Acetylation of 4c. Preparation of 10. Compound 4c (1 g) was heated under reflux for 12 h with acetic anhydride (20 mL). The excess acetic anhydride was evaporated and the residue poured into ethanol–water (50:50). The precipitate was filtered and recrystallized from ethanol/water (50:50) to give 1 g (71%) of 10: mp 148 °C; mass spectrum, *m/e* 294 (M^+); ^1H NMR spectrum ($CDCl_3$) δ (Me_4Si) 2.03 (s, 3 H, CH_3), 2.58 (s, 3 H, CH_3), 7.3–9 (m, 8 H, C_6H_5, H_5, H_7, H_8). Anal. Calcd for $C_{16}H_{14}N_4O_2$: C, 65.30; H, 4.79; N, 19.04. Found: C, 65.20; H, 4.96; N, 18.90.

Acknowledgment. We thank Mr. Granger and Mrs. Chapelle of Centre de Mesures Physiques, Université de Rouen, for assistance in attaining and interpreting some NMR spectral data and Mrs. M. J. Pouet (ENSCP), who performed the NOE experiments.

Registry No. 1, 59850-36-1; 2, 40848-48-4; 3c, 60097-00-9; 4c, 60445-75-2; 5, 78149-61-8; 6, 6133-44-4; 7, 78149-62-9; 8, 78149-63-0; 9, 78149-64-1; 10, 78149-65-2; 3-(2′-furyl)pyrido[3,4-*e*]-*as*-triazine, 78149-66-3; 3-(2′-thienyl)pyrido[3,4-*e*]-*as*-triazine, 78149-67-4; 3-(2′-pyrrolyl)pyrido[3,4-*e*]-*as*-triazine, 78149-68-5; 3-(2′-indolyl)-pyrido[3,4-*e*]-*as*-triazine, 78149-69-6.

Chemistry of 1,5-Diazapentadienium (Vinamidinium) Salts: Alkylation Reactions to Multifunctional Dienamines and Dienaminones[1]

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Received April 24, 1981

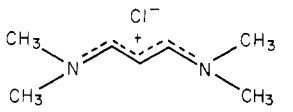
1,5-Diazapentadienium chloride 1 is a push–pull 6-π-electron system. It reacts selectively and in high yields with enolates of cyclic and acyclic ketones, esters, lactones, and lactams to produce multifunctional dienaminones. Heterocyclic systems containing activated methylene groups such as 2-ethyl-2-oxazoline, 2-picoline, and 2-methylfuran are converted to reactive dienamines. Derivatives of γ,δ-unsaturated β-keto esters, useful intermediates in organic synthesis, can be synthesized directly by selective alkylation with 1 of the dianion derived from ethyl acetoacetate. Cyclopentane-1,3-dione methyl ether reacts with 1 to produce both *E,E* and *Z,E* alkylated products.

One of the major synthetic applications of compounds containing activated methylene groups is the selective alkylation of the carbon α to the carbonyl group.[2,3] The enols and enolates of these carbonyl compounds have been alkylated with a variety of alkyl and allyl halides, as well as alkyl sulfonates, tosylates, oxonium ions and other reagents. We report the use of vinamidinium salts[4] in the alkylation of carbonyl enolates to produce dienaminones. The reaction appears to have generality, and we have applied it successfully to diesters, keto esters, cyclic and acyclic ketones, lactones, lactams, and other compounds containing activated methylene groups. The dienaminones and dienamines formed in these reactions are multifunctional compounds that have potential as intermediates in the synthesis of some natural products.

The vinamidine system (1,5-diaza-1,3-pentadiene) is present in natural products such as the betacyanin pigments found in red beets, many cacti, pokeberry and other plants[5] and in the porphyrin and corrin ring systems of chlorophyll, hemoglobin, cytochromes, and vitamin B_{12}.[6] Vinamidinium salts such as 1 are examples of push–pull alkenes, compounds that are stabilized by groups which can donate or accept electrons. They are vinylogues of amidinium salts and have an alternation of electron density; the α-carbons are electron poor and are attacked by nucleophilic reagents, and the β-carbon is electron rich and is attacked by electrophilic reagents.[7,8] The enhanced stability and push–pull nature of the vinamidinium system gives it regenerative character which makes it prone to substitution rather than addition reactions. The regenerative character of the vinamidinium salts has been demonstrated in both electrophilic reactions such as halogenation, nitration, and Vilsmeier type alkylations,[9] and in nucleophilic reactions with amines and carbon nucleophiles. The nucleophilic reactions have been exploited the most and have led to the synthesis of some polycyclic aromatic and heterocyclic compounds.[10–12] Vinamidinium salts have been used to alkylate the activated methylenes of various nitriles,[12,13] but there is only one report of the alkylation of other types of activated methylene compounds.[14]

Results and Discussion

In previous work with vinamidines, the perchlorate salts were used.[15] In this work we found a convenient method for the preparation of the tetramethylvinamidinium chloride salt 1 in good yield using readily available com-



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mercial reagents. This procedure involved the preparation of β-(dimethylamino)acrolein by a Vilsmeier reaction on

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Table I. Procedures and Product Yields in the Reaction of the Vinamidinium Salt 1 with Various Substrates

substrate	method	reaction conditions: temp, °C	reaction conditions: time	product	yield, %	mp, °C
diethyl malonate	A	reflux	10 h	**2**	73	51-53
ethyl acetoacetate	B	25	25 h	**4a, 4b**	57	88-90
3-pentanone	C	25	33 h	**3**	66	102-103
2-butanone	B	25	46 h	**5a, 5b**	78	84-87
2-butanone	D	0	4.5 h	**5a, 5b**	78	84-87
cyclopentanone	B	25	26 h	**9a**	88	89-90
cyclopentanone	D	25	5 h	**9a**	88	89-90
cyclohexanone	B	25	30 h	**10**	73	86-89
cycloheptanone	C	25	51 h	**11**	60	oil
cycloheptanone	D	0	4 h	**11**	60	oil
dl-camphor	C	reflux	40 h	**16**	33	oil
estrone 3-methyl ether	B	25	5 days	**15**	56	209-210
estrone 3-methyl ether	D	25	18 h	**15**	80	209-210
γ-butyrolactone	B	25	48 h	**12**	91	100-101
γ-butyrolactone	D	25	6 h	**12**	91	100-101
δ-valerolactone	C	25	38 h	**13**	86	101-103
δ-valerolactone	D	25	4 h	**13**	86	101-103
1-ethyl-2-pyrrolidinone	D	0	3 h	**14**	51	75-78
2-ethyl-2-oxazoline	D	−70	4 h	**6**	44	97-100
2-picoline	D	0	1.5 h	**7**	50	oil

ethyl vinyl ether.[16] The β-(dimethylamino)acrolein was isolated in 57% yield and was characterized by ^1H and ^{13}C NMR data and by mass spectrometry. The vinamidinium salt **1** was obtained by heating the β-(dimethylamino)-acrolein and dimethylamine hydrochloride in absolute ethanol under reflux. The reaction was monitored by UV spectroscopy and was stopped when the UV absorption maximum reached 309 nm. The product, a white solid which was isolated in 70% yield, must be recrystallized twice to avoid contamination with dimethylamine hydrochloride. The salt **1** was found to be hygroscopic, similar to the vinamidinium perchlorates, was dried over P_2O_5, and was stored in a desiccator. Once dried, the salt is stable indefinitely and can be handled in air for short periods of time. Its ^{13}C NMR spectrum showed the resonance for the α-carbons at 164.2 ppm and the resonance for the β-carbon at 90.3 ppm typical of the alternation of electron density in push–pull alkene systems.[17] The ^1H NMR spectrum also had only one resonance for H_α, a doublet at 8.60 ppm (J = 12.0 Hz). The β-carbon proton was observed as a triplet at 5.26 ppm (J = 12.0 Hz). The single resonance observed for H_α and C_α in the ^1H and ^{13}C NMR spectra and the coupling constant of 12.0 Hz are consistent with an all-trans or W form for the stereochemistry of **1** in nonpolar solvents. This geometry is typical of tetrasubstituted vinamidinium salts.[17,18] As the salt **1** contains a cation, the mass spectrum does not produce a parent peak, but the parent minus the chloride anion is observed and is, in fact, the base peak. The UV max (EtOH) at 309 nm of **1** provided a very convenient marker for monitoring the alkylation reactions.

When the vinamidinium salt **1** was treated with enolates generated in situ by reaction of sodium hydride with cyclic or acyclic carbonyl compounds in triethylamine or pyridine, dienaminones were isolated in good yields. The results are shown in Table I. It is essential to keep these reactions free from water in that sodium hydroxide produced by reaction of sodium hydride with water rapidly converts salt **1** to β-(dimethylamino)acrolein. The sodium hydride itself does not appear to attack the vinamidinium system even at elevated temperatures for several days.

In our preliminary work,[1] the reactions with **1** were carried out with enolates generated in situ by reaction of sodium hydride with the carbonyl compounds. In subsequent work, we investigated the possibility of using lithium diisopropylamide (LDA) as an alternative to sodium hydride particularly for substrates with low acidity. We found LDA to be an excellent base which generated anions readily where sodium hydride did not (e.g., lactam, oxazoline, picoline). In addition, there was no evidence of amine exchange between LDA and the vinamidinium salt under the reaction conditions used, a consideration that had dictated initially our use of sodium hydride in this work. We then reinvestigated with LDA several of the reactions with carbonyl compounds in which sodium hydride was used as base. An improvement in yield was noted in only one case (**15**). However, dramatic reductions in reaction times were observed in all cases. For example, the reaction time for the conversion of cyclopentanone to its dienaminone decreased from 26 h to 5 h, and the reaction time for the conversion of δ-valerolactone was reduced from 38 to 4 h. The greater effectiveness of LDA as the base in these alkylation reactions is probably due to its higher solubility in the reaction medium.

The reactions were extended to include the alkylation of heterocyclic systems containing activated methylene groups such as 2-ethyl-2-oxazoline, 2-picoline, and 2-methylfuran. The anion of 2-ethyl-2-oxazoline reacts with the salt **1** at −70 °C to give the dienamine **6**. It is necessary to run this reaction at low temperature because of the known tendency of oxazoline anions to rearrange thermally.[19] The anion of 2-picoline generated by reaction with LDA rapidly turns dark blue after addition of **1**, and at the termination of the reaction (~1 h), the solution slowly turns yellow, allowing visual monitoring of the transformation. In the presence of LDA, 2-methylfuran reacts rapidly with **1** as evidenced by the appearance of an intense peak at 414 nm in the UV–visible spectrum. However, the instability of the dienamine products precluded further investigation of this reaction at this time.[20]

When dry reagents and solvents are used, high yields of dienamines and dienaminones are obtained in all of the

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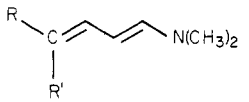
(20) Spectroscopic data and mechanistic considerations suggest two possible structures for these products. They result from alkylation at the 5-carbon (**8a**) and from alkylation at the 2-methyl carbon (**8b**).

reactions except in cases of inherent product instability. All of the reactions referred to above could be monitored very conveniently by UV spectroscopy. The substrates absorbed at wavelengths shorter than those for 1 (in the range 250–300 nm), and the products absorbed at wavelengths longer than those for 1 (in the range 350–420 nm). The absorption maxima of the products could be predicted readily by using Woodward's UV rules.[21] However, as no value was available for a dimethylamino group δ to a carbonyl, a value of 135 nm was assigned. This gave good agreement between the predicted and observed wavelengths of the products in all cases.

Close inspection of the spectral data for the dienamines and the dienaminones revealed several common characteristics. The ^{1}H NMR data (in $CDCl_3$) indicate that these compounds exist in the all-trans or W stereochemistry ($J \approx 12$ Hz). The chemical shifts for the proton on the carbon β to the amino group were all similar, with the resonance observed as a triplet at 4.87–6.41 ppm. The proton on the carbon α to the amino group characteristically appeared as a doublet at 6.32–7.33 ppm. Similar trends were found in the ^{13}C NMR data. The mass spectra of all of these compounds gave parent ions (by EI or CI methods) and fragmentation patterns consistent with their structures.

Symmetrical compounds such as diethyl malonate and 3-pentanone formed single dienaminone products. In the case of 3-pentanone, only one geometric isomer (*E,E*) was observed (rationale for the stereochemical assignments is discussed below for the cyclopentanone case). Ethyl acetoacetate reacted with 1 to produce the *Z,E* and *E,E* isomers **4a** and **4b** in a 44:56 ratio, respectively. When an



2, R = R′ = $CO_2CH_2CH_3$
3, R = $COCH_2CH_3$; R′ = CH_3
4a, R = $COCH_3$; R′ = $CO_2CH_2CH_3$
4b, R = $CO_2CH_2CH_3$; R′ = $COCH_3$
5a, R = $COCH_2CH_3$; R′ = H
5b, R = $COCH_3$; R′ = CH_3

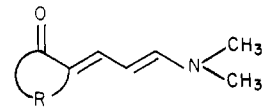
6, R =  R′ = CH_3

7, R =  R′ = H

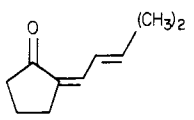
unsymmetrical ketone such as 2-butanone was treated with the vinamidinium salt 1, two products, **5a** and **5b**, were isolated by HPLC on silica gel in a 70:30 ratio respectively. The products are formed in a ratio consistent with the operation of kinetic control in this reaction. This type of regioselectivity could be exploited in a synthetic scheme involving unsymmetrical compounds.

The reaction of cyclopentanone with the vinamidinium salt 1 was of particular interest to us because of the possible ramifications of the resulting dienaminone **9a** (Chart I) in natural product synthesis. The structure of **9a** was established by ^{1}H and ^{13}C NMR data and by its mass spectrum. A detailed ^{1}H NMR analysis showed that only one compound was formed. The coupling constant of 12.5 Hz was consistent with the all-trans or W arrangement seen in the other dienaminones. Further, in the case of cyclopentanone (and other cyclic carbonyl containing systems), the structure was shown to be **9a** (*E,E*) and not its stereoisomer **9b** (*Z,E*) by comparison of chemical shift data with related ring systems containing exocyclic double

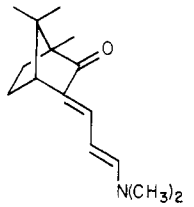
Chart I



9a, R = $-(CH_2)_3-$
10, R = $-(CH_2)_4-$
11, R = $-(CH_2)_5-$
12, R = $-O(CH_2)_2-$
13, R = $-O(CH_2)_3-$
14, R = $CH_3CH_2N(CH_2)_2-$



9b



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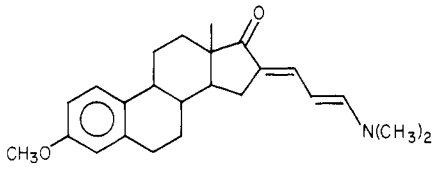

15

bonds.[22,23] On this comparative basis the exocyclic methylene proton of structure **9a** would be expected to have chemical shift of 6.8 ppm or more. The observed value was 7.08 ppm. The *Z,E* isomer **9b** would be expected to have a chemical shift for the exocyclic methylene proton of 5.6 to 5.9 ppm, much less than our observed value. Also present was a trans allylic coupling constant of 2.0 Hz between the C-3 ring protons and the exocyclic methylene proton (doublet of triplets).[24] The ^{13}C NMR spectrum exhibited one resonance for each carbon. Assignment of these resonances was aided by off-resonance and delayed ^{1}H decoupling experiments. The carbon α to the amine appeared at 152.3 ppm, and the carbon β to the amine appeared at 95.3 ppm. The resonance at 123.8 ppm (singlet in off-resonance decoupled spectrum) was assigned as the carbon δ to the amine. The resonance at 136.3 ppm (doublet) was assigned to the γ-carbon. The carbon resonances of the dienaminone appear to have an alternation of electron density similar to that observed in the vinamidinium system. This alternation of electron density is consistent with the generation of a new meneidic system in dienaminone formation.

Another interesting carbonyl system studied was γ-butyrolactone. We were particularly interested in this compound because of the possibility of entry into analogues of natural products containing the α-methylene-γ-butyrolactone moiety.[25] The γ-butyrolactone was an excellent substrate for 1 and gave the dienaminone **12** in 91% yield. As observed for the dienaminones of cyclopentanone, cyclohexanone, and cycloheptanone, the products from the reaction with γ-butyrolactone and δ-valerolactone also had the stereochemistry represented in **12** and **13** as evidenced from ^{1}H and ^{13}C NMR data.

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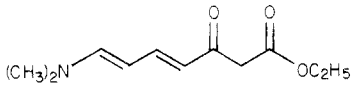
An example of the alkylation reaction with a bicyclic ketone was the transformation of camphor to **16**. The yield obtained is comparable to the yields observed with other alkylations of camphor.[26] Reaction of **1** with a more complex ketone, estrone 3-methyl ether, gave the product **15** (Chart I). It is of interest to note that estrone derivatives with alkyl substitution at position 16 have been found to have antiandrogenic properties.[27]

γ,δ-Unsaturated β-keto esters are useful intermediates in organic synthesis.[28] The direct synthesis of related keto esters can be realized by selective alkylation by **1** of the dianion from ethyl acetoacetate. This methodology allows the alkylation of the less stable of the two enolates.[29,30] Thus, when ethyl acetoacetate was converted to its dianion by reaction with sodium hydride followed by *n*-butyllithium, the resulting dianion reacted smoothly with sodium hyride followed by *n*-butyllithium, the resulting dianion reactes smoothly with the vinamidinium salt to give the unsaturated keto ester **17** in 74% conversion as determined by UV spectroscopy. The actual isolated yield was much lower than this because of product instability.



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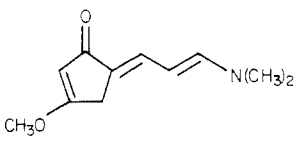
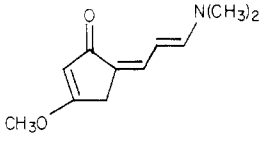
The methyl ether of cyclopentane-1,3-dione reacted with **1** to give **18a** (*E,E*) and **18b** (*Z,E*) in 19% and 12% pure



18a

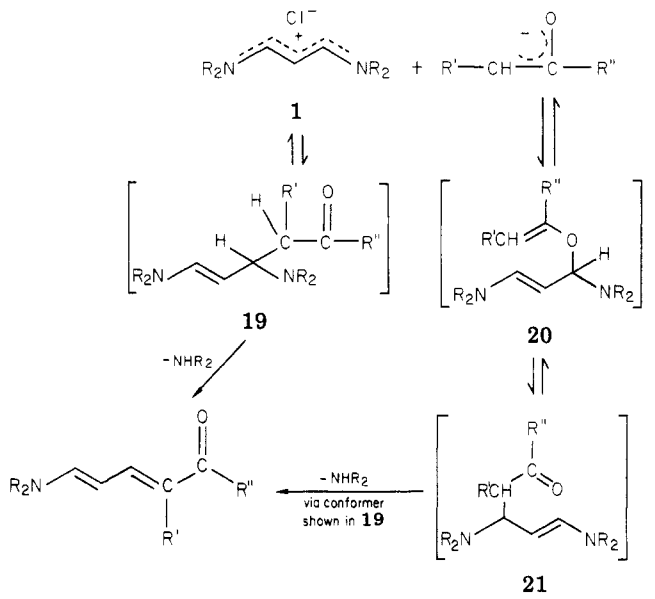


18b

isolated yields, respectively. Considerable decomposition occurred during the workup of this reaction, and the isolated yields were much lower than the spectrophotometrically determined percent conversions. The dianion of cyclopentane-1,3-dione gave even lower yields than that observed for the methyl ether. It should be mentioned with respect to **18b** that this was the only example of a dienaminone with *Z,E* stereochemistry isolated in this study.

All of the reactions discussed above involve nucleophilic attack of enolate (or other stabilized carbanionic species) on the α-carbon of the vinamidinium salt. The intermediate σ complex **19** formed, for example, in the case of the carbonyl-activated methylenes can eliminate a molecule of dimethylamine with the assistance of a tertiary amine such as triethylamine (Scheme I). Elimination of the amine from the σ complex drives the equilibrium forward and produces a new push–pull system. For elimination of the molecule of amine, the σ complex must have a hydrogen atom on the carbon β to the amino group. O-Alkylation, a troublesome side reaction in many direct alkylations of carbonyl-activated methylenes,[3] is not important in these alkylations. The intermediate formed, **20**, cannot eliminate a molecule of dimethylamine readily and probably collapses to give starting materials. This O-alkylated intermediate may undergo a [3,3]sigmatropic

Scheme I. Mechanism of Formation of Dienaminones and Dienamines



rearrangement to give **21** which could eliminate dimethylamine through a conformer similar to **19** to give the dienaminone product. The Claisen rearrangement may not be a significant pathway in most of these alkylations because of the relative low temperatures (generally 25 °C) used in this work.[31]

In summary, the reactions of the vinamidinium salt **1** with activated methylene groups result in the selective introduction of a conjugated three-carbon moiety in these molecules. We are presently examining some interesting transformations of these compounds including their utilization in natural products synthesis.

Experimental Section

The melting points reported are uncorrected and were taken on a Thomas-Hoover melting point apparatus fitted with a microscope. The infrared spectra were recorded on a Beckman IR-20A. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker HX-90E pulse Fourier transform NMR spectrometer interfaced with a Nicolet 1080 computer and disk unit or on a JEOL FX90Q pulse Fourier transform NMR spectrometer. Tetramethylsilane was the internal reference. The mass spectrometers employed were a Hitachi RMU-6E instrument and a Hewlett-Packard 5985 GC/MS system. The ultraviolet data were taken with a Cary Model 219 ultraviolet–visible spectrophotometer. Elemental analyses were performed by the University of Iowa Microanalytical Service on an automated Perkin-Elmer Model 240 carbon, hydrogen, and nitrogen analyzer. HPLC separations were done with an Altex Model 100 pump with preparative heads and an Altex Model 905-19 injector with a 10.2-mL loop and were monitored with a Tracor 970 detector with a Corasil (37–50 μm) silica gel column (1.0 cm 0.0 × 35 cm).

β-(Dimethylamino)acrolein. This compound was prepared by the method of Makin, Shavrygina, and co-workers[16] except that the product was obtained by extraction with methylene chloride instead of a benzene–alcohol mixture. The product, a clear amber liquid, was obtained in 58% yield: bp 121–123 °C (2.5 torr); IR (neat) 1680 (C=O), 1675 (C=C, trans); ^{1}H NMR ($CDCl_3$) δ 2.86 (s, 3 H), 3.15 (s, 3 H), 5.12 (dd, 1 H, J = 8.5, 12.7 Hz), 7.19 (d, 1 H, J = 12.7 Hz), 9.04 (d, 1 H, J = 8.5 Hz); mass spectrum, m/z (relative intensity) 99 (M^+, 100), 84 ($M^+ - CH_3$, 45), 71 (M^+ – CHO, 15), 55 ($M^+ - N(CH_3)_2$, 44).

1,1,5,5-Tetramethyl-1,5-diazapentadienium Chloride (1). β-(Dimethylamino)acrolein (17.5 g, 0.17 mol) and dry dimethylamine hydrochloride (14.4 g, 0.17 mol) in absolute ethanol

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(120 mL) were heated under reflux in a Soxhlet extractor, thimble charged with 3-Å molecular sieves, for 8.5 h under a positive N_2 atmosphere. The solvent was then removed under reduced pressure. The residue, an orange oil, was slurried with ether (3 × 120 mL), and the resulting solid was recrystallized twice from acetone. The product was hygroscopic and was isolated by filtration under N_2. The product was an off-white solid: 20.0 g (70%); mp 187–189 °C (lit.[32] mp 188–190 °C); UV max (EtOH) 309 nm (ε 47 115); ^{1}H NMR ($CDCl_3$) δ 3.17 (s, 6 H), 3.42 (s, 6 H), 5.26 (t, 1 H, J = 12.0 Hz), 8.60 (d, 2 H, J = 12.0 Hz); ^{13}C NMR ($CDCl_3$) δ 38.5, 46.5, 90.3, 164.2; mass spectrum, m/z (relative intensity) 127 (M^+ – Cl, 100), 112 (M^+ – Cl, CH_3, 13), 97 (M^+ – Cl, $2CH_3$, 9), 82 (M^+ – Cl, $3CH_3$, 66).

Methods for the Preparation of Dienaminones. Four different experimental procedures were used for the synthesis of the dienaminones. In all of these procedures the reactions were run in oven-dried glassware under a positive nitrogen atmosphere. The vinaminidinium salt was dried over P_2O_5 in vacuo prior to use. The solvents were also dried prior to use. THF was distilled from $LiAlH_4$. Triethylamine and pyridine were distilled from NaH under N_2. Mineral oil was removed from the NaH dispersion by rinsing with dry hexane before the addition of other reagents. The reaction progress was monitored by UV spectroscopy. The starting materials absorbed in the range of 250–310 nm, and the products absorbed in the range of 370–423 nm. The results of these reactions are summarized in Table I. All reactions were worked up by removal of the solvent under reduced pressure, addition of saturated NaCl solution (15 mL) to the residue (cautiously!), and extraction with CH_2Cl_2 (4 × 20 mL). The combined organic layers were dried over Na_2SO_4. After removal of the solvent, the products were purified by preparative layer chromatography on either E. Merck silica gel-PF-254 or aluminum oxide 60-PF-254 plates.

In method A the carbonyl compound (1.1 mmol) in THF (3 mL) was added dropwise with stirring to the vinamidinium salt (1.0 mmol) and NaH (1.5 mmol) in pyridine (7 mL) at 0 °C. This was followed by stirring at 0 °C for 30 min and then stirring under the specified conditions (Table I). The products were isolated by the standard workup procedure and were purified by the specified chromatographic procedures. In method B the carbonyl compound (1.1 mmol) in THF (3 mL) was added dropwise with stirring to the vinamidinium salt (1.0 mmol) and NaH (1.5 mmol) in triethylamine (7 mL) at 0 °C. This was followed by stirring at 0 °C for 30 min and then stirring under the specified conditions. The products were isolated by the standard workup procedure and were purified by the specified chromatographic procedures. In method C the carbonyl compound (1.1 mmol) in THF (3 mL) was added dropwise with stirring to the vinamidinium salt (1.0 mmol) and NaH (1.5 mmol) in triethylamine (7 mL) over 4-Å molecular sieves (0.3 g) at 0 °C. This was followed by stirring at 0 °C for 30 min and then stirring under the specified conditions. The products were isolated by the standard workup procedure and were purified by the specified chromatographic procedures. In method D the carbonyl compound (1.1 mmol) in dry THF (3 mL) was added dropwise to a stirred solution of lithium diisopropylamide (LDA). [The LDA was generated by adding 1.3 M n-BuLi (1.0 mL) to dry diisopropylamine (1.3 mmol) in dry THF (5 mL) at 0 °C and stirring the mixture at 0 °C for 20 min after the addition was complete.] To this was added dry triethylamine (4 mL) and the vinamidinium salt (1.0 mmol). The reaction was stirred at 0 °C for 30 min and then under the specified conditions. The reaction was quenched by carefully pouring the reaction mixture into saturated NaCl solution (20 mL) followed by the standard aqueous workup. The products were purified by the specified chromatographic procedures. Unless stated otherwise, all crystalline products were recrystallized from hexane or hexane/ether.

Dienaminone of Diethyl Malonate 2. Method A. The residue after the workup was chromatographed on silica gel preparative-layer plates which were developed with 3% MeOH/acetone. The band with R_f 0.52 was cut out and eluted with 5% MeOH/acetone. The dienaminone **2** was obtained as yellow crystals: UV max (EtOH) 372 nm (ε 54 990); ^{1}H NMR ($CDCl_3$) δ 1.25 (t, 3 H, J = 7.5 Hz), 1.30 (t, 3 H, J = 7.5 Hz), 3.00 (s, 6 H), 4.25 (q, 2 H, J = 7.5 Hz), 4.30 (q, 2 H, J = 7.5 Hz), 6.05 (t, 1 H, J = 13.0 Hz), 7.00 (d, 1 H, J = 13.0 Hz), 7.70 (d, 1 H, J = 13.0 Hz); ^{13}C NMR ($CDCl_3$) δ 14.5, 59.7, 59.8, 97.1, 106.3, 153.6, 156.9, 167.0; mass spectrum, m/z (relative intensity) 241 (M^+, 100), 196 (M^+ – $HN(CH_3)_2$, 85), 168 (M^+ – CO_2Et, 33), 97 (39), 94 (55), 82 (92).

Anal. Calcd for $C_{12}H_{19}NO_4$: C, 59.73; H, 7.94; N, 5.81. Found: C, 59.73; H, 7.60; N, 5.67.

Dienaminones of Ethyl Acetoacetate, 4a,b. Method B. The residue after the workup was chromatographed on silica gel preparative-layer plates which were developed with 5% acetone/EtOAc. The band with R_f 0.50 was cut out and eluted with 7% acetone/EtOAc. The dienaminones **4a,b** were obtained as a tan solid: UV max (EtOH) 393 nm (ε 54 798); ^{1}H NMR ($CDCl_3$) δ 1.30 (t, 3 H, J = 7.8 Hz), 1.35 (t, 3 H, J = 7.8 Hz), 2.39 (s, 3 H), 2.43 (s, 3 H), 3.07 (s, 12 H), 4.23 (q, 4 H, J = 7.8 Hz), 6.41 (t, 1 H, J = 12.7 Hz), 6.77 (t, 1 H, J = 12.7 Hz), 7.33 (d, 2 H, J = 12.7 Hz), 7.51 (d, 1 H, J = 12.7 Hz), 7.76 (d, 1 H, J = 12.7 Hz); isomers observed in 44% and 56% yields by NMR; ^{13}C NMR ($CDCl_3$) δ 14.5, 29.7, 31.8, 35.0, 59.6, 98.7, 99.3, 113.3, 115.0, 154.4, 155.0, 160.3, 168.3, 196.2, 198.7, both isomers observed; mass spectrum, m/z (relative intensity) 211 (M^+, 50), 196 (M^+ – CH_3, 27), 168 (M^+ – CH_3CO, 33), 167 (M^+ – $N(CH_3)_2$, 67), 124 (30), 94 (37), 45 ($(CH_3)_2NH^+$, 100), 44 ($CH_2NHCH_3^+$, 67).

Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.53; H, 8.11; N, 6.63. Found: C, 62.21; H, 7.83; N, 6.56.

Dienaminone of Cyclopentanone, 9a. Method B. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were developed with 3% acetone/EtOAc. The band with R_f 0.50 was cut out and eluted with 5% acetone/EtOAc. The dienaminone **9a** was obtained as yellow crystals: UV max (EtOH) 396 nm (ε 42 515); ^{1}H NMR ($CDCl_3$) δ 1.88 (m, 2 H), 2.33 (m, 2 H), 2.51 (m, 2 H), 2.91 (s, 6 H), 4.91 (t, 1 H, J = 12.5 Hz), 6.73 (d, 1 H, J = 12.5 Hz), 7.08 (dt, 1 H, J = 12.5, 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 19.8, 27.2, 38.7, 40.7, 95.3, 123.8, 136.3, 152.3, 206.0; mass spectrum, m/z (relative intensity) 165 (M^+, 100), 164 (M^+ – H, 27), 150 (M^+ – CH_3, 33), 121 (–M^+ – $N(CH_3)_2$, 70), 109 (61), 108 (24), 94 (44), 93 (33).

Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.24; H, 8.99; N, 8.48.

Dienaminone of Cyclohexanone, 10. Method B. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were developed with 3% acetone/EtOAc. The band with R_f 0.58 was cut out and eluted with 5% acetone/EtOAc. The dienaminone **10** was obtained as a brown solid: UV max (EtOH) 397 nm (ε 37 901); ^{1}H NMR ($CDCl_3$) δ 1.76 (m, 4 H), 2.68 (m, 4 H), 2.91 (s, 6 H), 5.00 (t, 1 H, J = 12.5 Hz), 6.76 (d, 1 H, J = 12.5 Hz), 7.41 (dt, 1 H, J = 12.5, 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 23.0, 23.2, 25.9, 38.8, 40.5, 94.1, 121.4, 140.8, 151.7, 198.1; mass spectrum, m/z (relative intensity) 179 (M^+, 91), 164 (M^+ – CH_3, 5), 136 (31), 135 (M^+ – $N(CH_3)_2$, 100), 134 (M^+ – $HN(CH_3)_2$, 33), 108 (26), 94 (28).

Anal. Calcd for $C_{11}H_{17}NO$: C, 73.69; H, 9.56; N, 7.81. Found: C, 73.18; H, 9.31; N, 7.53.

Dienaminone of 3-Pentanone, 3. Method C. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were developed with 25% EtOAc/$CHCl_3$. The band with R_f 0.69 was cut out and eluted with 27% EtOAc/$CHCl_3$. The dienaminone **3** was obtained as yellow crystals: UV max (EtOH) 385 nm (ε 44 081); ^{1}H NMR ($CDCl_3$) δ 1.10 (t, 3 H, J = 7.5 Hz), 1.82 (s, 3 H), 2.61 (q, 2 H, J = 7.5 Hz), 2.93 (s, 6 H), 5.13 (t, 1 H, J = 12.2 Hz), 6.70 (d, 1 H, J = 12.2 Hz), 7.21 (d, 1 H, J = 12.2 Hz); ^{13}C NMR ($CDCl_3$) δ 9.9, 11.2, 29.8, 40.6, 95.0, 123.5, 142.2, 149.9, 200.7, mass spectrum, m/z (relative intensity) 167 (M^+, 15), 123 (35), 122 (M^+ – $HN(CH_3)_2$, 100), 121 (88), 107 (M^+ – CH_3, $HN(CH_3)_2$, 37), 94 (29), 93 (40), 79 (67).

Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.38. Found: C, 71.74; H, 10.15; N, 8.09.

Dienaminones of 2-Butanone, 5a,b. Method B. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were developed with EtOAc. The band with R_f 0.60 was cut out and eluted with 2% acetone/EtOAc. The dienaminones **5a,b** were obtained as a yellow oil. The isomers **5a** and **5b** were separated by HPLC silica gel with 5% EtOAc/CH_2Cl_2. The separation was monitored at 395 nm. The flow

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rate of 5.6 mL/min was used. The first peak had a retention time of 13 min and was identified as **5b** which was 30% of the mixture. The second peak had a retention time of 22 min and was identified as **5a** which was 70% of the mixture. For the dienaminone **5a**: UV max (EtOH) 370 nm (ϵ 44 702); ^{1}H NMR ($CDCl_3$) δ 1.10 (t, 3 H, J = 7.5 Hz), 2.46 (q, 2 H, J = 7.5 Hz), 2.89 (s, 6 H), 5.12 (t, 1 H, J = 12.1 Hz), 5.85 (d, 1 H, J = 14.6 Hz), 6.70 (d, 1 H, J = 12.1 Hz), 7.31 (dd, 1 H, J = 12.1, 14.6 Hz); ^{13}C NMR ($CDCl_3$) δ 9.3, 29.7, 40.6, 96.8, 116.8, 146.3, 151.7, 230.9 For the dienaminone **5b**: UV max (EtOH) 380 nm (ϵ 44 300); ^{1}H NMR ($CDCl_3$) δ 1.81 (s, 3 H), 2.27 (s, 3 H), 2.92 (s, 6 H), 5.11 (t, 1 H, J = 12.1, 11.7 Hz), 6.69 (d, 1 H, J = 11.7 Hz), 7.15 (d, 1 H, J = 12.1 Hz); ^{13}C NMR ($CDCl_3$) δ 11.0, 29.6, 40.6, 95.1, 124.5, 143.5, 150.1, 229.5; mass spectrum, m/z (relative intensity) 108 (M^+ - $HN(CH_3)_2$, 92), 107 (M^+ - $HN(CH_3)_2$ - H, 100), 79 (M^+ - $HN(CH_3)_2$ - C_2H_6, 35), 77 (M^+ - Et - $HN(CH_3)_2$, 33), 54 (10), 52 (14), 51 (M^+ - EtCO - $HN(CH_3)_2$, 17).

Anal. Calcd for $C_9H_{15}NO{\cdot}H_2O$: C, 63.12; H, 10.01; N, 8.18. Found: C, 63.55; H, 9.76; N, 7.97.

Dienaminone of Estrone 3-Methyl Ether, 15. Method B. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were developed with 1% acetone/$CHCl_3$. The band with R_f 0.50 was cut out and eluted with 3% acetone/$CHCl_3$. The dienaminone **15** crystallized as a pale yellow solid: UV max (EtOH) 390 nm (ϵ 45 778); ^{1}H NMR ($CDCl_3$) δ 0.90 (s, 3 H), 1.23 (m, 4 H), 1.50 (m, 4 H), 2.18 (m, 2 H), 2.87 (s, 6 H), 3.73 (s, 3 H), 4.93 (t, 1 H, J = 13.4 Hz), 6.68 (d, 1 H, J = 13.4 Hz), 7.14 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 14.9, 26.1, 26.8, 29.6, 31.9, 37.8, 40.6, 44.6, 48.1, 55.0, 95.1, 111.3, 113.8, 123.6, 126.1, 132.5, 136.4, 137.7, 151.5, 157.4, 208.6; mass spectrum, m/z (relative intensity) 365 (M^+, 100), 350 (M^+ - CH_3, 4), 321 (M^+ - $(CH_3)_2N$, 12), 286 (M^+ - C_5H_5N, 6), 186 (6), 160 (2), 110 (12), 73 (13).

Anal. Calcd for $C_{24}H_{31}O_2N{\cdot}0.5H_2O$: C, 76.97; H, 8.61; N, 3.74. Found: C, 77.18; H, 8.61; N, 3.44.

Dienaminone of Cycloheptanone, 11. Method C. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were developed with 4% EtOAc/CH_2Cl_2. The band with R_f 0.45 was cut out and eluted with 10% EtOAc/CH_2Cl_2. The dienaminone **11** was isolated as a yellow oil: UV max (EtOH) 383 nm (ϵ 33 969); ^{1}H NMR ($CDCl_3$) δ 1.68 (s, 8 H), 2.55 (m, 2 H), 2.89 (s, 6 H), 5.09 (t, 1 H, J = 12.5, 12.1 Hz), 6.75 (d, 1 H, J = 12.5 Hz), 7.28 (d, 1 H, J = 12.1 Hz); ^{13}C NMR ($CDCl_3$) δ 25.4, 27.2, 29.6, 34.9, 40.7, 43.5, 94.2, 126.8, 139.9, 151.8, 200.0; mass spectrum, m/z (relative intensity) 193 (M^+, 1), 163 (M^+ - Et, 1), 149 (M^+ - $N(CH_3)_2$, 100), 133 (18), 123 (1), 121 (4), 104 (11).

This compound was too unstable to give satisfactory elemental analysis.

Dienaminone of δ-Valerolactone, 13. Method C. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were developed with 4% EtOAc/CH_2Cl_2. The band with R_f 0.48 was cut out and eluted with 10% EtOAc/CH_2Cl_2. After crystallization the dienaminone **13** was obtained as a pale yellow solid: UV max (EtOH) 365 nm (ϵ 38 422); ^{1}H NMR ($CDCl_3$) δ 1.91 (m, 2 H, J = 5.1 Hz), 2.44 (t, 2 H, J = 5.1 Hz), 2.92 (s, 6 H), 4.24 (t, 2 H, J = 5.1 Hz), 4.96 (t, 1 H, J = 12.5, 12.1 Hz), 6.72 (d, 1 H, J = 12.5 Hz), 7.51 (dt, 1 H, J = 12.1, 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 22.8, 23.5, 40.6, 67.9, 93.7, 108.6, 145.1, 151.6, 168.6; mass spectrum, m/z (relative intensity) 181 (M^+, 100), 166 (M^+ - CH_3, 5), 137 (M^+ - CO_2, 28), 108 ($C_6H_5O_2^+$, 25) 94 (43), 82 (37), 44 (11).

Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.58; H, 8.54; N, 7.46.

Dienaminone of γ-Butyrolactone, 12. Method C. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were developed with EtOAc. The band with R_f 0.50 was cut out and eluted with 2% acetone/EtOAc. The dienaminone **12** was obtained as yellow crystals: UV max (EtOH) 358 nm (ϵ 33 319); ^{1}H NMR ($CDCl_3$) δ 2.80 (m, 2 H), 2.99 (s, 6 H), 4.35 (t, 2 H, J = 7.5 Hz), 4.87 (t, 1 H, J = 12.2 Hz), 6.73 (d, 1 H, J = 12.2 Hz), 7.19 (dt, 1 H, J = 12.2, 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 25.9, 40.7, 65.2, 94.5, 108.6, 139.2, 151.3, 173.7; mass spectrum, m/z (relative intensity) 167 (M^+, 100), 166 (M^+ - H, 62), 138 (M^+ - C_2H_4, 51), 122 (M^+ - $HN(CH_3)_2$, 11), 109 (22), 108 (22), 94 (43).

Anal. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.83. Found: C, 64.50; H, 7.89; N, 8.25.

Dienaminone of *dl*-Camphor, 16. Method B. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were developed with 8% EtOAc/$CHCl_3$. The band with R_f 0.46 was cut out and eluted with 10% EtOAc/$CHCl_3$. The dienaminone **16** was obtained as a yellow oil: UV max (EtOH) 380 nm (ϵ 33 602); ^{1}H NMR ($CDCl_3$) δ 0.81–1.25 (m, 9 H), 1.46–2.69 (m, 5 H), 2.87 (s, 6 H), 4.95 (t, 1 H, J = 12.2 Hz), 6.32 (d, 1 H, J = 12.2 Hz), 6.88 (d, 1 H, J = 12.2 Hz); ^{13}C NMR ($CDCl_3$) δ 9.5, 18.8, 20.4, 26.6, 31.3, 40.6, 47.2, 48.0, 57.8, 94.3, 130.5, 131.5, 131.5, 150.3, 207.2; mass spectrum, m/z (relative intensity) 233 (M^+, 22), 218 (M^+ - CH_3, 2), 205 (M^+ - CO, 16), 190 (M^+ - CH_3, CO, 18), 136 (90), 121 (70), 107 (100), 95 (60), 94 (68), 93 (99).

Anal. Calcd for $C_{15}N_{23}NO$: C, 71.68; H, 10.03; N, 5.57. Found: C, 71.92; H, 10.25; N, 5.31.

Dienamine of 2-Ethyl-2-oxazoline, 6. Method D. The salt **1** was added to a solution of the oxazoline anion at −70 °C, and the reaction was stirred at this temperature for 4 h. The reaction was then allowed to slowly warm to room temperature and was then quenched. The residue after the workup was chromatographed on aluminum oxide preparative-layer plates which were eluted with 4% acetone/EtOAc. The band with R_f 0.71 was cut out and eluted with 10% acetone/EtOAc. The product was then sublimed at 55–60 °C (0.02 torr), and the dienamine **6** was isolated as an off-white solid: UV max (EtOH) 336 nm (ϵ 41 499); ^{1}H NMR ($CDCl_3$) δ 1.89 (s, 3 H), 3.02 (s, 6 H), 4.05 (m, 2 H), 4.54 (m, 2 H), 5.19 (t, 1 H, J = 12.4 Hz), 7.14 (d, 1 H, J = 12.4 Hz), 7.85 (d, 1 H, J = 12.4 Hz); ^{13}C NMR ($CDCl_3$) δ 13.1, 40.5, 54.1, 67.1, 94.9, 109.7, 137.7, 148.3, 167.9; mass spectrum, m/z (relative intensity) 180 (M^+, 5), 137 (M^+ - $HN(CH_3)_2$, 11), 136 (M^+ - $N(CH_3)_2$, 100), 122 (M^+ - $CH_2N(CH_3)_2$, 31, 108 (7), 92 (27), 71 (10).

Anal. Calcd for $C_{10}H_{16}N_2O$: C, 66.63; H, 8.95, N, 15.55. Found: C, 66.03; H, 8.28; N, 15.06.

Dienamine of 2-Picoline, 7. Method D. The residue after the workup was distilled in a micromolecular still. The product distilled with an oil bath temperature of 130–135 °C (0.3 torr) [lit.[33] 120–122 °C (0.1 torr)]. The product rapidly decomposed on exposure to air. It is best stored in a freezer under N_2: UV max (EtOH) 369 nm (ϵ 29 350); ^{1}H NMR ($CDCl_3$) δ 2.97 (s, 6 H), 5.04 (dd, 1 H, J = 11.0, 13.0 Hz), 6.00 (d, 1 H, J = 15.0 Hz), 6.32 (d, 1 H, J = 13.0 Hz), 7.00 (m, 2 H), 7.13 (dd, 1 H, J = 15.0, 11.0 Hz), 7.35 (m, 1 H), 8.37 (m, 1 H).

Dienaminone of 1-Ethyl-2-pyrrolidinone, 14. Method D. The residue after the workup was chromatographed on aluminum oxide preparative layer plates which were developed with 5% acetone/EtOAc. The band with R_f 0.41 was cut out and eluted with 10% acetone/EtOAc. The dienaminone **14** was isolated as a yellow solid: UV max (EtOH) 343 nm (ϵ 34 143); ^{1}H NMR ($CDCl_3$) δ 1.12 (t, 3 H, J = 7.3 Hz), 2.66 (m, 2 H), 2.82 (s, 6 H), 3.43 (m, 4 H), 4.80 (t, 1 H, J = 12.6, 12.0 Hz), 6.54 (d, 1 H, J = 12.6 Hz), 6.87 (dt, 1 H, J = 12.0, 2.5 Hz); ^{13}C NMR ($CDCl_3$) δ 12.6, 22.3, 37.6, 40.5, 43.8, 94.3, 118.7, 130.8, 148.0, 169.9; mass spectrum, m/z (relative intensity) 194 (M^+, 96), 179 (M^+ - CH_3, 17), 165 (M^+ - Et, 9), 150 (M^+ - $N(CH_3)_2$, 54), 122 (39), 94 (100), 82 (60), 58 (37), 43 (50).

Anal. Calcd for $C_{11}H_{18}N_2O$: C, 68.00; H, 9.34; N, 14.43. Found: C, 67.74; H, 9.16; N, 14.28.

Dienaminone from the Ethyl Acetoacetate Dianion, 17. An oven-dried round-bottomed flask with a septum inlet, pressure-equalized addition funnel, and gas stopcock was evacuated and flushed with N_2, and the reaction was run under a positive N_2 atmosphere. The flask was charged with NaH (0.072 g, 1.5 mmol)/mineral oil which was rinsed with dry hexane to remove the oil. To this was added 5 mL of dry THF. The reaction was cooled in an ice bath, and ethyl acetoacetate (0.17 mL, 1.3 mmol) in 5 mL dry THF was added dropwise with stirring. After the addition was complete the reaction was stirred at 0 °C for 30 min, and *n*-BuLi (1.0 mL, 1.4 mmol) was added dropwise by syringe. The dianion solution was bright orange. After the addition was complete, the reaction was stirred at 0 °C for 20 min. To the dianion solution was added 0.16 g (1.0 mmol) of the vinamidinium

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salt. After being stirred at 0 °C for 3 h, the reaction mixture was slowly warmed to room temperature and was stirred for an additional 2 h. It was then poured onto 20 mL of saturated NH_4Cl solution and extracted with CH_2Cl_2 (3 × 25 mL). Solvent was removed from the dried (Na_2SO_4) extracts under reduced pressure, and the residue was chromatographed on two silica gel preparative-layer plates, which were eluted with 3% acetone/EtOAc. The band with R_f 0.47 was cut out and eluted with 6% acetone/EtOAc. The dienaminone **17** was isolated as a yellow oil: 0.035 g (17% yield); UV max (EtOH) 388 nm (ε 43 346); ^1H NMR ($CDCl_3$) δ 1.26 (t, 3 H, J = 7.3 Hz), 2.92 (s, 6 H), 3.47 (s, 2 H), 4.13 (q, 2 H, J = 7.3 Hz), 5.15 (t, 1 H, J = 12.1, 14.5 Hz), 5.86 (d, 1 H, = 14.5 Hz), 6.76 (d, 1 H, J = 12.1 Hz), 7.34 (dd, 1 H, J = 14.5, 12.1 Hz).

Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.53; H, 8.11; N, 6.63. Found: C, 62.25; H, 7.84; 6.34.

Dienaminones of 3-Methoxy-2-cyclopentenone, 18a,b. The 3-methoxy-2-cyclopentenone was prepared by the method of House and Rasmusson.[34] The reaction residue, an amber oil, was purified by sublimation at 50–55 °C (bath temperature; 0.5 torr). The product, a white solid, was isolated in 81% yield: mp 49–51 °C (lit.[34] mp 51–52 °C); mass spectrum, m/z (relative intensity) 112 (M^+, 100), 83 (M^+ – CHO, 44), 81 (M^+ – OCH_3, 41), 69 (M^+ – C_2H_3O, 97), 57 (38).

The reaction of the vinamidinium salt 1 with 3-methoxy-2-cyclopentenone was carried out by method D. The residue after workup was chromatographed on aluminum oxide preparative-layer plates which were developed with 10% acetone/EtOAc. Two compounds were isolated, **18a** and **18b**, as yellow oils.

The band with R_f 0.40 was removed and eluted with 2% CH_3OH/EtOAc. The dienaminone **18b** was isolated as a yellow oil: 12% yield; UV max (EtOH) 395 nm (ε 45 400); ^1H NMR ($CDCl_3$) δ 2.85 (s, 6 H), 2.96 (m, 2 H), 3.86 (s, 3 H), 4.85 (t, 1 H, J = 12.1 Hz), 5.33 (s, 1 H), 6.51 (d, 1 H, J = 12.1 Hz), 6.60 (d, 1 H, J = 12.1 Hz); mass spectrum, m/z (relative intensity) 193 (M^+, 11), 178 (M^+ – CH_3, 7), 167 (M^+ – C_2H_2, 29), 149 (M^+ – $N(CH_3)_2$, 88), 97 (21), 70 (60), 43 (100).

The band with R_f 0.30 was cut out and eluted with 2% MeOH/EtOAc. The dienaminone **18a** was isolated as a yellow oil: 19% yield; UV max (EtOH) 395 nm (ε 45 431); ^1H NMR ($CDCl_3$) δ 2.88 (s, 6 H), 3.12 (m, 2 H), 3.82 (s, 3 H), 4.87 (t, 1 H, J = 12.1 Hz), 5.41 (s, 1 H), 6.66 (d, 1 H, J = 12.1 Hz), 7.02 (d, 1 H, J = 12.1 Hz); mass spectrum, m/z (relative intensity) 193 (M^+, 10), 178 (M^+ – CH_3, 4), 167 (M^+ – C_2H_2, 32), 149 (M^+ – $N(CH_3)_2$, 100), 97 (6), 70 (10), 43 (10).

Both of these compounds were too unstable to give satisfactory elemental analysis. However, mass, UV, and NMR spectral data provided excellent confirmation of the structure in each case.

Acknowledgment is made to the NSF for Grant No. CHE 79-058865 and to the University of Iowa Graduate College for a Research Assistantship to C.S.C.

Registry No. (*E*)-1, 70669-77-1; (*E*)-**2**, 78804-79-2; (*E,E*)-**3**, 75834-03-6; (*Z,E*)-**4a**, 78804-80-5; (*E,E*)-**4b**, 78804-81-6; (*E,E*)-**5a**, 75847-94-8; (*E,E*)-**5b**, 78804-82-7; (*E,E*)-**6**, 78804-83-8; (*E,E*)-**7**, 78804-84-9; (*E,E*)-**9a**, 75833-99-7; (*E,E*)-**10**, 75834-00-3; (*E,E*)-**11**, 78804-85-0; (*E,E*)-**12**, 75834-01-4; (*E,E*)-**13**, 78804-86-1; (*E,E*)-**14**, 78804-87-2; (*E,E*)-**15**, 75834-05-8; (±)-(*E,E*)-**16**, 78804-88-3; (*E,E*)-**17**, 78804-89-4; (*E,E*)-**18a**, 78804-90-7; (*Z,E*)-**18b**, 78804-91-8; β-(dimethylamino)acrolein, 927-63-9; dimethylamine·HCl, 506-59-2; diethyl malonate, 105-53-3; ethyl acetoacetate, 141-97-9; 3-pentanone, 96-22-0; 2-butanone, 78-93-3; cyclopentanone, 120-92-3; cyclohexanone, 108-94-1; cycloheptanone, 502-42-1; *dl*-camphor, 21368-68-3; estrone 3-methyl ether, 1624-62-0; γ-butyrolactone, 96-48-0; δ-valerolactone, 542-28-9; 1-ethyl-2-pyrrolidinone, 2687-91-4; 2-ethyl-2-oxazoline, 10431-98-8; 2-picoline, 109-06-8; 3-methoxy-2-cyclopentenone, 4683-50-5.

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Identification of Modified Nucleosides by Secondary-Ion Mass Spectrometry

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Received April 29, 1981

Argon ion bombardment of nucleosides produces mass spectra of high quality from which the molecular weight and the nature of the sugar can readily be determined. The most intense peak corresponds to the base itself, and ions representing the base attached to Na^+, or other cations, are obtained by addition of the appropriate salt. Parallels with fragmentations observed in electron impact exist and help to define molecular structures. Detection limits of a few nanograms are demonstrated and it is shown that ions characterizing the base can be greatly enhanced by simple acid pretreatment of the sample. Comparisons are made with pyrolysis mass spectrometry/mass spectrometry and it is concluded that modified bases cannot be identified in intact DNA by pyrolysis MS/MS without the possibility of isomerization although MS/MS does provide isomer specificity for pure modified bases.

The characterization of alkylated nucleosides at submicrogram levels has become increasingly important to nucleic acids and cancer research since most alkylating agents possess mutagenic activity and it is now recognized that most, if not all, chemical carcinogens are mutagens.[1,2] Nucleic acids generally have been considered prime target molecules for mutagenic and carcinogenic agents.[3,4] This paper deals with the capabilities of one of the newer ionization methods in mass spectrometry, secondary-ion mass spectrometry (SIMS),[5,6] for identification and quantification of methylated nucleosides. The companion paper[7]

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