(C), 125.59 (C), 127.3 (C), 127.41 (C), 128.46 (CH), 128.54 (CH), 128.79 (CH), 131.6 (C), 131.81 (C), 142.43 (C), 145.46 (C), 161.93 (C, C=N), 172.93 (C, C=N); MS, m/e 378 (M^+), 347, 363, 205; IR (CCl_4) 2980, 2940, 1660 cm^{-1}; Anal. Calcd for $C_{25}H_{34}N_2O$: C, 79.32; H, 9.05; N, 7.40. Found: C, 79.39; H, 9.00; N, 7.44.

Reactions of the Oxazinone (11). A. Pyrolysis and Addition of CO_2 or Methanol. The compound 11 (0.2 g, 0.51 mmol) was heated in an oil bath at 190–195 °C for 2 min under gentle suction. After the completition of CO_2 evolution, the oily residue was quickly frozen at 0 °C. Its mass spectrum revealed an intense peak at m/e 346 (2 M^+ of **1d**) and the complete disappearance of the peak at 390 (M^+ of 11); IR (CCl_4) showed an intense band at 2010 cm^{-1} (C=C=N), while the bands at 1770 and 1667 cm^{-1} of 11 were absent. The crude residue (0.15 g), dissolved in CH_2Cl_2 (50 mL), was bubbled with dry (H_2SO_4, silica) CO_2 for 40 min. The IR spectrum (CCl_4) of the reaction mixture revealed the absence of the band at 2010 cm^{-1} and the appearance of the bands at 1770 and 1667 cm^{-1} of 11. Evaporation of the solvent and chromatography of the residue (SiO_2, CH_2Cl_2) gave the oxazinone 11 (0.050 g, 0.128 mmol, 25%). In another experiment, using the same amount of 11, the oil from pyroylis was dissolved in 5 mL of MeOH and the solution refluxed for 1 h. Evaporation of the solvent and chromatography (SiO_2, CH_2Cl_2) gave 12 (0.07 g, 0.185 mmol, 36.3%).

B. Reaction of 11 with Methanol. Compound 11 (0.2 g, 0.59 mmol) was heated in a refluxing mixture of xylene (110 mL) and methanol (10 mL). The disappearance of 11 was monitored by IR at 1770 cm^{-1} on samples withdrawn at intervals. After compound 11 had totally disappeared, the solvent was evaporated and the oily residue was chromatographed (SiO_2, CH_2Cl_2) to give compound 12 (0.47 mmol, 78%).

Registry No. 1a, 18779-86-7; 1b, 42463-98-9; 1c, 74331-60-5; 1d, 89827-16-7; 3, 89827-17-8; 4, 52223-07-1; 5, 89827-18-9; 6, 89848-02-2; 7, 89827-19-0; 11, 89827-20-3; 12, 89827-21-4; $AlCl_3$, 7446-70-0; Et_2AlCl, 96-10-6.

N- vs. O-Acylation of 1,2-Diazetidin-3-one: 4,5-Dihydro-1,3-oxadiazin-6-ones by Ring Enlargement

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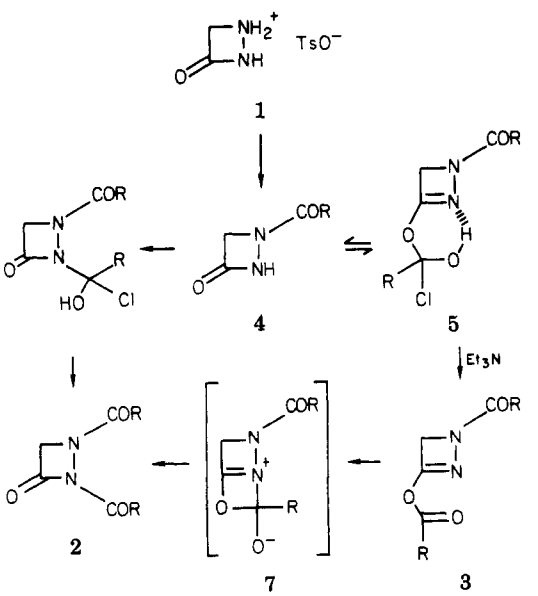
Received September 23, 1983

Treatment of 1,2-diazetidin-3-one with acid chlorides in the presence of 2,6-lutidine led to 1,2-diacyl-1,2-diazetidin-3-ones (N,N-diacylation), while the use of triethylamine as base gave 1-acyl-3-(acyloxy)-1,4-dihydro-1,2-diazetes (N,O-diacylation). Several 1-benzhydryl-2-acyl-1,2-diazetidin-3-ones were found to rearrange smoothly upon treatment with ethyl chloroformate to give 2-substituted 4-benzhydryl-4,5-dihydro-1,3,4-oxadiazin-6-ones.

We are currently engaged in a program aimed at the synthesis of highly strained aza analogues of the β-lactam antibiotics, starting from the readily accessible 3-oxo-1,2-diazetidinium tosylate (1).[1] We report in this paper some surprising results obtained from attempts to introduce acyl and aroyl substituents at N-1 and/or N-2.

It is well-known that azetidin-2-ones (β-lactams) unsubstituted on nitrogen readily polymerize in base in the presence of a catalytic amount of an acylating agent.[2] This sensitivity is shared by 1,2-diazetidin-3-one. All attempts to effect monoacylation of 1 under a wide variety of reaction conditions led only to a colorless solid of indefinite melting point that was clearly polymeric in nature. By contrast, however, treatment of a stirred suspension of 1 with 2 equiv of benzoyl chloride and 3 equiv of 2,6-lutidine in methylene chloride at −78 °C led to the formation in modest yield of 1,2-dibenzoyl-1,2-diazetidin-3-one (**2a**), which is characterized by IR carbonyl absorption bands at 1810, 1667, and 1652 cm^{-1}.[3] Under the same reaction conditions, 1 could be reacted with 4-anisoyl chloride, 4-nitrobenzoyl chloride, and cyclohexanecarbonyl chloride to give the respective 1,2-diacyl derivatives **2b–d** (Scheme I). Since only polymeric materials were isolated from attempts to effect diacylation with less electrophilic reagents (i.e., benzyl chloroformate, acetic anhydride), we

Scheme I



a, R = C_6H_5; b, R = $C_6H_4OCH_3$-4; c, R = $C_6H_4NO_2$-4; d, R =  ; e, R = $C(CH_3)_3$

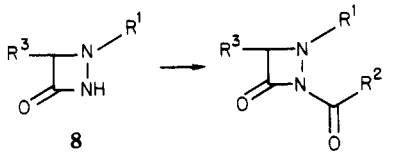
(1) Taylor, E. C.; Haley, N. F.; Clemens, R. J. *J. Am. Chem. Soc.* **1981**, *103*, 7743.

(2) Graf, R.; Lohaus, G.; Borner, K.; Schmidt, E.; Bestia, H. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 481.

(3) In our preliminary communication on this work the structure of this product was incorrectly assigned: Taylor, E. C.; Davies, H. M. L.; Clemens, R. J.; Yanagisawa, H.; Haley, N. F. *J. Am. Chem. Soc.* **1981**, *103*, 7660.

0022-3263/84/1949-2204$01.50/0

Table I. Acylation of 1-Substituted 1,2-Diazetidin-3-ones



8 9

starting material	R^1	R^2	R^3	product	yield, %	IR (Nujol), cm^{-1}
8a	$CH_2C_6H_4Cl$-4	CH_3	H	**9a**	70	1800, 1680
8b	$CH_2CH{=}CHC_6H_5$	CH_3	H	**9b**	74	1800, 1692
8c	c-$C_6H_{10}CH_3$	CH_3	H	**9c**	40	1810, 1710
8d	$C(CH_3)_2CH{=}CHC_6H_5$	CH_3	H	**9d**	76	1790, 1712
8e	$CH(C_6H_5)_2$	CH_3	H	**9e**	75	1822, 1790, 1732, 1695
8e	$CH(C_6H_5)_2$	C_6H_5	H	**9f**	76	1805, 1710
8e	$CH(C_6H_5)_2$	$OCH_2C_6H_5$	H	**9g**	74	1826, 1750
8e	$CH(C_6H_5)_2$	$NHC_6H_4CH_3$-4	H	**9h**	67	1812, 1700
8f	$CH(C_6H_5)_2$	CH_3	CH_3	**9i**	75	1795, 1728
8f	$CH(C_6H_5)_2$	C_6H_5	CH_3	**9j**	46	1815, 1695
8f	$CH(C_6H_5)_2$	$C_6H_4NO_2$-4	CH_3	**9k**	40	1820, 1700
8g	$C(CH_3)(C_6H_5)_2$	CH_3	H	**9l**	76	1800, 1720

conclude that 1,2-diazetidin-3-one is unstable as the free base and undergoes rapid polymerization unless trapped in situ by an extremely reactive acylating agent.

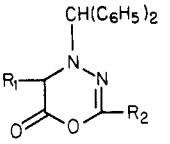
The reaction of 3-oxo-1,2-diazetidinium tosylate (**1**) with acylating agents proved to be critically dependent upon the nature of the base employed. Although, as described above, 1,2-diacyl derivatives were readily obtained when 2,6-lutidine was used as the acid scavenger, the use of pyridine led only to uncharacterized products in which the aza-β-lactam ring had been destroyed, presumably through ring opening by the more nucleophilic base. On the other hand, acylation of **1** with 2 equiv of 4-anisoyl chloride in the presence of triethylamine led to the formation of a new compound, isomeric with 1,2-di-4-anisoyl-1,2-diazetidin-3-one, which exhibited IR carbonyl absorption bands at 1750, 1640, and 1620 cm^{-1}. This compound was shown by X-ray crystallographic analysis to be the O-acylated derivative **3b**.[3] In analogous fashion, acylation of **1** with 2 equiv of benzoyl chloride, 4-nitrobenzoyl chloride, or pivaloyl chloride, again in the presence of triethylamine, led to the N,O-diacylated derivatives **3a**, **3c**, and **3e**, respectively.

The stabilities of the 1,2-diacyl-1,2-diazetidin-3-ones **2** and their N,O-diacylated isomers **3** vary considerably with solvent. For example, we were unable to obtain NMR spectra of either **2b** or **3b** in Me_2SO-d_6 because of rapid decomposition. Both **2b** and **3b** were stable in acetone-d_6, but in the same solvent the N,O-diacylated derivative **3c** rearranged quantitatively to **2c** within 24 h. Although the IR spectra of the crude products obtained from the diacylation reactions indicated that, in most cases, a single isomer was obtained in high yield, isolated yields were often considerably lower as a consequence of subsequent decomposition during isolation.

The remarkable dependency of the reaction pathway upon the nature of the base employed deserves special mention. It seems reasonable to suggest that the acylation reactions leading to **2** and **3** probably occur as depicted in Scheme I. Initial acylation undoubtedly occurs at N-1, which is more nucleophilic and more basic than N-2. Kinetic acylation of this 1-acyl derivative then presumably takes place at oxygen. In the absence of a base of sufficient basicity, intramolecular proton transfer to N-2 initiates the interconversion of **4** and **5**, and under these equilibration conditions, the thermodynamically favored pathway **4** → **6** → **2** dominates. In the presence of triethylamine, however, deprotonation of the kinetic product **5** leads directly to **3**, the observed product under these conditions. Isolation of isoimides under standard acylating conditions normally appears to be limited to systems that are sufficiently sterically strained that rearrangement through a four-membered intermediate is difficult (cf. **7**).[4] It should be noted that the *N,O*-dianisoyl derivative **3b** was unchanged after storage for 2 years at room temperature.

We have also briefly explored the reaction of 1-substituted 1,2-diazetidin-3-ones (**8**)[1,5] with acylating agents (anhydrides, acid chlorides, benzyl chloroformate, *p*-tolyl isocyanate). In these cases, more vigorous conditions are required (20–40 °C), and as expected from the above results, the thermodynamically favored N-acylated products (**9**) were isolated even in the presence of triethylamine (see Table I). The only anomalous results were obtained upon pivaloylation. For example, although the reaction of **8a**, **8c**, and **8d** with pivaloyl chloride led to the *N*-pivaloyl derivatives **10a**, **10c**, and **10d**, reaction of **8e–g** under the same reaction conditions led exclusively to the *O*-pivaloyl derivatives **11a–c** (see Table II). Steric factors appear to have a critical if unpredictable effect upon the formation of N- vs. O-products.

A further rearrangement was observed when **9j** was treated with ethyl chloroformate or with hydrogen chloride (gas) in toluene. An isomer (IR 1815, 1695 cm^{-1}) was obtained in high yield, which was shown to be 2-phenyl-4-benzhydryl-5-methyl-4,5-dihydro-1,3,4-oxadiazin-6-one (**12a**) by an X-ray crystallographic analysis. In analogous

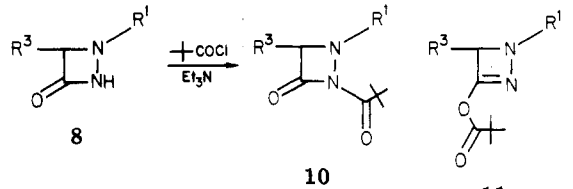


12a, $R_1 = CH_3$; $R_2 = C_6H_5$
b, $R_1 = H$; $R_2 = C_6H_5$
c, $R_1 = CH_3$; $R_2 = C_6H_4NO_2$-4

fashion, **9f** and **9k** underwent ring expansion upon treatment with ethyl chloroformate to give **12b** and **12c**, respectively. Although several intramolecular ring expansions of azetidin-2-ones (β-lactams) are known,[6] there are

(4) Hedaya, E.; Hinman, R. L.; Theodoropulos, S. *J. Org. Chem.* **1966**, *31*, 1317.
(5) Taylor, E. C.; Davies, H. M. L. *J. Org. Chem.*, submitted for publication.
(6) Manhas, M. S.; Amin, S. G.; Bose, A. K. *Heterocycles* **1976**, *5*, 669.

Table II. Pivaloylation of 1-Substituted 1,2-Diazetidin-3-ones



8 10 11

starting material	R^1	R^3	product	yield, %	product	yield, %	IR (Nujol), cm^{-1}
8a	$CH_2C_6H_4Cl$-4	H	10a	52			1800, 1676
8c	c-$C_6H_{10}CH_3$	H	10b	33			1798, 1698
8d	$C(CH_3)_2CH{=}CHC_6H_5$	H	10c	33			1807, 1684
8e	$CH(C_6H_5)_2$	H			11a	78	1760, 1620
8f	$CH(C_6H_5)_2$	CH_3			11b	57	1756, 1616
8g	$C(CH_3)(C_6H_5)_2$	H			11c	60	1758, 1620

no examples to our knowledge of the ring expansion of N-acylated azetidin-2-ones to 4,5-dihydro-1,3-oxazin-6-ones (a reaction comparable to the rearrangement of **9** to **12**). Our observation that 1,2-diazetidin-3-ones appear to be more reactive then comparable β-lactams may have interesting potential pharmacological consequences.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 467 spectrophotometer, and NMR spectra were recorded on Perkin-Elmer R-32 (90 MHz) or JEOL Model FX 90Q spectrometers. Mass spectra were determined on an AEI MS-9 instrument. Elemental analyses were carried out by Eli Lilly & Co., Indianapolis, IN.

Synthesis of N,N-Diacylated 1,2-Diazetidin-3-ones. General Procedure. 2,6-Lutidine (3 mmol) and the acid chloride (2 mmol) were added to a stirred suspension of 3-oxo-1,2-diazetidinium tosylate (0.244 g, 1 mmol) in 10 mL of methylene chloride at −78 °C, and the mixture was stirred for 1 h. Extraction first with dilute hydrochloric acid and then with a saturated sodium bicarbonate solution, followed by drying of the organic phase over $MgSO_4$ and evaporation in vacuo, afforded the product, which was then recrystallized.

1,2-Dibenzoyl-1,2-diazetidin-3-one (2a): mp 91–93 °C (from hexane), 35% yield; IR (Nujol) 1810, 1667, 1652 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80–7.35 (m, 10 H, 10 Ar H), 4.65 (s, 2 H, NCH_2CO); ^{13}C NMR ($CDCl_3$) δ 169.7, 159.9, 143.2, 131.9, 131.8, 130.5, 129.0, 128.1, 126.6, 42.8; LRMS (70 eV), *m/e* (relative intensity) 280 (observed M^+, 15), 236 (1), 149 (1), 122 (1), 105 (100), 77 (100).

Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.57; H, 4.32; N, 10.00. Found: C, 68.30; H, 4.25; N, 9.83.

1,2-Di-4-anisoyl-1,2-diazetidin-3-one (2b): mp 125 °C dec (from ether/pentane), 64% yield: IR (Nujol) 1830, 1700, 1670 cm^{-1}; ^1H NMR (acetone-d_6) δ 8.01, 7.99, 7.09 and 7.08 (d, 2 H, *J* = 9 Hz, 2 Ar H), 5.24 (s, 2 H, NCH_2CO), 3.93 and 3.92 (s, 3 H, OCH_3); LRMS (70 eV), *m/e* (relative intensity) 340 (observed M^+, 50), 152 (10), 135 (100), 107 (30).

Anal. Calcd for $C_{18}H_{16}N_2O_5$: C, 63.53; H, 4.74; N, 8.23. Found: C, 63.32; H, 4.82; N, 8.47.

1,2-Bis(4-nitrobenzoyl)-1,2-diazetidin-3-one (2c): mp 158–165 °C dec (from toluene), 43% yield; IR (Nujol) 1810, 1660, 1650 cm^{-1}; ^1H NMR (acetone-d_6) δ 8.45–7.98 (m, 8 H, 8 Ar H), 4.90 (s, 2 H, NCH_2CO); LRMS (70 eV), *m/e* (relative intensity) 370 (observed M^+, 30), 340 (3), 326 (3), 312 (4), 172 (30), 167 (50), 150 (100); HRMS calcd for $C_{16}H_{10}N_4O_7$ 370.0549, found 370.0530 ± 0.0019.

1,2-Bis(cyclohexylcarbonyl)-1,2-diazetidin-3-one (2d): mp 69–71 °C (from pentane), 52% yield; IR (Nujol) 1800, 1700, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.40 (s, 2 H, NCH_2CO), 3.0–1.0 (m, 22 H); ^{13}C NMR ($CDCl_3$) δ 176.7, 160.3, 149.6, 41.8, 40.5, 40.3, 29.2, 28.8, 25.7, 25.4; LRMS (70 eV), *m/e* (relative intensity) 292 (observed M^+, 15), 248 (3), 182 (30), 155 (10), 137 (5), 111 (80), 83 (100); HRMS calcd for $C_{16}H_{24}N_2O_3$ 292.1787, found 292.1782 ± 0.0015.

Synthesis of N,O-Diacylated 1,2-Diazetidin-3-ones. General Procedure. Triethylamine (3 mmol) and the acid chloride (2 mmol) were added to a stirred suspension of 3-oxo-1,2-diazetidinium tosylate (0.244 g, 1 mmol) in dichloromethane (20 mL) at −78 °C, and the mixture was stirred for 1 h. Extraction first with dilute hydrochloric acid and then with saturated sodium bicarbonate solution, followed by drying of the organic phase over $MgSO_4$ and evaporation in vacuo, afforded the product, which was then recrystallized.

1-Benzoyl-3-(benzoyloxy)-1,4-dihydro-1,2-diazete (3a): mp 111–113 °C (from hexane), 42% yield; IR (Nujol) 1760, 1660, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.1–7.4 (m, 10 H, 10 Ar H), 5.67 (s, 2 H, NCH_2CO); ^{13}C NMR ($CDCl_3$) δ 170.8, 167.3, 161.0, 135.3, 132.3, 130.7, 129.4, 129.1, 128.3, 63.8; LRMS (70 eV), *m/e* (relative intensity) 280 (observed M^+, 15), 252 (10), 236 (5), 122 (15), 105 (100), 77 (100).

Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.57; H, 4.32; N, 10.00. Found: C, 68.37; H, 4.31; N, 9.69.

1-(4-Anisoyl)-3-(4-anisoyloxy)-1,4-dihydro-1,2-diazete (3b): mp 142 °C dec (from ethyl acetate), 23% yield; IR (Nujol) 1750, 1640, 1620 cm^{-1}; ^1H NMR (acetone-d_6) δ 8.09, 7.99, 7.13 and 7.01 (d, 2 H, *J* = 9 Hz, 2 Ar H), 5.65 (s, 2 H, NCH_2CO), 3.93 and 3.87 (s, 3 H, OCH_3); LRMS (70 eV), *m/e* (relative intensity) 340 (observed M^+, 20), 312 (1), 286 (10), 132 (50), 135 (100); HRMS calcd for $C_{18}H_{16}N_2O_5$ 340.1059, found 340.1045 ± 0.0017.

X-ray Data. The compound crystallizes as colorless needles from chloroform–hexane: space group $P2_12_12_1$, four molecules per unit cell, *a* = 6.780 ± 0.001 Å, *b* = 11.167 ± 0.002 Å, *c* = 21.565 ± 0.006 Å, calculated density 1.38 g cm^{-3}. With use of monochromatic copper Kα radiation, 1365 reflections were measured on a four-angle automated diffractometer. The structure was solved by direct methods (SHELXTL) and refined by the least-squares method to *R* = 0.036 for 1299 observed reflections. See supplementary material for ORTEP drawing of molecule (Figure 1), atom coordinates, and bond distances and angles (Tables III–VII).

1-(4-Nitrobenzoyl)-3-[(4-nitrobenzoyl)oxy]-1,4-dihydro-1,2-diazete (3c): mp 110 °C dec (from toluene), 21% yield; IR (Nujol) 1765, 1620 cm^{-1}; ^1H NMR (acetone-d_6) δ 8.7–8.2 (m, 8 H, 8 Ar H), 5.8 (s, 2 H, NCH_2CO); LRMS (70 eV), *m/e* (relative intensity) 370 (observed M^+, 3), 342 (0.5), 316 (5), 272 (3), 220 (5), 167 (100), 150 (100); HRMS calcd for $C_{16}H_{10}N_4O_7$ 370.0549, found 370.0544 ± 0.0019.

1-Pivaloyl-3-(pivaloyloxy)-1,4-dihydro-1,2-diazete (3e): mp 70–70.5 °C (from pentane), 70% yield; IR (Nujol) 1782, 1648, 1618 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.33 (s, 2 H, NCH_2CO), 1.35 (s, 18 H, 6 CH_3); ^{13}C NMR ($CDCl_3$) δ 179.7, 172.9, 165.9, 63.0, 39.4, 27.0, 26.6; LRMS (70 eV), *m/e* (relative intensity) 240 (observed M^+, 2), 212 (2), 156 (5), 128 (15), 113 (70), 57 (100), 41 (100).

Anal. Calcd for $C_{12}H_{20}N_2O_3$: C, 59.99; H, 8.40; N, 11.66. Found: C, 59.83; H, 8.40; N, 11.77.

Acetylation of 1,2-Diazetidin-3-ones. General Procedure. A solution of the 1,2-diazetidin-3-one (1 mmol) in acetic anhydride (5 mL) was stirred for 12 h. Evaporation of the solvent in vacuo gave the product, which was then recrystallized.

1-(4-Chlorobenzyl)-2-acetyl-1,2-diazetidin-3-one (9a): mp 103–105 °C (from hexane), 70% yield; IR (Nujol) 1800, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33 (s, 4 H, 4 Ar H), 4.74 and 3.64 (d, 1 H, *J* = 14 Hz, total NCH_2Ar), 4.26 and 3.82 (d, 1 H, *J* = 14 Hz, total NCH_2CO), 2.39 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 164.9, 161.1,

134.2, 130.6, 128.9, 65.0, 61.8, 22.9.

Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74; Cl, 14.85. Found: C, 55.36; H, 4.56; N, 11.65; Cl, 14.93.

1-(3-Phenylprop-2-enyl)-2-acetyl-1,2-diazetidin-3-one (9b): mp 114–115 °C (from ethyl acetate/hexane), 74% yield; IR (Nujol) 1800, 1692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (s, 5 H, 5 Ar H), 6.65 (d, 1 H, J = 16 Hz, C=CH), 6.22 (dt, 1 H, J = 16, 5 Hz, C=CH), 4.39 and 3.92 (d, 1 H, J = 14 Hz, total NCH_2CO), 4.27 and 3.38 (q, 1 H, J = 16, 5 Hz, total NCH_2), 2.38 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 164.9, 161.5, 136.2, 135.6, 128.7, 128.2, 126.6, 121.7, 65.0, 60.9, 22.9.

Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.48; H, 6.43; N, 11.98.

1-(1-Methylcyclohexyl)-2-acetyl-1,2-diazetidin-3-one (9c): mp 50–52 °C (from hexane), 40% yield; IR (Nujol) 1810, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.21 (br s, 2 H, NCH_2CO), 2.38 (s, 3 H, CH_3), 2.1–1.1 (m, 10 H, 5 CH_2), 1.07 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 167.1, 164.9, 61.2, 59.3, 55.5, 34.8, 25.6, 23.5, 22.2, 17.2.

Anal. Calcd for $C_{11}H_{18}N_2O_2$: C, 62.83; H, 8.63; N, 13.32. Found: C, 62.59; H, 8.62; N, 13.24.

1-(3-Methyl-1-phenylbut-1-en-3-yl)-2-acetyl-1,2-diazetidin-3-one (9d): mp 67–68 °C (from hexane), 76% yield; IR (Nujol) 1790, 1712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (m, 5 H, 5 Ar H), 6.59 and 6.31 (d, 1 H, J = 16 Hz, C=CH), 4.30 and 4.06 (d, 1 H, J = 14 Hz, total NCH_2CO), 2.40 (s, 3 H, CH_3), 1.40 (s, 6 H, 2 CH_3); ^{13}C NMR ($CDCl_3$) δ 166.9, 164.3, 136.5, 131.4, 130.8, 128.7, 128.0, 126.5, 62.8, 61.2, 24.3, 23.4.

Anal. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.84. Found: C, 69.52; H, 6.76; N, 10.96.

1-Benzhydryl-2-acetyl-1,2-diazetidin-3-one (9e): mp 109–112 °C (from petroleum ether (bp 30–60 °C)), 75% yield; IR (Nujol) 1822, 1790, 1732, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31 (s, 10 H, 10 Ar H), 5.29 (s, 1 H, Ph_2CHN), 4.41 and 3.85 (br d, 1 H, J = 15 Hz, total NCH_2CO), 2.13 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 165.3, 162.4, 128.5, 128.1, 74.5, 64.1, 22.8.

Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; N, 5.75; N, 9.99. Found: C, 73.07; H, 5.73; N, 10.01.

1-Benzhydryl-2-benzoyl-1,2-diazetidin-3-one (9f). 2,6-Lutidine (0.14 mL, 1.25 mmol) and benzoyl chloride (0.12 mL, 1.05 mmol) were added to a stirred solution of **8a** (0.238 g, 1 mmol) in dichloromethane, and the mixture was heated under reflux for 5 h. Extraction of the mixture with dilute hydrochloric acid and saturated sodium bicarbonate solution, followed by drying over $MgSO_4$ and evaporation in vacuo, gave 0.26 g (76%) of **9f**, which was crystallized from ethyl acetate: mp 203–204 °C; IR (Nujol) 1805, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80–7.39 (m, 15 H, 15 Ar H), 5.27 (s, 1 H, Ph_2CH), 4.52 and 4.04 (br d, 1 H, J = 15 Hz, total NCH_2CO); ^{13}C NMR ($CDCl_3$) δ 163.7, 162.0, 133.5, 131.5, 129.9, 128.7, 128.2, 75.8, 75.2.

Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.26; H, 5.08; N, 8.22.

1-Benzhydryl-2-(benzyloxycarbonyl)-1,2-diazetidin-3-one (9g). 2,6-Lutidine (0.15 mL, 1.35 mmol) and benzyl chloroformate (0.155 mL, 1.1 mmol) were added to a stirred solution of **8a** (0.238 g, 1 mmol) in dichloromethane, and the mixture was heated under reflux for 5 h. Extraction of the mixture with dilute hydrochloric acid and saturated sodium bicarbonate solution, followed by drying over $MgSO_4$ and evaporation in vacuo, gave 0.265 g (74%) of **9g**, which was crystallized by trituration with petroleum ether (bp 30–60 °C): mp 108–110 °C; IR (Nujol) 1826, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (br s, 15 H, 15 Ar H), 5.05 (m, 3 H, $PhCH_2$ + Ph_2CHN), 4.48 and 3.86 (br d, 1 H, J = 15 Hz, total NCH_2CO); ^{13}C NMR ($CDCl_3$) δ 162.5, 148.6, 141.2, 134.7, 128.7, 128.4, 128.2, 128.0, 127.4, 127.2, 77.6, 68.3, 65.9.

Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52. Found: C, 74.12; H, 5.54; N, 7.60.

1-Benzhydryl-2-(4-toluidinocarbonyl)-1,2-diazetidin-3-one (9h). *p*-Tolyl isocyanate (0.14 mL, 1.1 mmol) was added to a stirred solution of **8a** (0.238 g, 1 mmol) in dichloromethane, and the mixture was heated under reflux for 5 h. Evaporation of the solvent in vacuo followed by trituration with ether gave 0.25 g (67%) of **9h**: mp 158–159 °C; IR (Nujol) 1812, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.5–7.1 (m, 14 H, 14 Ar H), 5.25 (s, 1 H, Ph_2CHN), 4.60 and 4.00 (d, 1 H, J = 15 Hz, total NCH_2CO), 2.30 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 164.6, 146.7, 139.2, 137.8, 133.8, 129.3, 128.7, 128.4, 128.2, 119.6, 76.5, 65.5, 20.7.

Anal. Calcd for $C_{23}H_{21}N_3O_2$: C, 74.37; H, 5.70; N, 11.31. Found: C, 74.55; H, 5.59; N, 11.11.

1-Benzhydryl-2-acetyl-4-methyl-1,2-diazetidin-3-one (9i): mp 88–89 °C (from hexane), 75% yield; IR (Nujol) 1795, 1728 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.6–7.2 (m, 10 H, 10 Ar H), 5.10 (s, 1 H, Ph_2CH), 4.05 (q, 1 H, J = 7 Hz, NCHCO), 2.09 (s, 3 H, CH_3), 1.51 (d, 3 H, J = 7 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 166.4, 165.4, 139.4, 138.1, 128.6, 128.5, 128.1, 127.9, 127.7, 76.7, 72.8, 22.7, 15.2.

Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.45; H, 6.20; N, 9.51.

1-Benzhydryl-2-benzoyl-4-methyl-1,2-diazetin-3-one (9j). 2,6-Lutidine (4.0 mL, 34 mmol) and benzoyl chloride (3.7 mL, 32 mmol) were added to a stirred solution of **8f** (6.6 g, 26 mmol) in dichloromethane (220 mL), and the mixture was stirred for 2 days at 25 °C. Extraction of the mixture with dilute hydrochloric acid and saturated sodium bicarbonate solution, followed by drying over $MgSO_4$, evaporation in vacuo, and recrystallization from toluene gave 4.35 g (46%) of **9j**: mp 158–161 °C; IR (KBr) 1815, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) 7.55 (m, 15 H), 5.15 (s, 1 H), 4.15 (q, 1 H, J = 7 Hz), 1.45 (d, 3 H, J = 7 Hz).

Anal. Calcd for $C_{23}H_{20}N_2O_2$: C, 77.52; H, 5.66; N, 7.86. Found: C, 77.83; H, 5.75; N, 7.70.

1-Benzhydryl-4-methyl-2-(4-nitrobenzoyl)-1,2-diazetidin-3-one (9k). 2,6-Lutidine (0.44 mL, 3.75 mmol) and 4-nitrobenzoyl chloride (0.585 g, 3.15 mmol) were added to a stirred solution of **8f** (0.755 g, 3.0 mmol) in dichloromethane (25 mL), and the mixture was stirred at 25 °C for 12 h. Extraction of the mixture with dilute hydrochloric acid and sodium bicarbonate solution, followed by drying over $MgSO_4$, evaporation in vacuo, and recrystallization from toluene gave 0.92 g (40%) of **9k**: mp 143–146 °C; IR (KBr) 1820, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) 8.24 and 7.95 (d, 2 H, J = 10 Hz), 7.34 (m, 10 H), 5.06 (s, 1 H), 4.08 (q, 1 H, J = 7 Hz), 1.50 (d, 3 H, J = 7 Hz).

Anal. Calcd for $C_{23}H_{19}N_3O_4$: C, 68.81; H, 4.77; N, 10.47. Found: C, 68.84; H, 4.72; N, 10.27.

1-(1,1-Diphenyl-1-ethyl)-2-acetyl-1,2-diazetidin-3-one (9l): mp 74–75 °C (from hexane), 76% yield; IR (Nujol) 1800, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (br s, 10 H, 10 Ar H), 4.16 (br s, 2 H, NCH_2CO), 2.23 (s, 3 H, CH_3), 1.96 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 166.2, 163.2, 143.5, 127.8, 127.4, 70.9, 62.3, 36.7, 23.1.

Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.62; H, 6.19; N, 9.53.

Pivaloylation of 1,2-Diazetidin-3-ones. General Procedure. Triethylamine (1 mmol) and pivaloyl chloride (1 mmol) were added to a stirred solution of the 1,2-diazetidin-3-one (1 mmol) in dichloromethane at 25 °C. After the mixture was stirred for a further 12 h, extraction of the mixture with saturated ammonium chloride solution and saturated sodium bicarbonate solution followed by drying over $MgSO_4$ and evaporation in vacuo afforded the product, which was then recrystallized.

1-(4-Chlorobenzyl)-2-pivaloyl-1,2-diazetidin-3-one (10a): mp 107–111 °C (from pentane), 52% yield; IR (Nujol) 1800, 1676 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33 (s, 4 H, 4 Ar H), 4.76 and 3.56 (d, 1 H, J = 14 Hz, total NCH_2Ar), 4.18 and 3.74 (d, 1 H, J = 14 Hz, total NCH_2CO), 1.34 (s, 9 H, 3 CH_3); ^{13}C NMR ($CDCl_3$) δ 174.1, 159.2, 134.2, 132.6, 130.8, 128.9, 62.4, 61.3, 39.3, 25.2.

Anal. Calcd for $C_{14}H_{17}ClN_2O_2$: C, 59.89; H, 6.10; N, 9.98; Cl, 12.63. Found: C, 59.71; H, 6.08; N, 10.26; Cl, 12.53.

1-(1-Methylcyclohexyl)-2-pivaloyl-1,2-diazetidin-3-one (10b): mp 97–98 °C (from pentane), 33% yield; IR (Nujol) 1798, 1698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.23 and 4.02 (d, 1 H, J = 14 Hz, total NCH_2CO), 2.1–1.1 (m, 10 H, 5 CH_2), 1.33 (s, 9 H, 3 CH_3), 1.06 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 176.4, 163.2, 61.8, 57.4, 40.2, 35.9, 34.7, 25.8, 25.6, 22.2, 16.8.

Anal. Calcd for $C_{14}H_{24}N_2O_2$: C, 66.63; H, 9.59; N, 11.10. Found: C, 66.35; H, 9.32; N, 10.86.

1-(3-Methyl-1-phenylbut-1-en-3-yl)-2-pivaloyl-1,2-diazetidin-3-one (10c): mp 78–80 °C (from hexane), 33% yield; IR (Nujol) 1807, 1684 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (m, 5 H, 5 ArH), 6.69 and 6.31 (d, 1 H, J = 16 Hz, C=CH), 4.25 and 3.88 (d, 1 H, J = 14 Hz, total NCH_2CO), 1.36 (s, 6 H, 2 CH_3), 1.35 (s, 9 H, 3 CH_3); ^{13}C NMR ($CDCl_3$) δ 176.0, 162.6, 136.5, 131.2, 131.0, 128.7, 128.0, 126.4, 63.3, 59.1, 40.1, 25.7, 24.3, 24.1.

Anal. Calcd for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.32. Found: C, 71.89; H, 8.15; N, 9.17.

1-Benzhydryl-3-(pivaloyloxy)-1,4-dihydro-1,2-diazete (11a): mp 112–113 °C (from dichloromethane/hexane), 78% yield; IR (Nujol) 1760, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.5–7.2 (m, 10 H, 10 Ar H), 4.57 (br s, 3 H, NCH_2CO + Ph_2CHN), 1.25 (s, 9 H, 3 CH_3).

Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.74; H, 6.99; N, 8.84.

1-Benzhydryl-3-(pivaloyloxy)-4-methyl-1,4-dihydro-1,2-diazete (11b): mp 86–87 °C (from pentane), 57% yield; IR (Nujol) 1756, 1616 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.7–7.2 (m, 10 H, 10 Ar H), 4.60 (s, 1 H, Ph_2CH), 4.50 (q, 1 H, J = 7 Hz, NCHCO), 1.28 (s, 9 H, 3 CH_3), 1.28 (d, 3 H, J = 7 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 173.7, 168.3, 141.2, 141.0, 128.4, 128.2, 127.7, 127.1, 75.9, 74.3, 39.0, 26.5, 14.5.

Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.32. Found: C, 74.68; H, 7.08; N, 8.59.

1-(1,1-Diphenyl-1-ethyl)-3-(pivaloyloxy)-1,4-dihydro-1,2-diazete (11c): mp 55–58 °C (from pentane), 60% yield; IR (Nujol) 1758, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.6–7.2 (m, 10 H, 10 Ar H), 4.48 (s, 2 H, NCH_2CO), 1.84 (s, 3 H, CH_3), 1.25 (s, 9 H, 3 CH_3); ^{13}C NMR ($CDCl_3$) δ 173.5, 163.4, 143.8, 128.0, 127.7, 126.8, 67.3, 61.4, 39.1, 26.5, 22.8.

Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.32. Found: C, 74.64; H, 7.51; N, 8.48.

Synthesis of 4,5-Dihydro-1,3,4-oxadiazin-6-ones (12). General Procedure. A solution of the N-2-acylated 1,2-diazetidin-3-one (2 mmol) in ethyl chloroformate (30 mL) was stirred overnight at 25 °C. Evaporation in vacuo followed by trituration with hexane afforded the product, which was then recrystallized.

2-Phenyl-4-benzhydryl-5-methyl-4,5-dihydro-1,3,4-oxadiazin-6-one (12a): mp 158–159 °C (from ethyl acetate), 80% yield; IR (Nujol) 1790, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.75–7.18 (m, 15 H), 5.45 (s, 1 H), 3.75 (q 1 H, J = 7 Hz), 1.37 (d, 3 H, J = 7 Hz).

Anal. Calcd for $C_{23}H_{20}N_2O_2$: C, 77.52; H, 5.66; N, 7.86. Found: C, 77.28; H, 5.60; N, 7.77.

X-ray Data. The compound crystallizes as colorless prisms from ethyl acetate: space group *Pn*, two molecules per unit cell, a = 9.353 ± 0.003 Å, b = 8.861 ± 0.002 Å, c = 11.638 ± 0.002 Å, β = 101.03 ± 0.02°, calculated density 1.25 g cm^{-3}. With use of monochromatic copper Kα radiation, 1492 reflections were measured on a four-angle automated diffractometer. The structure was solved by direct methods (SHELXTL) and refined by the least-squares method to R = 0.041 for 1352 observed reflections. See supplementary material for ORTEP drawing of molecule (Figure 2), atom coordinates, bond distances and bond angles (Tables VIII–XII).

2-Phenyl-4-benzhydryl-4,5-dihydro-1,3,4-oxadiazin-6-one (12b): mp 126.5–128.5 °C (from ethyl acetate/hexane), 80% yield; IR (KBr) 1800, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.79–7.24 (m, 15 H), 5.31 (s, 1 H), 3.45 (s, 2 H).

Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.14; H, 5.05; N, 7.91.

2-(4-Nitrophenyl)-4-benzhydryl-5-methyl-4,5-dihydro-1,3,4-oxadiazin-6-one (12c): mp 167 °C dec, 95% yield; IR (Nujol) 1800, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.18 and 7.81 (d, 2 H, J = 9 Hz), 7.4–7.2 (m, 10 H), 5.50 (s, 1 H), 3.80 (q, 1 H, J = 7 Hz), 1.44 (d, 3 H, J = 7 Hz).

Anal. Calcd for $C_{23}H_{19}N_3O_4$: C, 68.81; H, 4.77; N, 10.47. Found: C, 68.61; H, 4.55; N, 10.46.

Acknowledgment. We are deeply indebted to Eli Lilly and Co., Indianapolis, IN, for financial support of this work.

Registry No. 1, 79289-49-9; **2a**, 80351-11-7; **2b**, 80351-13-9; **2c**, 80351-12-8; **2d**, 89773-55-7; **3a**, 89773-56-8; **3b**, 89773-57-9; **3c**, 89773-58-0; **3e**, 89773-59-1; **8a**, 89773-80-8; **8b**, 79559-06-1; **8c**, 80351-05-9; **8d**, 89773-81-9; **8e**, 79289-53-5; **8f**, 21083-14-7; **8g**, 80351-18-4; **9a**, 89773-60-4; **9b**, 89773-61-5; **9c**, 89773-62-6; **9d**, 89773-63-7; **9e**, 89773-64-8; **9f**, 89773-65-9; **9g**, 89773-66-0; **9h**, 89773-67-1; **9i**, 89773-68-2; **9j**, 89773-69-3; **9k**, 89773-70-6; **9l**, 89773-71-7; **10a**, 89773-72-8; **10b**, 89773-73-9; **10c**, 89773-74-0; **11a**, 89773-75-1; **11b**, 89773-76-2; **11c**, 89773-77-3; **12a**, 89773-78-4; **12b**, 80351-23-1; **12c**, 89773-79-5; C_6H_5COCl, 98-88-4; 4-$CH_3OC_6H_4COCl$, 100-07-2; 4-$O_2NC_6H_4COCl$, 122-04-3; $(CH_3)_3CCOCl$, 3282-30-2; $C_6H_5CH_2OCOCl$, 501-53-1; 4-$CH_3C_6H_4NCO$, 622-58-2; cyclohexanecarbonyl chloride, 2719-27-9; $(CH_3CO)_2O$, 108-24-7.

Supplementary Material Available: Tables of the final atomic parameters, bond lengths, and bond angles and structures for compounds **3b** and **12a** (13 pages). Ordering information is given on any current masthead page.

Polyaza Cavity-Shaped Molecules. Annelated Derivatives of 2-(2′-Pyridyl)-1,8-naphthyridine and 2,2′-Bi-1,8-naphthyridine

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Received November 22, 1983

A two-step method is presented for the oxidation of the 2-methylene position of 2,3-cycloalkenopyridines. The pyridyl ketones thus obtained may be reacted with 2-aminonicotinaldehyde to yield 3,3′-annelated derivatives of 2-(2′-pyridyl)-1,8-naphthyridine. Treatment of cyclic α-diketones in a similar manner provided 3,3′-annelated derivatives of 2,2′-bi-1,8-naphthyridine. Analyses by NMR indicate that when the 3,3′ bridge contains four methylene units the molecule is conformationally rigid at room temperature. UV and pK_a data indicate interactions between the two heteroaromatic rings which vary as a function of the dihedral angle between the rings.

The effectiveness of 2,2′-bipyridine as a coordinating ligand stems from its having two pyridine rings joined such that their nitrogen lone pair orbitals bear a 1,4 relationship to one another, thus enabling the system to function in a bidentate fashion. Similarly 1,8-naphthyridine, although less basic than 2,2′-bipyridine, can also function as a bidentate ligand where the nitrogen lone pairs are now fixed nearly parallel and coplanar in a 1,3 relationship. By joining a pyridine and 1,8-naphthyridine ring at their 2-positions as in **1** or two 1,8-naphthyridine rings at their 2-positions as in **2**, one is able to create a molecule capable of functioning either as a 1,3 or 1,4 diaza ligand.

The effectiveness of coordination is a function of both the availability of the nitrogen lone pair electrons (basicity) as well as the spatial orientation of these lone pairs with respect to one another. It was of interest to us, therefore, to prepare and study the annelated derivatives of 2-(2′-pyridyl)-1,8-naphthyridine (**3a–c**) and 2,2′-bi-1,8-

0022-3263/84/1949-2208$01.50/0