(C-2), 55.9 (C-9), 23.8 (C-7), 22.0 (C-4), 21.0 and 20.3 (C-1 and C-6), 16.4 (C-5), and 13.4 (C-8).

7-*endo*-Methyl-7-*exo*-(2-hydroxy-4-methyl-3-pentenyl)bicyclo[4.1.0]hept-2-ene (15). An ether solution of isobutenyllithium (ca. 20 mmol, prepared from isobutenyl bromide and lithium wire) was added to 750 mg (5.0 mmol) of aldehyde **14** in 10 ml of ether at 0 °C. This mixture was stirred for 6 h and then poured into ether. The ether solution was washed with saturated ammonium chloride solution, bicarbonate, and brine. The ether was dried ($MgSO_4$), filtered, and concentrated. The resulting oil was chromatographed on a short silica gel column (ether/hexane) to yield 920 mg (89%) of alcohol **15**: IR (film) 3350 cm^{-1}; ^1H NMR δ 1.6 (bs, 2 olefinic methyls), 4.5 (m, CHOH), 5.1 (broad doublet, J = 9 Hz, C-1 vinyl proton), and 5.8 (bs, ring olefinic protons); ^{13}C NMR δ 133.8 (C-12), 128.6 (C-3), 126.3 (C-11), 125.2 (C-2), 67.5 (C-10), 50.1 (C-9), 25.9 (C-7 and C-13), 22.2 (C-4), 21.6 and 20.8 (C-1 and C-6), 18.2 (C-14), 16.5 (C-5), and 12.9 (C-8).

7-*endo*-Methyl-7-*exo*-(2-acetoxy-4-methyl-3-pentenyl)bicyclo[4.1.0]hept-2-ene (16). A solution of 540 mg (2.62 mmol) of alcohol **15**, 2 mL of pyridine, and 10 mL of acetic anhydride was refluxed for 3 h. This solution was poured into ether and washed several times with water, bicarbonate, and brine. The aqueous extracts were washed with ether and the combined ether extracts were dried ($MgSO_4$), filtered, and concentrated. The residue was evaporatively distilled (120 °C (0.1 mm)) to yield 550 mg (85%) of acetate **16**: IR (film) 1725 cm^{-1}, no OH; ^1H NMR δ 2.0 (s, O_2CCH_3).

Demethylsesquicarene (3).[12] Acetate **16** (540 mg, 2.18 mmol) was added to 25 mL of ethylamine (distilled from a small piece of sodium) and 60 mg (8.6 mg-atoms) of lithium. This solution was stirred until the lithium had completely reacted and then ammonium chloride was added. The solution was poured into ether and washed with water (3×), acid (2×), bicarbonate, and brine. The ether solution was dried ($MgSO_4$), filtered, and concentrated. The residual oil was evaporatively distilled to yield 400 mg (97%) of product: IR (film) 3040, 1640, 1450, and 1375 cm^{-1}; ^1H NMR δ 0.9 (s, CH_3), 0.7–2.2 (m), 1.60 and 1.65 (s, two olefinic methyls), 5.1 (t, J = 7 Hz, 1 H), and 5.7 ppm (bs, olefinic protons on ring); ^{13}C NMR δ 130.9 (C-12), 127.1 (C-3), 125.8 (C-11), 124.8 (C-2), 43.1 (C-9), 25.7, 22.3, 22.1 21.3, 21.0, 17.6, 16.9, 16.6, and 12.6; MS m/e (rel intensity) 190 (M^+, 7), 121 (19), 107 (55), 105 (50), 93 (33), 91 (38), 82 (21), 81 (21), 80 (19), 79 (67), 77 (26), 69 (60), 67 (29), 55 (43), 53 (24), 41 (100), 39 (33). Anal.[13] Calcd for $C_{14}H_{22}$: 190.172150. Found: 190.171598 (MS); 2.9 ppm error.

Acknowledgements. We thank the Robert A. Welch Foundation for generous financial support of this research. The JEOL PFT-100 NMR spectrometer was purchased with grant support from the National Science Foundation (GP-32912).

Registry No.—**3**, 63764-90-9; **4**, 63813-94-5; **5**, 63813-95-6; **10**, 63764-91-0; **11**, 63764-92-1; **12**, 63764-93-2; **13**, 63764-94-3; **14**, 63764-95-4; **15**, 63764-96-5; **16**, 63764-97-6; 8-chloro-8-*exo*-methyl-*cis*-bicyclo[4.2.0]oct-2-ene-7-one, 63813-96-7; isobutenyllithium, 29917-94-0.

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Pyridopyrimidines. 8. A Novel Ring Opening during the Acylation of 6-Amino-1,3-dimethyluracil

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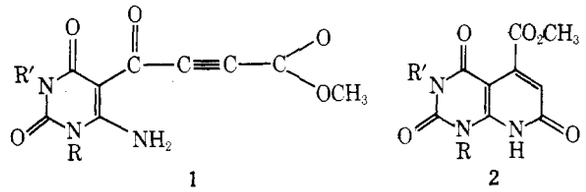
The use of dimethyl acetylenedicarboxylate (DMAD) in the synthesis of pyrido[2,3-*d*]pyrimidines has been the subject of several recent papers.[1-4] During the course of these investigations, it was found that the reaction of 1-alkyl-6-aminouracil derivatives with DMAD under aprotic conditions gave rise to 5-(3-carbomethoxy-2-propynoyl)uracils (**1**).[4] When the same reaction was carried out in a protic solvent (water, methanol), on the other hand, the pyridopyrimidine (**2**) was formed.[1-3]



1 **2**

a, R = R′ = CH_3
b, R = CH_3; R′ = H

In an attempt to gain additional insight into the mechanism of the formation of ketones having the general structure **1**, the reaction of 1,3-dimethyl-6-aminouracil (**3**) with DMAD was followed by ^1H NMR spectroscopy using $(CD_3)_2SO$ as solvent. Spectra were obtained at various time intervals and revealed the disappearance of **3** and the ultimate formation of **1a**. However, a number of additional peaks appeared in the spectrum such that, about 1 h after the initiation of the reaction, the spectrum was a composite of all the peaks (and only the peaks) seen in Figure 1a–c. After 6 h the spectrum (Figure 1c) corresponded to that of the propynoyl adduct **1a**.

The most striking feature of the composite spectrum was the disappearance of one *N*-methyl resonance at δ 3.27 and its replacement by a doublet at δ 2.60. Addition of a small amount of D_2O to the solution caused an immediate collapse of the δ 2.60 doublet to a singlet with the concomitant disap-

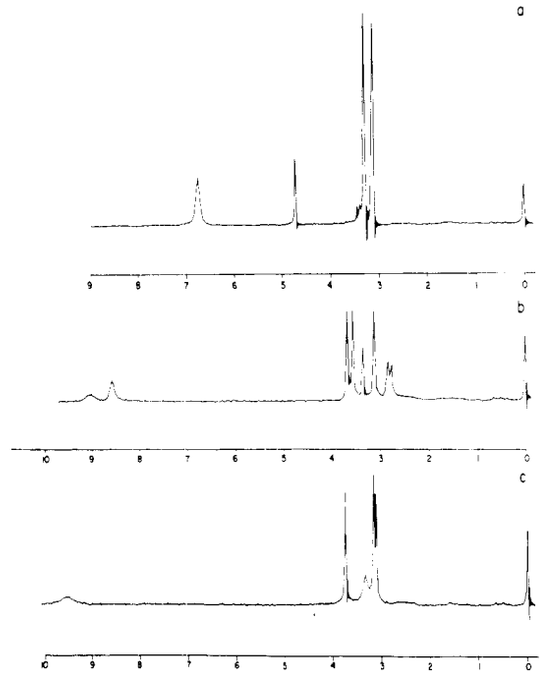


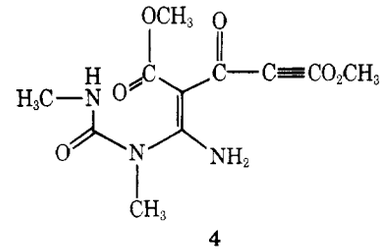
Figure 1. ^1H NMR spectra in $(CD_3)_2SO$ with DSS as internal reference (multiplet at δ 2.5 due to solvent was eliminated for the sake of clarity): (a) 6-amino-1,3-dimethyluracil; (b) reaction mixture; (c) 5-(3-carbomethoxypropynoyl)-1,3-dimethyl-6-aminouracil.

pearance of a broad doublet at δ 9.03 attributable to a single N–H proton.

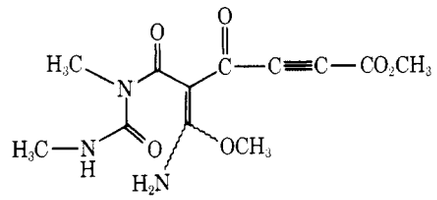
The reaction was repeated on a larger scale in $(CH_3)_2SO$. Addition of methanol to the reaction mixture after 1 h led to the precipitation of a pale yellow solid which was recovered in 57% yield. The ^1H NMR spectrum of this solid (Figure 1b) showed very clearly the presence of the δ 2.60 doublet. In addition there were seen two low-field signals (δ 9.03 and 8.55) which disappeared rapidly upon addition of D_2O and which corresponded to one and two protons, respectively. These data are consistent only with an $NHCH_3$ moiety which must have resulted from opening the pyrimidine ring. The ring-opened intermediate was unstable and was converted to the intensely orange propynoyl derivative **1a** simply by gentle warming or allowing the solution to stand at room temperature in either protic or aprotic solvents. Even at −10 °C the pure solid intermediate was converted to **1a** within a few months.

The intermediate gave an elemental analysis consistent with a simple adduct of **3** and DMAD, but electron impact or chemical ionization mass spectrometry gave only the molecular ion (*m/e* 265) of the cyclized final product **1a**. Although this result was not surprising in view of the marked instability of the intermediate, it was clearly desirable to demonstrate that the true molecular ion did contain the additional elements of methanol (*m/e* 297). A freshly prepared sample of the intermediate was subjected to field desorption mass spectrometry which did lead to the demonstration of a prominent molecular ion at *m/e* 297.

To account for these observations, two ring-opened intermediates could be proposed. Cleavage of the N3–C4 bond, a reaction well-documented in the 5,6-dihydrouracil series,[5,6] would lead to ester **4**. Cleavage of the N1–C6 bond, on the other hand, would lead to the ketene acetal-type structure **5**. In order to determine which mode of ring opening was operative, the same reaction was followed by ^1H NMR using 6-amino-1-methyluracil (**1b**). Again the *N*-methyl signal (in this case the only such signal) moved to higher field as a doublet. This observation is consistent *only* with ring opening at the N1–C6 bond.



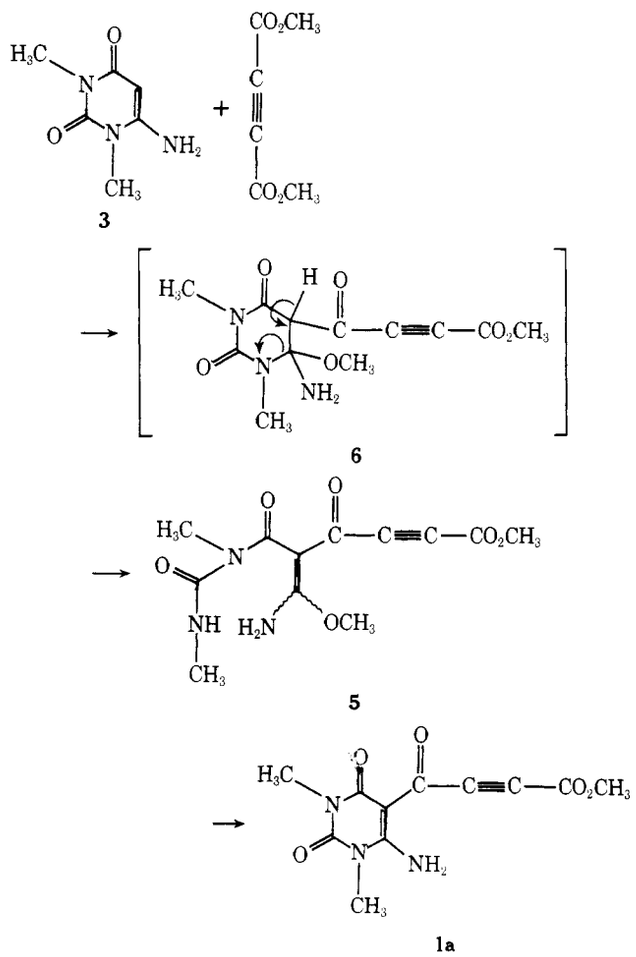
4



5

Based upon the above data, a logical mechanism for the formation of intermediate **5** is presented (Scheme I). The first step is presumed to involve addition of DMAD across the 5,6 double bond giving intermediate **6**. The subsequent elimination reaction should proceed with rupture of the bond leading to the greatest stabilization of negative charge (the least basic anion). The only anion subject to resonance stabilization is that resulting from cleavage of the 1,6 bond; such a cleavage leads to intermediate **5**. Upon recyclization, again the least basic anion is eliminated (in this case methoxide) to give **1a** as the final product. The cyclization is very similar to that recently reported by Shealy and O'Dell[7] whereby uracil derivatives were readily prepared by the cyclization of 3-methoxyacryloylureas.

Scheme I



3 **6** **5** **1a**

Experimental Section

The ^1H NMR spectra were recorded on a JEOL C60H spectrometer with 2,2-dimethyl-2-silapentanesulfonic acid, sodium salt as internal reference. Mass spectra were obtained using an LKB-GC/MS Model 9000S (electron impact), a Varian 112S MS (chemical ionization), and a Varian MAT 731MS (field desorption). 1,3-Dimethyl-6-aminouracil was purchased from Het-Chem Co., Harrisonville, Mo.

***N,N'*-Dimethyl-*N*-[3-amino-3-methoxy-2-(3-carbomethoxypropynoyl)acryloyl]urea (5).** To a suspension of 1,3-dimethyl-6-aminouracil (1.55 g, 10 mmol) in $(CH_3)_2SO$ (20 mL) was added dimethyl acetylenedicarboxylate (1.35 mL, 11 mmol). The suspension was stirred at 25 °C for 1 h. Methanol (30 mL) was added. After 8 h at −5 °C, the pale yellow solid was filtered and washed with Et_2O to give 1.68 g (57%) of **5**: MS, *m/e* 265 (EI, CI), 297 (field desorption); ^1H NMR [$(CD_3)_2SO$] δ 9.03 (br d, 1 H, NH), 8.55 (br s, 2 H, NH_2), 3.68 (s, 3 H, OCH_3), 3.57 (s, 3 H, OCH_3), 3.12 (s, 3 H, NCH_3), 2.60 (d, 3 H, NCH_3, J_{H,CH_3} = 4 Hz). The signal appearing at δ ~3.4 arose from H_2O in the solvent.

Anal. Calcd for $C_{12}H_{15}N_3O_6 \cdot 0.5H_2O$: C, 47.05; H, 5.27; N, 13.71. Found: C, 47.35; H, 5.26; N, 13.54.

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Registry No.—**1a**, 32970-29-9; **3**, 6642-31-5; **5**, 63744-45-6; dimethyl acetylenedicarboxylate, 762-42-5.

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Identification of Alkaloids in Crude Extracts by Mass-Analyzed Ion Kinetic Energy Spectrometry

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Complex mixtures can be analyzed by a new method[2] based upon ion kinetic energy measurements. We show here that this procedure, which does not require chromatography and involves minimal sample pretreatment, is applicable to the identification of alkaloids in crude plant extracts.

The procedure involves the following steps. (i) The mixture is ionized by electron impact (EI) or by chemical ionization (CI). (ii) An ion of interest, usually the molecular ion or the protonated alkaloid, is selected by mass analysis. (iii) The mass-analyzed ion is excited by collision which causes it to fragment. (iv) The fragments are identified by kinetic energy analysis. Mass-analyzed ion kinetic energy (MIKE) spectra were obtained in this way for selected ions from crude extracts of the cacti *Dolichothele longimamma* (DC.) Br. and R., *Dolichothele uberiformis* (Zucc.) Br. and R., *Lophophora williamsii* (Lem.) Coult., and *Opuntia spinosior* (Eng.) Toumey. Alkaloid structures were deduced either directly from these spectra in the cases of new alkaloids or by comparison with MIKE spectra of authentic alkaloids.

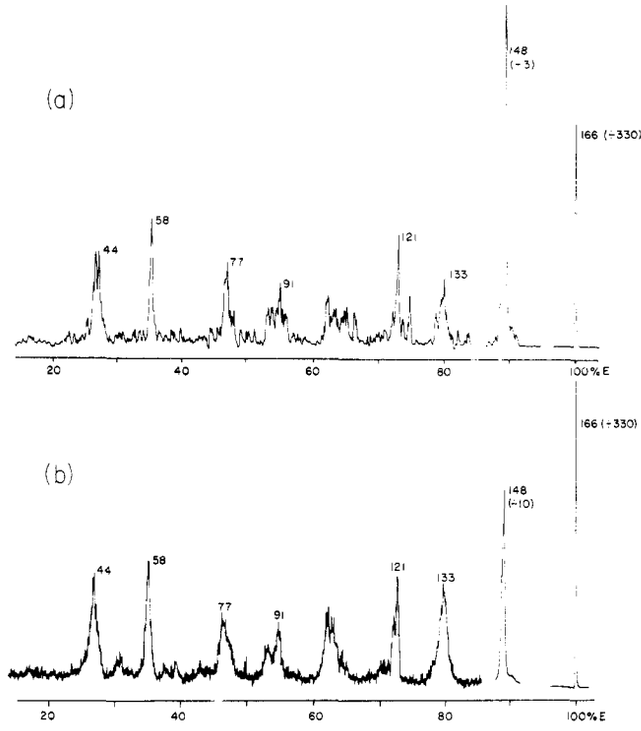

Figure 1. MIKE spectra of *m/e* 166 obtained from (a) a crude *D. longimamma* extract and (b) ubine hydrochloride. The major fragment ions are indicated on the spectra and their origins explained in Scheme I.

Experimental Section

The MIKE spectrometer has been described elsewhere.[3] Samples were introduced from a direct insertion probe at a source temperature (100–200 °C) appropriate for evaporation of the component of interest. Chemical ionization reagent gases were methane or isobutane as indicated. The ion accelerating voltage was 7 kV, the electron emission current was 0.1–0.2 mA (CI and EI), and the indicated pressure of collision gas (always introduced for these studies) was 5 × 10^{-5} Torr.

The alkaloid extract used in the EI study was the phenolic fraction obtained from *D. uberiformis* as described elsewhere.[4] The other extracts were obtained from 1 g of freeze-dried cactus from which lipids were removed by overnight Soxhlet extraction with cyclohexane. Extraction with chloroform–methanol–ammonium hydroxide (2:2:1) and evaporation yielded an alkaloid-containing mixture which was analyzed without further work-up. Only a small portion of the extract was used in the analysis.

Results and Discussion

The power of the ion kinetic energy method can be illustrated by the identification of ubine (1) in *D. longimamma*. Studies by traditional chromatographic and spectroscopic methods[5] revealed a number of new as well as previously known alkaloids in this plant not including ubine. The CI (isobutane) mass spectrum of the plant extract shows an ion which corresponds in mass to protonated ubine (*m/e* 166). The MIKE spectrum of this ion (Figure 1a) was interpreted as requiring the ubine structure for the alkaloid. Scheme I summarizes the fragmentation pattern upon which this assignment was based. The MIKE spectrum of authentic protonated ubine (Figure 1b) confirmed the assignment. It is noteworthy that these results were obtained in a few hours using a very crude plant extract. Other constituents of *D. longimamma* studied in this way will be discussed elsewhere.

Our procedure can be used in a survey of plant materials for