(0.392 g, 4 mmol) and **1a** (0.76 g, 4.06 mmol) in 10 mL of benzene was heated at reflux temperature for 2 h. Removal of the solvent gave a pale brown oil (0.877 g), which was a 54:18:28 mixture of **3d**, **4d**, and **5d** (by NMR analysis). TLC analysis (two developments on silica gel GF_{254}, 3:1 hexane:acetone) showed three spots present very closely at R_f values 0.36, 0.42, and 0.48, respectively. Preparative TLC (silica gel PF_{254}, 3:1 hexane:acetone) yielded 0.126 g (16%) of **4d** (R_f 0.48), 0.379 g (49%) of **3d** (R_f 0.42), and 0.196 g (25%) of **5d** (R_f 0.36). Spectral data of **3d** and **4d** are shown in Tables I–IV.

5d: IR (neat) 1645, 1620, 1595, 1420, 1000 cm^{-1}; ^1H NMR (CCl_4) δ 0.92 (t, 3 H, J = 6 Hz, CH_3), 1.40 (m, 2 H, CH_3CH_2), 1.7–2.3 (m, 6 H, $CH_2CH_2NCH_2CH_2$ and $CH_2CH=$), 3.43 (m, 4 H, CH_2NCH_2), 5.96 (d, 1 H, J = 15 Hz, C_2-H), 5.8–6.2 (m, 2 H, C_4-H and C_5-H), 7.09 (m, 1 H, C_3-H); mass spectrum, m/e (relative intensity) 193 (M^+, 43), 178 (8), 164 (27), 150 (95), 123 (100), 98 (22), 95 (45), 84 (45), 81 (75). Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25%. Found: C, 74.72; H, 9.82; N, 7.05%.

1-(1-Oxo-3,4-tetradecadienyl)pyrrolidine (3h). A solution of 1-dodecyn-3-ol (**2h**)(0.40 g, 2.2 mmol) and **1a** (0.535 g, 2.86 mmol) in 72 mL of xylene was heated under reflux for 16 h. After removal of the solvent, the residual oil (0.90 g) was subjected to preparative TLC (silica gel, 3:1 hexane:acetone) to yield 0.35 g (57%, 74% yield from consumed **2h**) of **3h** (R_f 0.28) along with the recovery of 88 mg of **2h** (R_f 0.51). Spectral data are shown in Tables I and II.

1-[5-(1,3-Benzodioxol-5-yl)-1-oxo-3,4-pentadienyl]-piperidine (3j) was prepared as described previously.[20] IR and ^1H NMR spectra have been reported previously.[20] ^{13}C NMR data are shown in Table II. Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91%. Found: C, 71.43; H, 6.60; N, 5.12%.

General procedure for the transformation of 3 to 4 was similar to that described in the previous paper.[24] Some representative experiments are shown below.

(2*E*,4*Z*)-1-(1-Oxo-2,4-octadienyl)pyrrolidine (4d). A mixed solution of 20 mg (0.109 mmol) of **3d**, 50 mg of alumina, and 3 mL of benzene was heated at reflux temperature for 2 h. The mixture was filtered, and the filtrate was concentrated in vacuo to give 16 mg (80%) of **4d** (pure by ^1H NMR). Spectral data are shown in Tables III and IV.

(2*E*,4*Z*)-1-(1-Oxo-2,4-decadienyl)piperidine (4f). A mixed solution of 106 mg (0.451 mmol) of **3f**, 520 mg of alumina, and 2 mL of benzene was heated at reflux temperature for 2 h. The mixture was worked up analogously to give 100 mg (95%) of **4f** (77% pure by ^{13}C NMR). Spectral data were shown in Tables III and IV.

(2*E*,4*Z*)-1-(1-Oxo-2,4-tetradecadienyl)pyrrolidine (4h) and (2*E*,4*E*)-1-(1-Oxo-2,4-tetradecadienyl)pyrrolidine (5h). A mixed solution of 57 mg (0.206 mmol) of **3h**, 150 mg of alumina, and 1 mL of benzene was heated at reflux temperature for 3 h. The mixture was worked up analogously to give 50 mg (88%) of **4h**, which was shown by ^{13}C NMR analysis to be a 74:26 mixture of **4h** and **5h**: mp 48–50 °C. The components were isolated by preparative TLC (silica gel PF_{254}, 3:1 hexane:acetone). A major fraction of R_f 0.34 gave pure **4h**: mp 62–63 °C; IR and NMR (see Tables III and IV). A minor fraction of R_f 0.27 yielded pure **5h**: mp 36–38 °C; IR (neat) 1622, 1598, 1425, 1005 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.2–7.6 (m, 1 H, C_3–H), 6.0–6.4 (m, 3 H, C_2–H, C_4–H, C_5–H), 3.55–3.75 (m, 4 H, $-CH_2NCH_2-$), 1.6–2.3 (m, 6 H, $CH_2CH=$ and $CH_2CH_2NCH_2CH_2$), 1.26 (br s, 14 h, $(CH_2)_7$), 0.90 (t, J = 7 Hz, 3 H, CH_3). Anal. Calcd for $C_{18}H_{31}NO$: C, 77.92; H, 11.26; N, 5.05. Found: C, 77.85; H, 11.12; N, 5.14.

(2*E*,4*Z*)-1-[5-(1,3-Benzodioxol-5-yl)-1-oxo-2,4-pentadienyl]piperidine (Isochavicine) (4j). A mixed solution of 23 mg (0.0807 mmol) of **3j**, 140 mg of alumina, and 2 mL of benzene was heated at reflux temperature for 2 h. The mixture was filtered, and the filtrate was concentrated in vacuo to give 20 mg (87%) of **4j** (pure by ^1H NMR). IR and ^1H NMR spectra were identical with those in the literature.[1d,f] ^{13}C NMR data are shown in Table IV.

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Registry No. **1a**, 88855-23-6; **1b**, 71627-25-3; **2a**, 107-19-7; **2c**, 2028-63-9; **2d**, 105-31-7; **2f**, 818-72-4; **2g**, 7383-20-2; **2h**, 81929-17-1; **2j**, 2620-47-5; **3a**, 88855-24-7; **3b**, 88855-25-8; **3c**, 88855-26-9; **3d**, 88855-27-0; **3e**, 88855-28-1; **3f**, 88855-29-2; **3g**, 88855-30-5; **3h**, 88855-31-6; **3i**, 88855-32-7; **3j**, 71627-26-4; **4c**, 88855-33-8; **4d**, 88855-34-9; **4e**, 88855-35-0; **4f**, 88855-36-1; **4g**, 88855-37-2; **4h**, 88855-38-3; **4i**, 88855-39-4; **4j**, 30511-77-4; **5d**, 88855-40-7; **5h**, 88855-41-8; 1-acetylpyrrolidine, 4030-18-6; 1-acetylpiperidine, 618-42-8.

Synthesis and Crystallography of 2,3,3,5,6,6-Hexamethyl-3,6-dihydropyrazine Hexahydrate and 3-Amino-3-methyl-2-butanone Hydrochloride

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The X-ray crystal structures and chemical reactions of 2,3,3,5,6,6-hexamethyl-3,6-dihydropyrazine hexahydrate and 3-amino-3-methylbutanone hydrochloride are described.

We previously reported on our synthetic attempts to prepare α-amino ketones.[1,2] We were intrigued by the fact that all attempts to hydrate propargyl derivatives led ultimately to material that is spectroscopically best described as a dimer (**1**) rather than monomer (**2**). For example, IR 1657 cm^{-1} (no 1680–1720 cm^{-1}), ^1H NMR δ 1.30 (s, 6 H), 2.00 (s, 3 H), and ^{13}C NMR 22.91, 28.45, 56.14, and 169.64 ppm were obtained.

This dimer had previously been prepared by Gabriel[3] from the well-known synthesis carrying his name and while

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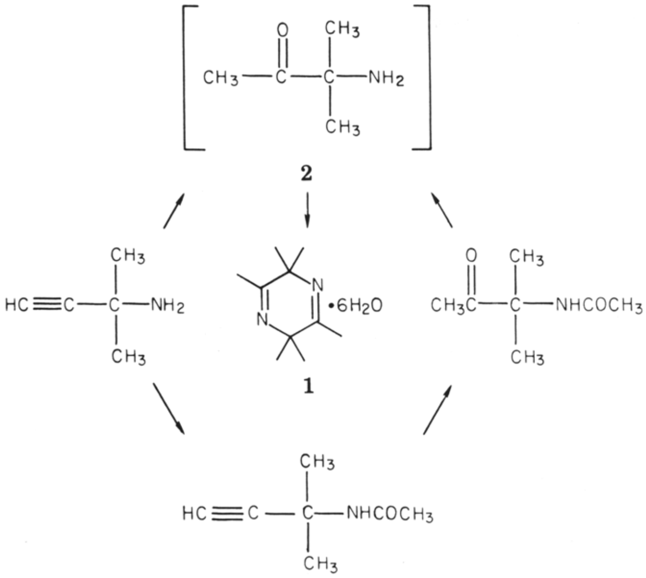
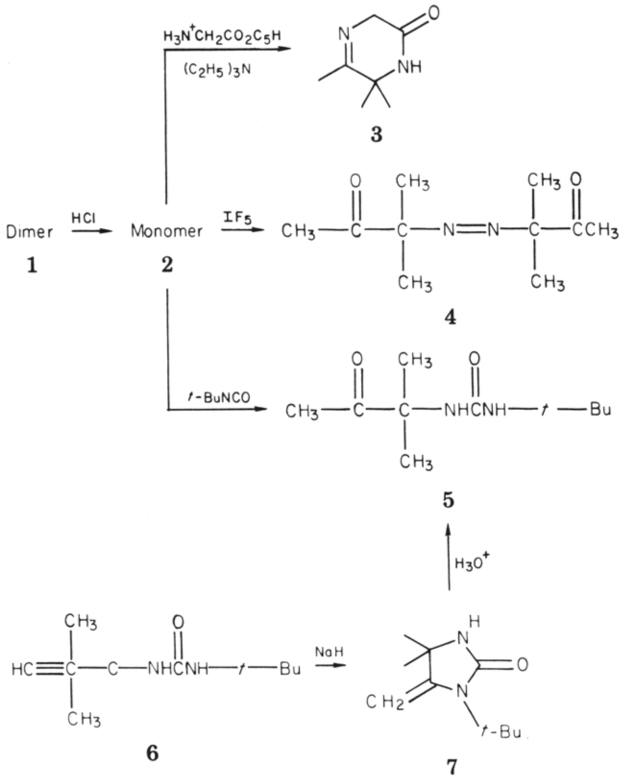
(1) Chiu, S. K.; Dube, M. F.; Keifer, L.; Szilagyi, S.; Timberlake, J. W. *J. Org. Chem.* **1978**, *43*, 61.

(2) Kovacic, P.; Lisiak, M.; Zawalski, R. C.; Luedtke, A.; Timberlake, J. W. *Tetrahedron Lett.* **1980**, *21*, 425.

(3) Gabriel, S. *Chem. Ber.* **1911**, *44*, 57.



it can be dehydrated at great material expense, its normal state appears to be that of a hexahydrate. We have found that hydrolysis of this dimer leads to monomer, isolated as the HCl salt. All attempts to derivatize the monomer under acidic conditions as the oxime or dinitrophenylhydrazone were unsuccessful. When similar reactions were tried under basic conditions, triethylamine or pyridine, the free amine **2** simply dimerized. However, the reaction of ethyl glycine and the hydrochloride salt of **2** gave 5,6,6-trimethyl-3,6-dihydro-2[1*H*]-pyrazinone (**3**). We were also able to prepare the *tert*-butylurea **5** by reaction with *tert*-butyl isocyanate and amine hydrochloride. The latter derivative we previously prepared by cyclization of propargylurea **6** and hydrolysis of the corresponding imidazolindione **7**.[1] The monomer can also be coupled to form the azo compound (**4**) by reaction with IF_5. This keto diazene was prepared as part of our continued interest in radical stabilizing effects[2] and its rate of thermal decomposition will be reported at a later date. This is the first case where the hydrochloride salt, rather than the free amine, has been coupled to the azoalkane using IF_5.



Organic molecules with such an extensive amount of hydration are rare and for this reason it was considered of interest to determine the single-crystal structure of this hexahydrated dimer, and because we were not positive of the monomeric nature of **2** the structure of this hydrochloride was also determined.[4]

Figure 1 shows the numbering system and one complete dimeric unit of 2,3,3,5,6,6-hexamethyl-3,6-dihydropyrazine hexahydrate including the six water molecules and their hydrogen bonds. This diagram shows more than two hydrogen atoms bonded to each water molecule, indicating each disordered position. The disorder in the positions of the hydrogen atoms on all three unique water molecules is extensive. Each oxygen atom is within bonding distance of three hydrogen atom positions. The oxygen–hydrogen bond lengths range from 0.62 (4) Å to 1.17 (6) Å. In each water molecule, one hydrogen atom occupies one unique position and the other hydrogen atom is disordered over two sites. Therefore, the inter-water hydrogen bond scheme depends on which of the two possible positions the second water hydrogen atom occupies.

The molecule crystallizes about an inversion center resulting in two cyclic dimers in the unit cell. The most

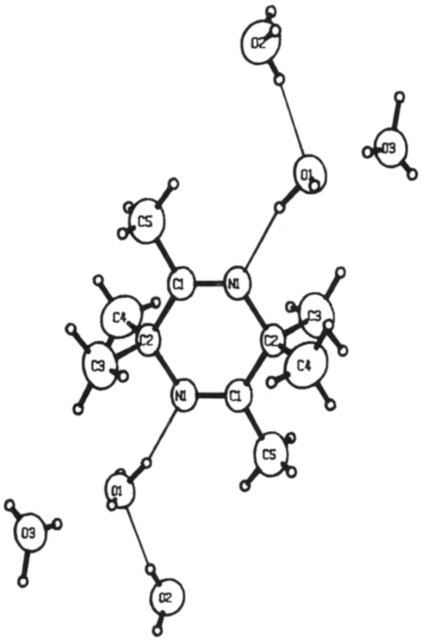


Figure 1.

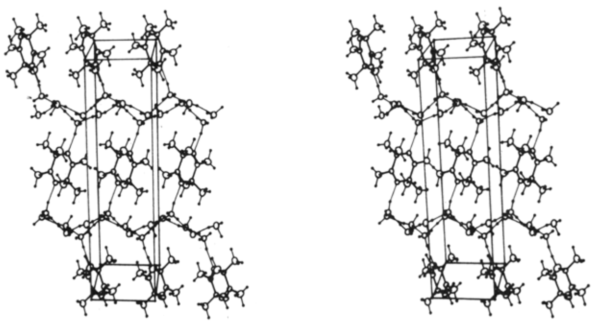


Figure 2.

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[4] The hydrolysis of the dimer gave rise to a compound whose analysis was consistent with it being the monomeric keto amine hydrochloride monohydrate or dimeric dihydrochloride tetrahydrate of **1**. The water of hydration was removed under vacuum for the X-ray determination.

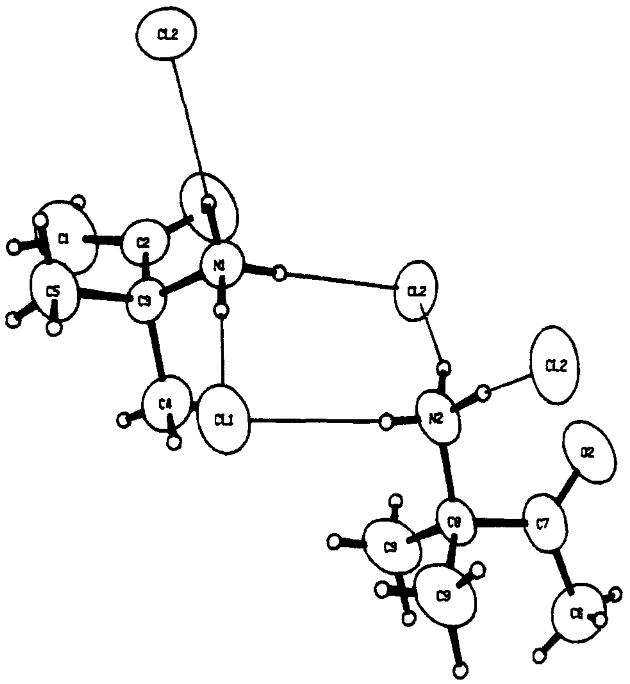

Figure 3.

unique feature of this dimeric structure is the way the dimer appears to have "parted the sea"[5] and is sandwiched between the two water layers as illustrated in the stereoscopic diagram in Figure 2. Within each sheet of water molecules, there is an extensive hydrogen bond network involving four crystallographically unique hydrogen bonds between water molecule oxygen atoms. The average O–O hydrogen bond distance is 2.805 (3) Å. The organic and water sheets are held together by only two hydrogen bonds, both between N1 and O1. The N1–O1 hydrogen bond length is 2.835 (3) Å.

Within the cylic dimer, a standard C1–N1 double bond distance of 1.276 (4) Å and C–C average single bond distance of 1.515 (5) Å indicate little delocalization of the C–N double bond in the ring. The remaining bond lengths and angles in this molecule are also comparable to those of other molecules with similar geometries.

The unusual asymmetric unit for 3-amino-3-methyl-2-butanone hydrochloride consists of one unique molecule at a general position and half of a molecule located on a mirror plane. The numbering system, two complete molecules, and a hydrogen bond scheme involving the chloride ions can be found in Figure 3. The unit cell contains twelve molecules crystallizing as monomeric units arranged in sheets which are bridged together by chloride ions hydrogen bonded to ammonium groups. The average N···Cl hydrogen bond length is 3.191 (6) Å. Within the monomeric unit, the bond lengths and bond angles are comparable to other molecules with similar geometries.

This study has established the structure of both the monomeric and dimeric forms 1 and 2. Furthermore, although the preferred structure of the free amine is the dimer, reactions can be conducted by using the HCl salt of the monomer.

Experimental Section

2,3,3,5,6,6-Hexamethyl-3,6-dihydropyrazine (1). To a stirred solution of 2.0 g (9.2 mmol) of red mercuric oxide in 120 mL of 28% sulfuric acid at 70 °C was added dropwise 10.0 g (120 mmol) of 1,1-dimethylpropargylamine. The mixture was stirred overnight at room temperature and 50 mL of methylene chloride was added. The mixture was stirred at 0 °C, made basic by the cautious addition of solid potassium carbonate, and filtered. The aqueous solution was then extracted several times with methylene chloride and then extracted continuously overnight. The combined extracts were dried ($MgSO_4$) and evaporated on a watch glass to yield 7.06 g (31.6%) of product as a white solid, mp 84–85 °C. The product may be further purified by sublimation.[1]

Table I. Intramolecular Bond Distances (Å) and Angles (deg) for 2,3,3,5,6,6-Hexamethyl-3,6-dihydropyrazine Hexahydrate

N1-C1	1.276 (4)	C2-N1-C1	120.9 (3)
C1-C2	1.504 (4)	N1-C -C2	125.2 (3)
C1-C5	1.505 (5)	N1-C1-C5	117.2 (3)
C2-C3	1.523 (5)	C2-C1-C5	117.7 (3)
C2-C4	1.526 (5)	C1-C2-N1	114.0 (2)
C2-N1	1.452 (2)	C1-C2-C3	110.3 (3)
		C1-C2-C4	109.5 (3)
		N1-C2-C3	120.7 (2)
		N1-C2-C4	119.9 (2)
		C3-C2-C4	109.7 (3)

3-Amino-3-methyl-2-butanone Hydrochloride Hydrate (2). A solution of 3.74 g (0.01 mol) of 3-amino-3-methyl-2-butanone hexahydrate dimer (1) and 25 mL of 15% hydrochloric acid was refluxed with stirring for 3 days. After removal of the solvent in vacuo the crude salt was washed with THF. Recrystallization of the residual solid from ethanol–ethyl acetate yielded 1.94 g (62.3%) of 3-amino-3-methyl-2-butanone hydrochloride monohydrate, mp 219–220 °C.

Anal. Calcd for $C_5H_{12}NClO{\cdot}H_2O$: C, 38.56; H, 9.08; N, 9.00; Cl, 22.80. Found: C, 38.87; H, 8.96; N, 8.98; Cl, 22.55.

Anal. Calcd for $C_5H_{12}NClO$ (after vacuum drying): C, 43.63; H, 8.81; N, 10.18. Found: C, 43.75; H, 8.96; N, 10.19.

5,6,6-Trimethyl-3,6-dihydro-2[1*H*]-pyrazinone (3). A mixture consisting of 3.5 g (0.025 mol) of glycine ethyl ester hydrochloride, 250 mL of benzene, and 10.1 g (0.1 mol) of triethylamine was stirred for 15 min at room temperature, then 3.9 g (0.025 mol) of 3-amino-3-methyl-2-butanone hydrate hydrochloride was added, and the mixture was stirred at reflux for 5 days. The reaction mixture was cooled to room temperature and filtered to remove the undissolved solid, and the solvent was removed in vacuo to give 2.8 g of crude product. Sublimation to remove the 3-amino-3-methyl-2-butanone hexahydrate dimer (1) gave 2.25 g (64%) of the desired product.

An analytical sample was prepared by recrystallizing the product twice from hexane–ethyl acetate and once from hexane–chloroform to give white crystals: mp 123–124 °C; NMR ($CDCl_3$) δ 1.40 (s, 6 H), (s, 3 H), 4.15 (s, 2 H), 8.25 (br s, 1 H).

Anal. Calcd for $C_7H_{12}N_2O$: C, 59.98; H, 8.63; N, 19.98. Found: C, 60.11; H, 8.63; N, 20.05.

***N-tert*-Butyl-*N'*-(2-methyl-3-oxo-2-butyl)urea (5).** A mixture of 0.40 g (0.0026 mol) of 3-amino-3-methyl-2-butanone hydrate hydrochloride, 7.26 g (0.07 mol) of triethylamine, and 0.30 g (0.003 mol) of *tert*-butyl isocyanate was stirred at reflux for 3 days. Removal of the solvent and unreacted isocyanate gave a while solid. Water was added and the mixture extracted with chloroform. The extracts were dried over $MgSO_4$ and the solvent removed in vacuo. The resulting solid was recrystallized from hexane–chloroform to give 0.21 g (40%) of the desired product as a white solid, mp 201–202 °C (lit.[1] mp 198–199).

***N,N'*-Bis(1,1-dimethyl-2-oxopropyl)diazine (4).** A solution containing 5 mL of freshly distilled pyridine in 50 mL of CH_2Cl_2 was cooled to −78 °C under nitrogen followed by the addition of 0.50 g (2.3 mmol) of IF_5. After stirring for 20 min, 0.30 g (2.2 mmol) of 1,1-dimethyl-2-oxopropylamine hydrochloride was added in one portion.

The reaction mixture was stirred for 5 h at −78 °C, allowed to slowly warm to 0 °C, and stirred an additional 2 h. The product mixture was carefully poured onto ice and separated, and the organic layer was washed with 5% HCl (5 × 30 mL). After drying over $MgSO_4$, the CH_2Cl_2 solution was concentrated leaving a light yellow liquid. Chromatography of the crude product on silica gel (CH_2Cl_2) provided 0.23 g (1.2 mmol, 55%) of pure diazene: ^1H

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(5) Exodus 14:21.

(6) R_w is the weighted reliabilty index. $R_w = [\sum w|k|F_o| - |F_c||^2/\sum w|kF_o|^2]^{1/2}$ where $w = 1/\sigma^2$ and $\sigma = {}^1/_2[F(1 + I_{Co}/I_{Ni})/(1 - I_{Co}/I_{Ni})]^{1/2}$.

Table II. Table of Bond Distances (Å) and Angles (deg) for 3-Amino-2-methyl-2-butanone Hydrochloride

O1-C2	1.204 (8)	O1-C2-C1	121.4 (7)
O2-C7	1.226 (13)	O1-C2-C3	119.1 (7)
N1-C3	1.494 (8)	C1-C2-C3	119.4 (7)
N2-C8	1.507 (12)	N1-C3-C2	107.5 (6)
C1-C2	1.468 (11)	N1-C3-C4	108.9 (6)
C2-C3	1.525 (9)	N1-C3-C5	107.3 (6)
C2-C4	1.516 (10)	C2-C3-C4	109.2 (6)
C3-C5	1.531 (9)	C2-C3-C5	113.2 (6)
C6-C7	1.527 (18)	C4-C3-C5	110.7 (7)
C7-C8	1.485 (14)	O2-C7-C6	118.4 (12)
C8-C9	1.508 (10)	O2-C7-C8	121.3 (11)
		C6-C7-C8	120.3 (11)
		N2-C8-C7	107.8 (8)
		N2-C8-C9	108.8 (7)
		C7-C8-C9	111.3 (6)
		C9-C8-C9	109.2 (7)

NMR ($CDCl_3$) δ 1.35 (s, 12 H) and 2.16 (s, 6 H); ^{13}C NMR ($CDCl_3$) 21.78, 26.49, 80.30, 208.38 ppm; IR (neat) 1720 cm^{-1}.

X-ray Structural Determination of 2,3,3,5,6,6-Hexamethyl-2,5-dihydropyrazine Hexahydrate (1) (Tables I and II). A single white rhombohedral-shaped crystal with dimensions no greater than 0.30 mm was mounted in a glass capillary in order to avoid rapid loss of water. This dimer crystallized in space group $P2_1/c$ with unit cell dimensions of a = 6.454 (3) Å, b = 6.462 (2) Å, c = 20.405 (6) Å, β = 102.03 (3) Å and V = 832.2 $Å^3$. The measured density was found to be 1.07 g/cm^3 by flotation in THF and chlorobenzene. The calculated density is 1.09 g/cm^3 with two molecules per unit cell. All X-ray data were collected by the stationary-crystal, stationary-counter method on a General Electric XRD-490 automated diffractometer using balanced nickel and cobalt filters and Cu K_α (λ = 1.5406 Å) radiation. A total of 1414 independent reflections were collected to a 2θ maximum of 120°. Of these 625 (44%) reflections were considered to be statistically significant by $[I_{Ni} - 2\sigma(I_{Ni})] - [I_{Co} - 2\sigma(I_{Co})] > 500$, with σ's based entirely on counting statistics.

The structure was solved by direct methods which revealed the locations of all nine non-hydrogen atoms on the initial E map. All hydrogen atom positions were located on a Fourier difference map. The hydrogen atom positions on the water molecules were found to be disordered, appearing as multiple peaks located in the proximity of the oxygen atoms with reasonable bond lengths and angles. The fractional occupancies for these water hydrogen atoms were then refined, idealized, and fixed so that each water molecule had a total of two hydrogen atoms. The structure was refined by using a block-diagonal least-squares program with anistropic thermal parameters for all non-hydrogen atoms and isotropic thermal parameters fixed at U = 0.1013 $Å^2$ (B = 8.0 $Å^2$) for all hydrogen atoms to R = 3.6% and R_w = 3.4% 5. The final difference Fourier map revealed no peaks greater than 0.17 e/$Å^3$.

X-ray Structural Determination of 3-Amino-3-methyl-2-butanone Hydrochloride (2). A single, white, needle-like crystal with dimensions 0.20 × 0.20 × 0.35 mm was mounted on an Enraf-Nonius CAD-4 diffractometer with a Mo target X-ray tube (λ = 0.71073 Å) and a graphite-crystal monochrometer. This monomer crystallized in space group *Pnma* with unit cell dimensions[7] of a = 10.505 (9) Å, b = 21.936 (4) Å, c = 10.035 (2) Å, and V = 2312.5 $Å^3$. All three-dimensional intensity data were collected in the ω:2θ scan mode. A total of 1915 independent reflections were collected to a 2θ maximum of 50° with 711 independent observed reflections with $I > \sigma(I)$.

The structure was solved by direct methods which revealed the locations of all fifteen non-hydrogen atoms on the initial E map. All hydrogen atom positions were located on a Fourier difference map. The structure was refined using a full-matrix least-squares program with anisotropic thermal parameters for all hydrogen atoms. All atomic coordinates were allowed to refine except those restricting the atom to a mirror plane. Temperature factors for ten hydrogen atoms were fixed at U = 0.1013 $Å^2$ (B = 8.0 $Å^2$) while the others were allowed to refine. The structure was refined down to a final value of R = 5.4% and R_w = 5.0%.[8] On the basis of twelve molecules of this monomer in the unit cell, the calculated density was 1.19 g/cm^3. The experimental density was measured to be 1.17 g/cm^3. The final difference Fourier map revealed no peaks greater than 0.30 e/$Å^3$.

Acknowledgment. Funds for the purchase of a new automated diffractometer were provided in part by a grant from the National Science Foundation (CHE8208754).

Registry No. 1, 36848-44-9; 2, 10201-15-7; 3, 79137-43-2; 4, 88842-48-2; 5, 88842-49-3; 1,1-dimethylpropargylamine, 2978-58-7; mercuric oxide, 21908-53-2; glycine ethyl ester, 459-73-4.

Supplementary Material Available: Fractional atomic coordinates (5 pages). Ordering informaton is given on any current masthead page.

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(7) All programs used in space group determination, unit cell dimension determination, and structure refinement and solution are part of the CAD-4 SDP structure determination package by B. Frenz (1982).

(8) R_w is the weighted reliability index as in ref 5 where $w = (1/\sigma(F)^2)$ and $\sigma(F^2) = [\sigma(F^2)_{cs} + (0.03)^2(F^2)^2]^{1/2}$.