7 - *en* - 3 - *one* - 5,6 - *dicarboxylic acid* **27**

A soln of 13.8 g (47 mmol) of the acid anhydride **26** in 200 ml of water containing 100 ml of tetrahydrofuran was stirred at room temperature under a $N_2$ atmosphere for 12 h. The resulting solution cooled to 0°C was made basic with 10% sodium hydroxide and washed with chloroform. The aqueous solution was acidified with 10% hydrochloric acid and extracted with chloroform. The combined chloroform extracts were dried and concentrated *in vacuo* giving a white solid which was recrystallized from water acetone yielding 13.1 g (90%) of the desired diacid **27**, m.p. 176–177°C. IR (KBr) 2600–3400, 1730, 1620, 1410, 1200 $cm^{-1}$; UV ($CH_3CN$) $\lambda_{max}$ 288 ($\epsilon$ 22,000); $^1H$ NMR ($d_6$-acetone) 3.5 (m, 2H, H-5 and H-6), 3.6 (m, 1H, H-4), 5.3 (m, 1H, H-1), 6.5 (d, 1H, J = 14 Hz, *N*-vinyl), 6.6 (m, 2H, H-7 and H-8 vinyl), 7.4 (m, 5H, aromatic), 7.5 (d, 1H, J = 14 Hz, *N*-vinyl). Anal. Calc. for $C_{17}H_{15}NO_5$: C, 65.17; H, 4.83; N, 4.47. Found: C, 65.17; H, 4.82; N, 4.48%.

*Dimethyl* 2 - (1 - *methoxy* - 2 - *phenyleth* - 1 - *yl*) - 2 - *azabicyclo*[2.2.2]*oct* - 7 - *en* - 3 - *one* - 5,6 - *dicarboxylate* **28**

A soln containing 1.11 g (9.7 mmol) of thionylchloride, 0.85 g (2.7 mmol) of the diacid **27** in 50 ml of anhydrous methanol was stirred at room temp. for 12 h and then poured into an ice-cooled water–benzene mixture. This mixture was basified with solid sodium carbonate and the benzene layer separated, dried and concentrated *in vacuo* yielding 1.36 g of a yellow oil which crystallized on standing. Recrystallization of this material from hexane–acetone gave 0.81 g (81%) of pure **28**, m.p. 124–125°C. IR ($CHCl_3$) 3020, 2960, 1745, 1660, 1445, 1200, 730 $cm^{-1}$; UV ($CH_3CN$) $\lambda_{max}$ 259 nm ($\epsilon$ 1870); $^1H$ NMR ($CDCl_3$) $\delta$ 2.9 (m, 2H, benzylic $CH_2$), 3.0 (m, 3H, H-4, H-5 and H-6), 3.1 (s, 3H, $OCH_3$), 4.6 (m, 1H, H-1), 5.6 (t, 1H, J = 7.0 Hz, CHNO), 6.5 (m, 2H, H-7 and H-8 vinyl), 7.3 (br s, 5H, aromatic); $^{13}C$ NMR ($CDCl_3$) ppm 172.9, 171.2 and 170.5 9s, C=O's), 136.0 (s, aromatic C-1), 133.1 and 131.0 (d, C-7 and C-8 vinyl), 128.8, 128.6 and 126.9 (d, o, m and p aromatic), 83.0 (d, CON), 56.2 and 52.1 (q, ester $OCH_3$), 49.1 and 48.8 (d, C-1 and C-4), 47.2 (d, C-5 and C-6), 42.9 (q, $OCH_3$), 39.3 (t, benzylic $CH_2$); MS *m/e* (rel intens) 342 (P-31) (3), 283 (14), 282 (100), 151 (14), 135 (26), 91 (20), 86 (39). Anal. Calc. for $C_{20}H_{22}NO_6$: C, 64.33; H, 6.21; N, 3.75. Found: C, 64.16; H, 6.12; N, 3.81%.

*Dimethyl* 2 - (trans - 2 - *phenylethen* - 1 - *yl*) - 2 - *azabicyclo*[2.2.2]*oct* - 7 - *en* - 3 - *one* - 5,6 - *dicarboxylate* **29** *from amino ether* **28**

A soln of 50 mg of *p*-toluenesulfonic acid and 2.70 g (7.3 mmol) of the amino ether **28** in 250 ml of benzene was refluxed for 5 h, cooled to room temp. and made basic with aqueous potassium carbonate and the benzene layer separated, dried and concentrated *in vacuo* giving a viscous oil which crystallized upon standing. Recrystallization from benzene gave 2.47 g (91%) of pure **29**, m.p. 127–128°C. The spectroscopic properties of material derived in this way are identical to those for the substance obtained by direct esterification of the diacid **27**.

*Dimethyl* 2 - (trans - 2 - *phenylethen* - 1 - *yl*) - 2 - *azabicyclo*[2.2.2]*oct* - 7 - *en* - 3 - *one* - 5,6 - *dicarboxylate* **29** *from diacid* **27**

A slurry obtained by mixing 5.17 g (16.7 mmol) of the diacid **27**, 8.42 g (67.0 mmol) of dimethyl sulfate, and 6.95 g (50.2 mmol) of

chloroform and the resulting soln filtered. The filtrate was washed with water and saturated sodium chloride, dried and concentrated *in vacuo* yielding a solid material which was recrystallized from benzene giving 4.17 g (73%) of pure **29**, m.p. 134.0–134.5°C. IR ($CHCl_3$) 3100, 1749, 1675, 1460, 730, 690 $cm^{-1}$; UV ($CH_3CN$) $\lambda_{max}$ 287 nm ($\epsilon$ 20,900); $^1H$ NMR ($CDCl_3$) $\delta$ 3.75 (m, 2H, H-5 and H-6), 4.1 (m, 1H, H-4), 4.0 (s, 6H, $OCH_3$), 5.4 (m, 1H, H-1), 6.4 (d, 1H, J = 16 Hz, *N*-vinyl), 6.9 (m, 2H, H-7 and H-8 vinyl), 7.6 (m, 5H, aromatic), 7.8 (d, 1H, J = 16 Hz, *N*-vinyl); $^{13}C$ NMR ($CDCl_3$) ppm 170.7, 170.4 and 169.5 (s, C=O), 135.9 (s), 131.8 (d), 131.5 (d), 128.7 (d), 126.7 (d), 125.7 (d), 122.7 (d), 110.8 (d), 52.2 (q), 51.7 (d), 48.1 (d), 46.9 (d), 43.4 (d). Anal. Calc. for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61; N, 4.10. Found: C, 66.85; H, 5.69; N, 3.91%.

*Retro π2+π4 reaction of dimethyl* 2 - (trans - 2 - *phenylethen* - 1 - *yl*) - 2 - *azabicyclo* - [2.2.2]*oct* - 7 - *en* - 3 - *one* - 5,6 - *dicarboxylate* **29**

*Thermal process.* A soln of 0.26 g (0.75 mmol) of the *N*-styrylisoquinuclidenone **29** in 10 ml of a mixture of *cis*- and *trans*-decalin was refluxed for 96 h under an Ar atmosphere. The reaction mixture was concentrated *in vacuo* (45°, 0.08 mm) yielding 0.14 g (97%) of a crystalline material, m.p. 148–151°C, which was identical in every respect with the known 1 - (*trans* - 2 - phenylethen - 1 - yl) - 2 - pyridone.

*Lewis acid catalyzed process.* A soln of 0.26 g (0.75 mmol) of the *N*-styrylisoquinuclidenone **29** in 25 ml of decalin containing 0.10 g (0.75 mmol) of aluminum trichloride was heated at 110°C for 10 h. The reaction mixture was cooled and poured into water. The aqueous mixture was extracted with chloroform. The chloroform extracts were washed with water, dried and concentrated *in vacuo* giving 0.14 g (95%) of pure 1-β-styryl-2-pyridone **2** as a crystalline material, m.p. 147–151°C.

2 - (trans - 1 - *Propenyl*) - endo *and* exo - 7 - *acetyl* - 2 - *azabicyclo*[2.2.2]*oct* - 5 - *ene* - 3 - *one* **31**

A mixture of 1.094 g (8.11 mmol) of 1 - (*trans* - 1 - propenyl) - 2 - pyridone and 2.4 ml (16.2 mmol) of methyl vinyl ketone was heated at 115°C for 120 h under a $N_2$ atmosphere. An additional 2.4 ml of methyl vinyl was added and heating was continued for another 57.5 h. The crude reaction mixture was concentrated *in vacuo* (room temp., 0.175 mm) using a Kugelrooor apparatus to remove unreacted methyl vinyl ketone and its thermal dimer. The residue obtained was separated by TLC on silica gel (elution was with 4:1 ether–hexane). A pale yellow oil (237 mg, 14%) was isolated from a band with an $R_f$ of 0.17. $^1H$ NMR analysis of this material showed it to be a 3:1 mixture of the 7-*exo*-acetylisoquinuclidenones **31**-*exo* and one of the respective regioisomers **32** (determined by comparison of the integration of the 4-protons at 3.50 ppm and 3.72 ppm respectively). Another pale yellow oil (488 mg, 29%) was obtained from a band with an $R_f$ of 0.32. $^1H$ NMR analysis indicated that the band was a 2:1 mixture of the 7-*endo*-acetyl isoquinuclidenone **31**-*endo* and one of the respective 8-acetyl isomers **32** (as determined by integration of the 4-protons as in the case of the 7-*exo*-acetyl isomer). Small quantities of the pure 7-*exo* and 7-*endo*-acetyl isomers were obtained by tedious silica gel column chromatography of a reaction mixture (obtained as described above), followed by preparative TLC. The 7-*exo*-acetyl isoquinuclidenone (**31**-*exo*) and the following spectral properties: IR ($CHCl_3$) 2976, 2924, 2899, 2857, 1715, 1664, 1416, 1385, 1359, 1263, 1206, 1206 $cm^{-1}$; UV (EtOH) $\lambda_{max}$ 223 nm ($\epsilon$ 8300); $^1H$ NMR ($CDCl_3$) $\delta$ 1.66 (dd, 3H, J = 7.0 Hz and 1.5 Hz, allylic $CH_3$), 1.73 (m, 1H, H-8 *endo*), 2.21 (m, 1H, H-8 *exo*), 2.20 (s, 3H, $-COCH_3$), 2.78 (ddd, 1H, J = 11.0 Hz, 5.0 Hz, and 2.0 Hz, H-7), 3.50 (m, 1H, H-1), 5.02 (dt, 1H, J = 5.0 Hz and 2.0 Hz, H-1), 5.18 (dq, 1H), J = 15.0 Hz and 7.0 Hz, –NC=CH–), 6.44 (ddd, 1H, J = 8.0 Hz, 5.0 Hz, and 2.0 Hz, H-5 or H-6), 6.56 (ddd, 1H, J = 8.0 Hz, 5.0 Hz, and 2.0 Hz, H-5 or H-6), 6.63 (dq, 1H, J = 15.0 Hz and 1.5 Hz, –NCH=); $^{13}C$ NMR ($CDCl_3$) ppm 15.2 (q, allylic $CH_3$), 23.8 (t, C-8), 28.9 (q, $-COCH_3$), 44.0 (d, C-7), 51.8 (d, C-4), 52.6 (d, C-1), 105.0 (d, NCH=CH–), 125.0 (d, N–CH=CH–), 132.7 and 133.6 (d, C-5 and C-6), 170.8 (s, –NCO–), 205.6 (s, $-COCH_3$–); MS *m/e* (rel intens) 205 P (34), 162 (29), 134 (15), 120 (78), 79 (100), 78 (39), 77 (28), 43 (59), 41 (16), 39 (20); High resol MS *m/e* 205.11077 ($C_{12}H_{15}NO_2$ requires: 205.11027).

The 7-*endo*-acetylisoquinuclidenone (**31**-*endo*) had the following spectral properties: IR ($CHCl_3$) 2976, 2959, 2924, 2857, 1718, 1667, 1458, 1424, 1385, 1364, 1209, 1178 $cm^{-1}$; UV (EtOH) $\lambda_{max}$ 224 nm ($\epsilon$ 7800); $^1H$ NMR ($CDCl_3$) $\delta$ 1.70 (dd, 3H, J = 6.8 Hz and 1.5 Hz, allylic $CH_3$), 1.76 (m, 1H, H-8 *endo*), 2.15 (m, 1H, H-8 *exo*), 2.15 (s, 3H, $-COCH_3$), 3.13 (ddd, 1H, J = 10.0 Hz, 6.0 Hz, and 2.8 Hz, H-7 *exo*), 3.43 (dq, 1H, J = 5.0 Hz and 2.8 Hz, H-4), 4.96 (dt, 1H, J = 4.0 Hz and 2.8 Hz, H-1), 5.22 (dq, 1H, J = 15.0 Hz and 6.8 Hz, NCH=CH), 6.42 (m, 2H, H-5 and H-6), 6.66 (dp, 1H, J = 15.0 Hz and 1.5 Hz, –NCH=); $^{13}C$ NMR ($CDCl_3$) ppm 15.1 (q, allylic $CH_3$), 25.6 (t, C-8), 28.4 (q, $-COCH_3$), 44.0 (d, C-7), 51.3 (d, C-4), 52.7 (d, C-1), 105.5 (d, –NCH=CH–), 123.7 (d, –NCH=CH–), 131.0 and 133.4 (d, C-5 and C-6), 171.0 (s, –NCO–), 206.2 (s, $-COCH_3$); MS *m/e* (rel intens) 205 P (47), 162 (37), 134 (17), 120 (88), 106 (12), 83 (18), 79 (100), 78 (38), 77 (21), 43 (28); High resol MS *m/e* 205.11097 ($C_{12}H_{15}NO_2$ requires: 205.11027).

2 - (5,5 - *Dimethyl* - 3 - *cyclohex* - 2 - *ene* - 1 - *onyl*) - endo - *and* exo - 7 - *acetyl* - 2 - *azabicyclo*[2.2.2]*oct* - 5 - *en* - 3 - *one* **33**

A mixture of 10.0 g (46.0 mmol) of 1 - (5,5 - dimethyl - 3 - cyclohex - 2 - ene - 1 - onyl) - 2 - pyridone and 4.0 ml (49.3 mmol) of methyl vinyl ketone in 15 ml toluene was heated to a vigorous reflux under an Ar atmosphere. This reaction was allowed to continue for a period of 8 days while adding 4.0 ml of methyl vinyl ketone once every 24 h. The reaction mixture was cooled to room temp. and toluene and the methyl vinyl ketone dimer were removed *in vacuo*. The concentrated reaction mixture was then subjected to column chromatography on Florisil (65 × 5 cm i.d.) by elution with ether and collection of 250 ml fractions. Concentration of fractions 9–62 yielded a mixture of the starting pyridone and *endo*-Diels–Alder product which was subjected to fractional crystallization from benzene. The crystalline material obtained consisted of 5.336 g (24.6 mmol) of starting pyridone. The mother liquor was subjected to evaporative distillation to remove any remaining starting material (65–70°C, 0.025 mm) and 1 890 g (6.59 mmol) of the crude *endo*-Diels–Alder product was obtained. This was recrystallized from benzene to yield 0.972 g (3.39 mmol) of the *endo* isomer **33**-*endo* (m.p. 144–146.5°C). IR ($CHCl_3$) 2976, 2849, 2933, 2849, 1704, 1653, 1597, 1412 $cm^{-1}$; UV (EtOH) $\lambda_{max}$ 289 nm ($\epsilon$ 16,300); H NMR ($CDCl_3$) $\delta$ 1.04 (s, 3H, $-C(CH_3)_2$–), 1.08 (s, 3H, $-C(CH_3)_2$–), 1.81 (ddd, 1H, J = 13.0 Hz, 6.0 Hz, and 3.0 Hz, H-8 *endo*), 2.10–2.50 (m, 1H, H-8 *exo*), 216 (s, 3H, $-COCH_3$), 2.20 (s, 2H, $-CH_2CO$–), 2.56 (d, 1H, J = 18.0 Hz, =C–(CH–H)–), 2.87 (dd, 1H, J = 18.0 Hz and 1.0 Hz, =C(CH–H)–), 3.27 (ddd, 1H, J = 10.0 Hz, 6.0 Hz and 3.0 Hz, H-7 *exo*), 3.57 (m, 1H, H-1), 5.02 (dt, 1H, J = 4.0 Hz and 3.0 Hz, H-4), 5 87 (broad s, 1H, =CH–CO–), 6.44–6.58 (m, 2H, –CH=CH–); $^{13}C$ NMR ($CDCl_3$) ppm 25.1 (t, C-8), 27.7 and 28.7 (q, $C(CH_3)_2$), 28.4 (q, $-COCH_3$), 33.6 (s, $C-(CH_3)_2$), 42.5 (t, $-CH_2CO$–), 45.6 (d, C-7), 50.5 (t, $-CH_2-C$=), 52.8 (d, C-4), 55.6 (d, C-1), 112.9 (d, =CHCO–), 131.6 and 133.2 (d, C-5 and C-6), 158.2 (s, N–C=), 172.9 (s, –N-CO–), 199.2 (s, =C–CO–), 205.3 (s, $-COCH_3$); MS *m/e* (rel intens) 287 P (51), 272 (51), 244 (19), 203 (23), 202 (30), 166 (17), 150 (21), 133 (53), 79 (100), 78 (47), 77 (36), 43 (83); High resol Ms *m/e* 287.15193 ($C_{17}H_{21}NO_3$ requires: 287.15213).

Column fractions 63–97 yielded 2.60 g (9.06 mmol) of the *endo* and *exo* Diels–Alder products **33**. This mixture was subjected to fractional crystallization from benzene yielding in the first crop 0.322 g (1.12 mmol) of the *exo*-Diels–Alder adduct: (m.p. 154–156°C), IR ($CHCl_3$), 2976, 2941, 2849, 1701, 1647, 1602, 1408 $cm^{-1}$; UV (EtOH) 288 ($\epsilon$ 15,100); H NMR ($CDCl_3$) $\delta$ 1.02 (s, 3H, $C(CH_3)_2$), 1.09 (s, 3H, $C(CH_3)_2$), 1.81 (ddd, 1H, J = 13.0 Hz, 10.5 Hz, and 3.0 Hz, H-8 *endo*), 2.11–2.35 (m, 1H, H-8 *exo*), 2.21 (s, 2H, $-CH_2CO$–), 2.23 (s, 3H, $-COCH_3$), 2.35 (d, 1H, J = 18.0 Hz, =C–CH–H), 2.85 (ddd, 1H, J = 10.5 Hz, 5.0 Hz, and 2 0 Hz, H-7 *endo*), 3.00 (dd, 1H, J = 18.0 Hz and 1.0 Hz, =C(CH–H)–), 3.55 (dq, 1H, J = 5.0 Hz and 2.5 Hz, H-4), 5.03 (dt, 1H, J = 5.0 Hz and 2.0 Hz, H-1), 5.82 (broad s, 1H, –COCH=), 6.42–6.71 (m, 2H, H-5 and H-6); $^{13}C$ NMR ($CDCl_3$) ppm 22.7 (t, C-8), 27.0 and 29.1 (q, $-C(CH_3)_2$–), 29.1 (q, $-COCH_3$), 33.6 (s, $-C(CH_3)_2$–), 42.1 (t, $-COCH_2$–), 45.3 (d, C-7), 50.5 (t, $=CCH_2$–), 51.1 (d, C-4), 56.3 (d, C-1), 113.4 (d, =CHCO–), 132.4 and 133.7 (d,

potassium carbonate in 100 ml of anhydrous acetone was refluxed for 5 h. The cloudy brown mixture was poured into C-5 and C-6), 159.1 (s, –NC=), 172.3 (–NCO–), 199.5 (–COC=), 205.6, –$COCH_3$): MS *m/e* rel intens), 287 P (69), 272 (80), 244 (26), 203 (27), 202 (62), 166 (21), 150 (22), 133 (62), 79 (100), 78 (43), 77 (36), 43 (52): High resol MS *m/e* 287.15137 ($C_{17}H_{21}NO_3$ requires: 287.15213). The mother liquor yielded 1.223 g (4.26 mmol) of *endo–exo* Diels–Alder product mixture giving a total yield of 41% of 33 based on recovered starting material.

1 - (5,5 - *Dimethyl* - 2 - (4 - *butan* - 2 - *onyl*) - 3 - *cyclohex* - 2 - *en* - 1 - *onyl*) - 2 - *pyridone* 35

The *N*-vinyl-2-pyridone, used in the Diels–Alder reaction of methyl vinyl ketone and 1 - (5,5 - dimethyl - 3 - cyclohex - 2 - en - 1 - onyl) - 2 - pyridone, is purified prior to the reaction by washing a $H_2CCl_2$ soln of the *N*-vinyl - 2 - pyridone with 10% aqueous KOH. The material obtained from concentration of the $H_2CCl_2$ fraction *in vacuo* is subjected to kugelroor distillation to obtain the pure starting material (65–70°C, 0.025 mm). If this procedure is not adhered to, varying amounts of the enamine addition product 35 appear in the reaction mixture and can only be separated by careful preparative TLC on silica gel via elution with 9:1 ether:hexane. This side product 35 has the following spectral properties: IR ($CHCl_3$) 2976, 2941, 2873, 2849, 1709, 1666, 1587, 1533 $cm^{-1}$; UV (EtOH) $\lambda_{max}$ 231 nm ($\epsilon$ 14,100) 306 nm ($\epsilon$ 5760); $^1$H NMR ($CDCl_3$) $\delta$ 1.11 (s, 3H, –$C(CH_3)_2$–), 1.16 (s, 3H, –$C(CH_3)_2$), 2.03 (s, 3H, –$COCH_3$), 2.05–2.80 (m, 4H, –$CH_2CH_2CO$–), 2.40 (s, 2H, –$COCH_2$–), 2.42 (d, 1H, J = 18 Hz, =C(CH–H)–), 2.78 (d, J = 18.0 Hz, =C(CH–H)–), 6.29 (td, 1H, J = 7.0 Hz and 1.0 Hz, H-5), 6.45 (broad d, 1H, J = 9.5 Hz, H-3), 7.18 (broad dd, 1H, J = 7.0 Hz and 2.0 Hz, H-6), 7.42 (ddd, 1H, J = 9.5 Hz, 7.0 Hz, and 2.0 Hz, H-4); $^{13}$C NMR ($CDCl_3$) ppm 19.2 (t, –$COCH_2CH_2C$=), 27.3 and 28.4 (q, $C(CH_3)_2$), 29.5 (q, –$COCH_3$), 32.8 (s, $C(CH_3)_2$), 41.2 (t, $H_3CCOCH_2$–), 43.8 (t, –$COCH_2$–), 51.3 (t, =$CCH_2$–), 106.5 (d, C-5), 121.9 (d, C-3), 134.7 (s, –COC=), 135.7 (d, C-4), 140.3 (d, C-6), 153.3 (s, –COC=C–), 160.8 (s, –NC=O–), 198.5 (s, –COC=), 207.3 (s, –$COCH_3$); MS *m/e* (rel intens) 287 P (14), 259 (100), 258 (32), 244 (17), 230 (19), 216 (53), 203 (50), 160 (58), 146 (42), 133 (29), 109 (26), 96 (44), 43 (39); High resol MS *m/e* 287.15137 ($C_{17}H_{21}NO_3$ requires: 287.15213).

*Acknowledgements*—Acknowledgement is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. Financial support for a portion of these studies derived from an NSF grant (CHE76-10892). We wish to acknowledge the competent technical assistance given by Michael Peters, John Frazer, and Dr. Emil Krochmal during initial phases of this research. We would like to thank Prof. Richard Hedges for assistance with the molecular orbital calculations.

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