Competing Reaction Pathways in the Cycloaddition of 3-(Dimethylamino)-2*H*-azirines with Ketenes

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Addition of diphenylketene (**2a**) to the azirines **1a,b** affords the isomeric cycloadducts **3a,b** and **4a,b** as well as the acyclic addition products **5a,b** in variable amounts. In the reaction with **1a**, the 3-benzazepine **6** is also formed and can be hydrolyzed to give **8** via **7** or trapped to furnish the Diels-Alder adduct **10**. The 2-vinylazirine **1c** and **2a** yield the pyrrolinone **4c** as the sole product. These compounds as well as the corresponding products **16** and **17** from **1b** and *tert*-butylcyanoketene (**2b**) all arise from cleavage of what was the original 1,2 bond in the azirine precursor with subsequent ring closure, hydrogen migration or intramolecular S_E reaction with a phenyl substituent and the cation of the intermediate zwitterion **21**. On the other hand, the 2,2-dimethylazirine **1a** and the cyanoketene **2b** afford the ketenimine **12** resulting from complete opening of the original 1,3 bond of the azirine. Thiolysis of **12** to give the urea **14** can be understood in terms of attack of hydrogen sulfide on a small equilibrium concentration of the intermediate zwitterion **11**.

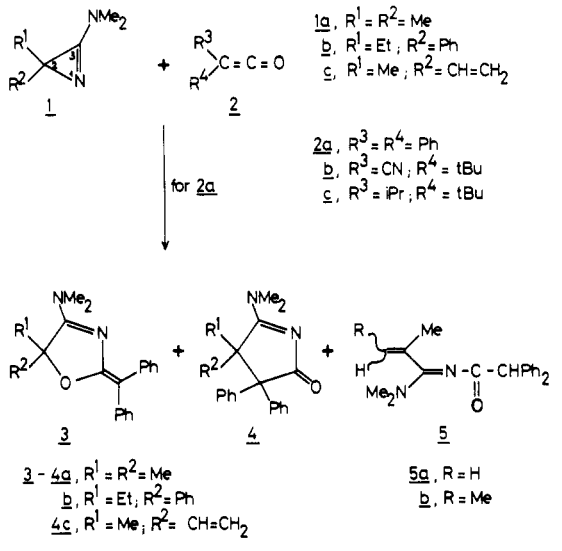
Numerous examples have been reported for the use of 3-alkyl- or 3-aryl-2*H*-azirines as building blocks for heterocyclic synthesis.[1] Most of the cycloadditions investigated take advantage of the facile photolytic 2,3 ring opening of these 2*H*-azirines to give 1,3-dipolar nitrile ylides as reactive intermediates.[2] On the other hand, the number of thermally induced cycloadditions is comparatively limited. The majority of these thermoreactions occur across the 1,3 (C=N) bond of the azirines. Exceptions are provided by the intramolecular cyclization of 2-vinylazirines[3] and by two types of products formed in the reaction of 2*H*-azirines with ketenes.[4]

Contrary to the 3-alkyl or 3-aryl compounds, 3-dialkylamino-substituted 2*H*-azirines are highly reactive nucleophiles in thermal reactions.[5] As for their cycloadditions with ketenes, a preliminary study[6] indicated divergent reaction pathways and stimulated the present more comprehensive study.

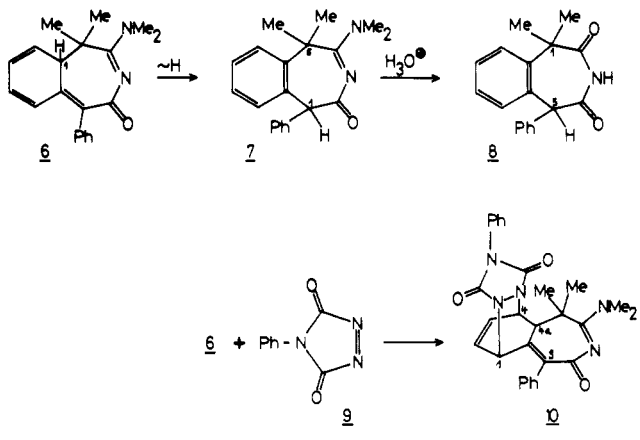
Results

Reactions with Diphenylketene (2a). Addition of diphenylketene (**2a**) to the azirine **1a** is reported to yield oxazoline **3a** as the main product[6] (see Scheme I). The ^{13}C NMR spectrum obtained now provides additional evidence for the proposed structure. Characteristic features are the signals of the exocyclic C=C moiety (Table I) when compared to a similar ketene *O,N*-acetal[7] and the peak of the amidine system incorporated into the five-membered ring.[8] The *N*-methyl groups are magnetically equivalent at room temperature, but the signal splits into two at −40 ± 2 °C (60 MHz) and, with $\Delta\nu$ = 4.5 Hz, a ΔG^* of 52.2 ± 0.4 kJ/mol (12.5 ± 0.1 kcal/mol) can be calculated for hindered rotation around the C–NMe_2 bond.[9]

Scheme I



Scheme II



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(2) A. Padwa, *Acc. Chem. Res.*, **9**, 371 (1976); *Chem. Rev.*, **77**, 37 (1977).
(3) A. Padwa, *Angew. Chem., Int. Ed. Engl.*, **15**, 123 (1976).
(4) A. Hassner, A. S. Miller, and M. J. Haddadin, *Tetrahedron Lett.*, 1353 (1972); M. J. Haddadin and A. Hassner, *J. Org. Chem.*, **38**, 3466 (1973).
(5) L. Ghosez and J. Marchand-Brynaert, *Adv. Org. Chem.*, **9**, 482 (1976); H. Heimgartner, *Chimia*, **33**, 111 (1979).
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(8) For data on cyclic amidines see ref 16, 17, and 20; carbon atoms of acyclic amidines show an upfield shift of 10–15 ppm: N. Naulet, M. L. Filleux, G. J. Martin, and J. Pornet, *Org. Magn. Reson.*, **7**, 326 (1975).

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Table I. IR and ^{13}C NMR Characterization of the Cycloadducts

	IR[a]			^{13}C NMR[b]			
compd	$\nu_{C=O}$	$\nu_{C=N}$	$\nu_{C=C}$	$\delta_{C=O}$	$\delta_{C=N}$	$\delta_{C=C}$	other shift values
3a		1580	1640		172.1	159.3, 98.5	141.6, 141.0, 130.4, 127.6, 127.2, 124.5, 124.1 (Ar), 83.7 (C-5), 38.8 (NMe_2), 25.1 (CMe_2)
3b		1560	1645		169.6	161.0, 98.6	141.8, 141.1, 139.2, 130.6, 128.8, 127.3, 126.3, 124.6, 124.1 (Ar), 89.8 (C-5), 38.7 (NMe_2), 27.2 (CH_2), 8.0 ($EtCH_3$)
4a[c]	1695	1560-1590					
4b[c]	1700	1570					
4c	1710	1580	?	185.1	188.4[d]	138.3, 116.9	140.0, 129.5, 129.2, 127.5, 127.3, 126.6, 126.2 (Ar), 71.2 (C-3), 55.9 (C-4), 41.2, 38.8 (NMe_2), 22.6 (4-Me)
7	1660	1575		171.7	177.1[d]		142.1, 141.2, 138.1, 133.1, 129.0, 128.2, 127.5, 126.7, 124.9 (Ar), 62.4 (C-1), 47.4 (C-5), 42.1 (NMe_2), 33.5, 31.8 (CMe_2)
8	1690, 1680			178.3, 171.7			140.4, 136.4, 133.7, 131.3, 128.8, 128.5, 127.7 (Ar), 57.8 (C-5), 49.2 (C-1), 29.9, 28.3 (CMe_2)
17[c]		1580	1640[e]				

[a] In KBr, except for 7, where a CH_2Cl_2 solution was used; wavenumbers, ν_{max}, in cm^{-1}. [b] All of the spectra (δ values in parts per million from Me_4Si) were recorded in $CDCl_3$. The full complement of aromatic ^{13}C peaks was not always resolved. [c] ^{13}C NMR was not measured. [d] The assignment of $\delta_{C=O}$ and $\delta_{C=N}$ may be reversed. [e] $\nu_{C\equiv N}$ 2220 cm^{-1}.

The nature of a second, highly labile product in which the geminal methyl groups of the parent azirine **1a** are diastereotopic[6] has not previously been elucidated. Chromatography of the crude reaction mixture provides the labile but isolable benzazepine **7**. Acid hydrolysis of the crude reaction mixture or of **7** afforded the stable benzazepinedione **8** (Scheme II).

Much of the evidence in support of the structural assignments of **7** and **8** rests on spectroscopic data. The ^1H NMR spectra of both compounds show signals of a highly deshielded methine proton at δ 5.50 and 4.98, respectively. Furthermore, in the ^1H NMR of **8** and in the ^{13}C NMR spectra of both compounds (Table I) the geminal methyl groups exhibit the expected magnetic nonequivalence. In the range of aromatic carbon atoms, the ^{13}C NMR spectra indicate the presence of three quaternary carbon atoms instead of two such signals for **3a**. Hence it appears that one of the phenyl residues of **2a** has been fused with the heterocyclic ring. Finally, the low-field ^{13}C signals of **7** and **8** (Table I) are compatible with the amide and the amidine units in the proposed structures.

Neither **7** nor **8** is present in the reaction mixture prior to workup, since the ^1H NMR spectrum gives no indication for the presence of either of the pertinent methine hydrogens. This suggests that the primary product contains a bicyclic system as in **6**. Though the aromaticity of the parent phenyl residue is lost in the six-membered ring of **6**, this compound seems to gain some stability from the sequence of conjugated π bonds. A chemical demonstration for the presence of **6** in the crude reaction mixture was achieved by addition of the highly reactive dienophile **9**. The Diels–Alder adduct **10** formed with **6** can now be separated from **3a**. The ^1H NMR spectrum of the compound shows the expected doublet at δ 3.45 for the methine proton on C-4a and three multiplets at δ 5.3, 5.6, and 6.6, in an intensity ratio of 1:1:2, which can be assigned to the two olefinic and the bridgehead hydrogens, respectively. A final proof of the structure **10** was obtained by an X-ray crystallographic analysis[10] (Figure 1) giving also an indirect confirmation of the structural assignments for **6**–**8**. Relative to the bridged ring, the triazolidine adopts the exo conformation. For the seven-membered ring, a flattened boat conformation is found with the most pronounced flattening at the sp^2-hybridized atoms C2 and C3 (Figure 1).

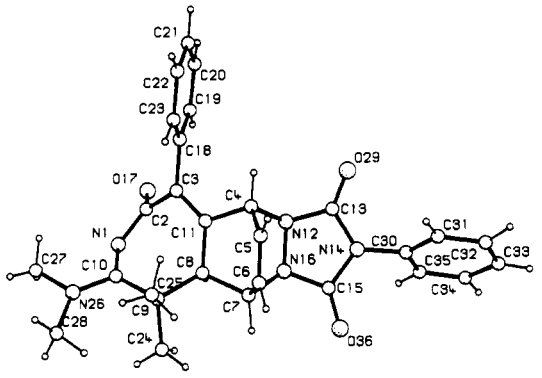


Figure 1. Drawing of compound **10**.

In addition to **3a** and **6**, extensive chromatography revealed the presence of **4a** and the *N*-acylamidine **5a**. The pyrrolinone **4a** is isomeric with **3a** but results from incorporation of the ketene precursor via the C=C bond. Characteristic spectroscopic features are the carbonyl absorption in the IR spectrum (Table I) and, contrary to **3a**, the magnetic nonequivalence of the *N*-methyl groups even at room temperature. From coalescence studies [$\Delta\nu$ = 11.5 Hz, t_c = 47 ± 2 °C in *o*-dichlorobenzene (ODC)], a ΔG^* for hindered internal rotation in the amidine moiety of 70.0 ± 0.5 kJ/mol (16.7 ± 0.1 kcal/mol) was derived. The amidine **5a** has been obtained previously by addition of diphenylacetyl chloride to the azirine **1a**.[11]

The reaction of the 2-phenyl-substituted azirine **1b** and diphenylketene (**2a**) at −40 °C affords an almost quantitative yield of **3b**. This structure is supported by the marked similarity of the characteristic IR and ^{13}C NMR data with those of **3a** (Table I). However, when the reaction is carried out at room temperature, as in the case with **1a**, a minor amount of the isomer **4b** can be isolated as well. Also traces of the acyclic addition product **5b** were detected by ^1H NMR spectroscopy.

(9) Cf. G. Mukherjee-Müller, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, **62**, 1429 (1979). These authors reinvestigated our earlier work[6] and reached the same conclusions.

(10) M. Van Meerssche, G. Germain, J. P. Declercq, R. Touillaux, E. Schaumann, and S. Grabley, *Cryst. Struct. Commun.*, (1980).

(11) E. Schaumann, E. Kausch, and W. Walter, *Chem. Ber.*, **108**, 2500 (1975).

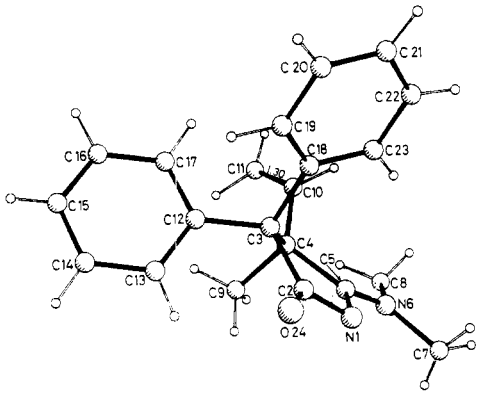
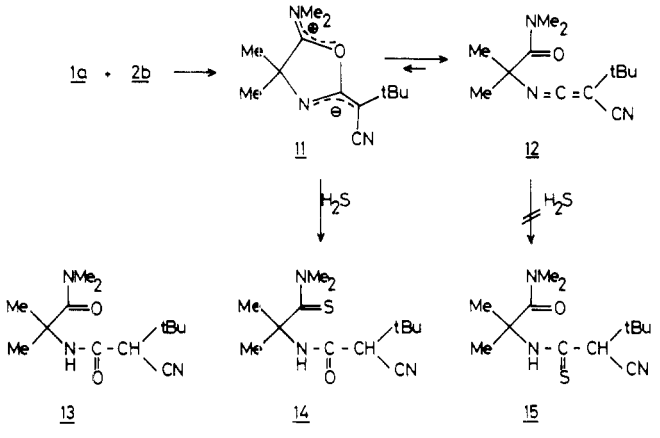


Figure 2. Drawing of compound **4c**.

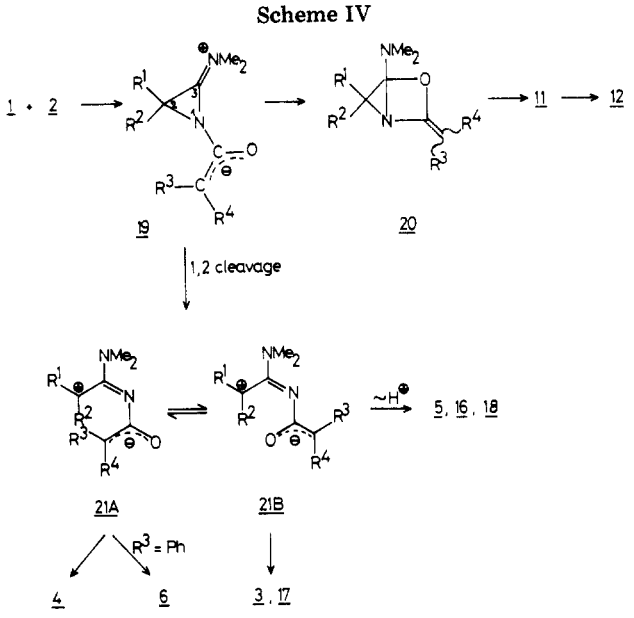
Scheme III



Whereas in the reactions with **1a,b** the C=O bond of the ketene **2a** is the preferred site of attack, a striking change in site selectivity is observed on mixing the 2-vinylazirine **1c** and **2a**. Here the only product isolated is the pyrrolinone **4c**. In addition to the spectroscopic data (Table I), the proposed structure is proven by an X-ray structural investigation[10] (Figure 2). The pyrroline ring is found to have a half-chair conformation. The bond lengths for N1–C5 and C5–N6 are almost identical, reflecting the electron delocalization in the amidine unit. This is also apparent from the magnetic nonequivalence of the *N*-methyl groups in the ^1H and ^{13}C NMR spectra (Table I).

Reactions with *tert*-Butylcyanoketene (2b). The 2,2-dimethylazirine **1a** and the ketene **2b** react to give the ketenimine **12**[6] (Scheme III). Addition of water to **12** yields the urea **13**,[6] which may form via hydrolysis of the ketenimine **12** or via attack of water at C-5 in the isomeric dipolar structure **11**. The latter mode of reaction was previously observed in the hydrolysis of (α-thiocarbamoyl)carbodiimides.[12-17] However, only isotopic labeling of oxygen would distinguish between the two mechanisms for the hydrolysis of **12**.

Scheme IV

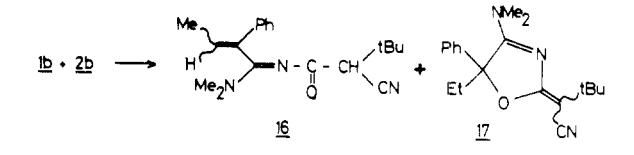


On the contrary, thiolysis of **12** did not furnish the thiourea **15**, which would form by attack of the nucleophile at the heteroallene unit in **12**, but furnished the urea **14**. This unusual course of thiolysis is suggested by the low-field position of the NMe_2 signal in the ^1H NMR spectrum (δ 3.57), indicating a neighboring thiocarbonyl group. Moreover, the carbonyl band is observed at 1655 cm^{-1} and not around 1620 cm^{-1} as expected for the amide structure in the isomeric **15**. Finally, from the mass spectrum, elimination of the dimethylthiocarbamoyl radical from the molecular ion can be deduced (*m/e* 181), whereas the peak corresponding to the loss of the dimethylcarbamoyl radical (*m/e* 197) from $15^{+\cdot}$ is not observed.

Thus, it appears that **11** and **12** exist in an equilibrium, in which **12** strongly predominates, making it the only species detectable by spectroscopy. However, isomer **11** is more reactive toward nucleophiles and is constantly re-formed from **12** in the thiolysis and probably also in the hydrolysis reactions.

Interestingly, the ketenimine **12** proved to be thermally stable up to 130 °C. Hence, neither transfer of the dimethylamino group[14,15] nor Dimroth rearrangement[17] as observed with similar compounds seems to be energetically feasible here.

In contrast to the reaction with **1a**, **1b** and the ketene **2b** afford products of the types obtained with diphenylketene (**2a**). In addition to the *N*-acylamidine **16**, the oxazoline **17** is isolated as a mixture of diastereomers. The



isomers can be separated by chromatography, but traces of acid induce equilibration to give predominantly the isomer with the ^1H *tert*-butyl signal at lower field. The isolated yield of **17** is rather low as the compound partly decomposes on chromatographic workup.

Reactions with *tert*-Butylisopropylketene (2c). For comparison with the cycloadditions of **2a,b**, the reaction between azirines **1** and the dialkylketene **2c** was of interest. Due to steric hindrance, **2c** is reluctant in its cycloadditions with azirines, and prolonged heating is required. Only from the reaction with **1b** was a stable product isolated, which the spectroscopic evidence proves to be the acyclic amidine

(12) E. Schaumann, E. Kausch, and W. Walter, *Chem. Ber.*, 110, 820 (1977).
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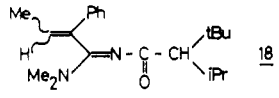
(16) E. Schaumann and S. Grabley, *Justus Liebigs Ann. Chem.*, 1568 (1978).
(17) E. Schaumann, H. Behr, and G. Adiwidjaja, *Justus Liebigs Ann. Chem.*, 1322 (1979).

18 resulting from 1,2 bond cleavage of **1b**.



1b + 2c ⟶ 18

Discussion

It seems reasonable to assume that the above reactions proceed via dipolar intermediates in which the cationic moiety is stabilized by the unshaired electron pairs of the nitrogen atoms and the anionic moiety derived from the ketenes is an enolate anion. This leads to the mechanism outlined in Scheme IV, with the zwitterion **19** being the primary intermediate. From here the inherent ring strain should favor bond cleavage to give **21**. However, starting from **1a** and the highly reactive ketene **2b**, the intermediate **19** may possess an anionic part with pronounced nucleophilicity[18] so that ring closure to give **20** and finally ketenimine **12** via **11** successfully competes with ring opening.

Contrary to **1a**, the azirines **1b,c** possess a substituent, R^2, which will be in conjugation with and thus provide additional stabilization to the positive charge in the 1,5-dipole **21**. Consequently, ring cleavage of **19** is even more favorable so that ketene **2b** takes this reaction pathway in the cycloaddition with the 2-phenylazirine **1b**. Similarly, heteroallenes containing a thiocarbonyl group lead to opening of the C=N bond in the reaction with **1a**, whereas 1,2 bond rupture is the preferred reaction mode with **1b**.[16,19]

Ring closure of **21** may occur in the conformations **21A** or **21B**, leading to cycloaddition across the original C=C or C=O bond of the ketene precursors. On steric grounds **21B** should be preferred, and, indeed, the resulting oxazolines **3** and **17** are the major products in most instances. However, the reaction between the 2-vinylazirine **1c** and **2a** to give the pyrrolinone **4c** exclusively constitutes an exception. Here the zwitterionic species **21** may be extended to a 1,7-dipolar system by inclusion of the vinyl substituent, but contrary to the cycloadditions of other reactants with **1c**,[20] formation of seven-membered rings is not observed. Nevertheless, the vinyl residue seems to exert some special effect on the conformational equilibrium of **21** in favor of **21A**.

An extension of the 1,5-dipolar framework in **21** may also occur by way of the substituents R^3 and R^4 in the anionic moiety. In fact, formation of the bicyclic system **6** indicates that some electron density is developed in the ortho positions of phenyl residues R^3 and R^4, resulting in cyclization to the seven-membered ring **6** which can be looked upon as the σ complex in an electrophilic aromatic alkylation. Similar ring closures to give six-membered rings by formal intramolecular cyclizations of 1,4-dipoles derived from diphenylketene via an ortho position have been reported.[21] However, formation of a seven-membered ring is exceptional and seems to be possible only by the special conformation of **21A** which results from **1a** and the ketene **2a**.

The acrylic amidines **5**, **16**, and **18** arise from stabilization of the cation by proton transfer to the anion by intra- or intermolecular pathways. The latter would be independent of the conformation of **21**, which, however, apparently has a subtle influence on the formation of the cycloadducts.

Experimental Section

All melting points are uncorrected. ^1H NMR spectra were taken on a Varian T-60, EM-360, or NV-14 instrument and ^{13}C measurements on a Bruker WP-60 spectrometer. IR spectra were recorded on a Perkin-Elmer 297 spectrometer. The mass spectra were measured on a Varian MAT CH 7 spectrometer. Preparative thin-layer chromatography (PTLC) was carried out with Merck Kieselgel 60 PF_{254} and aluminum plates (20 × 90 cm, 2 mm thick).

Reaction of Azirine 1a with Diphenylketene (2a). To a solution of **1a**[22] (0.78 g, 7 mmol) in 40 mL of dry ether was added dropwise **2a**[23] (1.36 g, 7 mmol) in 30 mL of dry ether at room temperature. After the mixture was stirred for 2 h, the precipitate (1.22 g) was removed by filtration and found by ^1H NMR analysis to consist of **3a**[6] and **6** in a ratio of 2:1; the following ^1H NMR peaks ($CDCl_3$) were assigned to **6**: δ 1.35, 1.48 (2 s, 3 H each, CMe_2), 3.20 (6 H, s, NMe_2), 3.6 (1 H, m, bridgehead H), 5.8–6.6 (4 H, olefinic H), 7.1–7.5 (5 H, aromatic H). PTLC (3:2 acetone/ether) of the precipitate led to **3a** (0.45 g, 21%) and 5,5-dimethyl-4-(dimethylamino)-1-phenyl-3,4-dihydro-1*H*-3-benzazepin-2-one (**7**; 0.31 g, 14%) as a semisolid material: ^1H NMR ($CDCl_3$) δ 1.75 (6 H, s, CMe_2), 2.85 (6 H, s, NMe_2), 4.98 (1 H, s, CHPh), 6.8–7.2 (9 H, aromatic H); for IR and ^{13}C NMR, see Table I.

PTLC (1:1 ethyl acetate/petroleum ether) of the filtrate gave an additional crop of **3a** (0.09 g, 4%) besides 5-(dimethylamino)-4,4-dimethyl-3,3-diphenyl-5-pyrrolin-2-one (**4a**; 0.18 g, 8%; mp 214–216 °C after recrystallization from 2-propanol/ether) and **5a** (0.37 g, 17%), which was identified by comparison with an authentic sample.[11] Compound **4a** showed the following spectroscopic characteristics: IR and ^{13}C NMR, see Table I; ^1H NMR ($CDCl_3$) δ 1.27 (6 H, s, CMe_2), 3.40, 3.45 (2 s, 3 H each, NMe_2), 7.43 (10 H, s, aromatic H); mass spectrum, *m/e* (relative intensity) 306 (22, M^+), 291 (14, M^+ - Me), 208 (9), 165 (12, fluorenyl$^+$), 139 (20), 115 (12), 111 (14), 109 (10), 99 (44), 98 (26), 97 (20), 95 (14), 91 (19), 70 (100, Me_2CN). Anal. Calcd for $C_{20}H_{22}N_2O$: C, 78.40; H, 7.24; N, 9.14. Found: C, 78.42; H, 7.33; N, 9.08.

1,1-Dimethyl-5-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine-2,4-dione (8). To 1.22 g of a 2:1 mixture of **3a** and **6** obtained as described above was added 20 mL of dilute HCl. After the mixture was stirred for 2 h at room temperature, the organic material was extracted with CH_2Cl_2, and the products were isolated by PTLC in ethyl acetate/petroleum ether, 1:1. Besides **3a** and its hydrochloride, **8** (0.27 g, 73% based on the percentage of **6** in the starting material; mp 153–154 °C, recrystallized from ethanol) was obtained: IR (KBr) ν_{max} 3190, 3090 (NH), 1690, 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.42, 1.82 (2 s, 3 H each, CMe_2), 5.50 (1 H, s, H-5), 7.2–7.6 with 7.35 (s, 9 H, aromatic H), 8.2 (1 H, br, NH); ^{13}C NMR, see Table I; mass spectrum, *m/e* (relative intensity) 279 (10, M^+), 236 (50, M^+ - HNCO), 210 (13), 209 (11), 208 (58), 193 (100), 191 (11), 178 (65), 165 (16). Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.32; H, 6.21; N, 5.02.

6-(Dimethylamino)-1,4-ethylene-5,5-dimethyl-8-oxo-*N*,9-diphenyl-2,3,4,4a,5,8-hexahydro-1*H*-pyridazino[4,5-*d*]azepine-2,3-dicarboximide (10). Compound **9**[24] (0.53 g, 3 mmol) in 15 mL of acetone was slowly added to 0.92 g of the above 2:1 mixture of **3a** and **6** dissolved in 15 mL of acetone at 0 °C. The mixture was allowed to warm to room temperature, evaporated to dryness, and separated by PTLC using acetone/ether (5:1) to give **10**, which solidified on treatment with ethanol/ether (0.20 g, 42%; mp 200–204 °C dec, recrystallized from CH_3CN): IR (KBr) ν_{max} 1780, 1720 (st, C=O), 1640 (w), 1610 (w), 1595 (w), 1560 cm^{-1} (st, C=N); ^1H NMR ($CDCl_3$) δ 1.22, 1.73 (2 s, 3 H each, CMe_2), 3.20 (6 H, s, NMe_2), 3.45 (1 H, d, J = 3 Hz, H-4a), 5.27, 5.57 (2 m, 1 H each, H-1, H-4), 6.62 (2 H, m, olefinic H), 7.4–7.5

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(10 H, aromatic H). Anal. Calcd for $C_{28}H_{27}N_5O_3$: C, 69.84; H, 5.65; N, 14.54. Found: C, 69.63; H, 5.60; N, 14.51.

Reactions of Azirine 1b with Ketene 2a. To **1b**[22] (0.56 g, 3 mmol) in 2 mL of dry THF was added dropwise **2a**[23] (0.58 g, 3 mmol) in 15 mL of dry ether at room temperature. After 2 h the precipitated solid was filtered by suction and found to be 4-(dimethylamino)-2-(diphenylmethylene)-5-ethyl-5-phenyl-3-oxazoline (**3b**): 0.53 g (46%); mp 198–198.5 °C; IR and ^{13}C NMR, see Table I; ^1H NMR ($CDCl_3$) δ 0.98 (3 H, t, J = 7 Hz, $EtCH_3$), 2.2 (2 H, m, $EtCH_2$), 2.73 (6 H, s, NMe_2), 6.7–7.3 (15 H, aromatic H); coalescence of the NMe_2 peaks in $CDCl_3$, $\Delta\nu$ = 29.5 Hz, t_c = −18 ± 2 °C, ΔG^* = 53.3 ± 0.4 kJ/mol (12.7 ± 0.1 kcal/mol); mass spectrum, m/e (relative intensity) 382 (100, M^+), 357 (7, M^+ − Et), 194 (65, **2a**$^+$·), 165 (80, fluorenyl$^+$), 117 (17, **2a** − Ph), 77 (26, Ph). Anal. Calcd for $C_{26}H_{26}N_2O$: C, 81.64; H, 6.85; N, 7.32. Found: C, 81.51; H, 6.77; N, 7.29.

^1H NMR ($CDCl_3$) of the evaporated filtrate revealed the presence of **3b**, **4b**, and a trace of **5b** as indicated by δ 1.55 (3 H, d, J = 7 Hz, CH_3), 2.80, 3.03 (2 s, 3 H each, NMe_2), 4.90 (1 H, s, $CHPh_2$), 6.1 (1 H, m, olefinic H), and 7.0–7.3 (15 H, aromatic H). PTLC using ethyl acetate/petroleum ether (1:2) yielded again **3b** (0.12 g, 10%) and 5-(dimethylamino)-4-ethyl-3,3,4-triphenyl-5-pyrrolin-2-one (**4b**): 0.18 g (16%); mp 97–99 °C, recrystallized from ether/hexane to gain crystals which retained a trace of ether; IR, see Table I; ^1H NMR ($CDCl_3$) δ 0.53 (3 H, t, J = 7 Hz, $EtCH_3$), 2.1, 2.7 (2 m, 1 H each, $EtCH_2$), 2.37, 3.23 (2 s, 3 H each, NMe_2), 6.8–8.1 (15 H, aromatic H); coalescence of the NMe_2 peaks in ODC, $\Delta\nu$ = 54.5 Hz, t_c = 101 ± 2 °C, ΔG^* = 77.4 ± 0.4 kJ/mol (18.5 ± 0.1 kcal/mol); mass spectrum, m/e (relative intensity) 382 (100, M^+), 367 (12, M^+ − CH_3), 354 (13), 353 (40, M^+ − Et), 284 (30), 208 (21), 206 (12), 194 (69, **2a**$^+$·), 191 (32). Anal. Calcd for $C_{26}H_{26}N_2O$: C, 81.64; H, 6.85; N, 7.32. Found: C, 80.42; H, 6.85; N, 7.17.

When the reaction between **1b** (3.3 g, 17 mmol) and **2a** (3.4 g, 17 mmol) was carried out at −40 °C in ether, only **3b** (6.1 g, 94%) was obtained.

5-(Dimethylamino)-4-methyl-3,3-diphenyl-4-vinyl-5-pyrrolin-2-one (4c). Compound **1c**[22] (0.57 g, 4.6 mmol) was added dropwise at −40 °C to **2a** (0.9 g, 4.6 mmol) in 60 mL of dry ether. The reaction mixture was allowed to warm to room temperature and was stirred for 1 h. The precipitate which had formed was filtered and washed with 15 mL of ether in two portions. Concentration of the mother liquor yielded a second fraction of the product **4c**: total yield 1.36 g (93%, recrystallized from CH_2Cl_2/petroleum ether); IR and ^{13}C NMR, see Table I; ^1H NMR ($CDCl_3$) δ 1.13 (3 H, s, 4-CH_3), 3.2, 3.32 (2 s, 3 H each, NMe_2), 4.93 (2 H, 2 d, $=CH_2$), 6.07 (1 H, 2 d, =CH), 6.8–7.63 (10 H, aromatic H); mass spectrum, m/e (relative intensity) 318 (100, M^+), 303 (19, M^+ − Me), 274 (9, M − NMe_2), 220 (14), 98 (17), 77 (8, Ph), 70 (41, Me_2CN). Anal. Calcd for $C_{21}H_{22}N_2O$: C, 79.21; H, 6.96; N, 8.79. Found: C, 79.16; H, 7.01; N, 8.82.

2-Cyano-*N*-[1-(dimethylthiocarbamoyl)-1-methylethyl]-3,3-dimethylbutyramide (14). H_2S was bubbled for 15 min through a solution of **12**[6] (0.35 g, 1.5 mmol) in 10 mL of dry ether. The precipitate was filtered by suction and recrystallized from CH_2Cl_2/hexane to give **14**: 0.38 g (94%); mp 144–147 °C; IR (KBr) ν_{max} 3300 (NH), 2240 (C≡N, very weak), 1655 (C=O), 1540–1500 (thioamide B band); ^1H NMR ($CDCl_3$) δ 1.25 (9 H, s, *t*-Bu), 1.78, 1.87 (2 s, 3 H each, CMe_2), 3.32 (1 H, s, CO—CH), 3.57 (6 H, s, NMe_2), 8.7 (1 H, br, NH); mass spectrum, m/e (relative intensity) 269 (15, M^+), 181 (66, M^+ − $CSNMe_2$), 173 (12), 130 (12, Me_2C–$CSNMe_2$), 125 (18). Anal. Calcd for $C_{13}H_{23}N_3OS$: C, 57.96; H, 8.61; N, 15.60; S, 11.90. Found: C, 57.92; H, 8.53; N, 15.64; S, 11.82.

Reaction of Azirine 1b with Ketene 2b. A solution of the ketene **2b** (3.3 mmol, generated according to the literature[25]) in 15 mL of dry toluene was added dropwise to **1b**[22] (0.62 g, 3.3 mmol), dissolved in 5 mL of dry toluene, with stirring and ice cooling. After 1.5 h at room temperature, the mixture was evaporated and separated by PTLC (2:2:1 ethyl acetate/petroleum ether/CH_2Cl_2) to afford N^2-(2-cyano-3,3-dimethylbutyryl)-N^1,N^1-dimethyl-2-phenylcrotonamidine (**16**; 0.11 g, 11%) and 2-[4-(dimethylamino)-5-ethyl-5-phenyl-3-oxazolin-2-ylidene]-3,3-dimethylbutyronitrile (**17**; 0.37 g, 36%).

16: mp 142–145 °C, recrystallized from hexane, mixture of E/Z isomers; IR (KBr) ν_{max} 2220 (C≡N), 1650 (C=O), 1560 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 1.08 (9 H, s, *t*-Bu), 1.8 (3 H, br d, J = 7 Hz, $=CCH_3$), 2.88, 2.93, 3.22, 3.25 (a total of 6 H, singlets, NMe_2), 3.05 (1 H, s, CHCN), 6.20 (1 H, br q, =CH), 7.2 (5 H, s, aromatic H). Anal. Calcd for $C_{19}H_{25}N_3O$: C, 73.28; H, 8.09; N, 13.49. Found: C, 72.94; H, 8.00; N, 13.42.

17: mp 123–125 °C, recrystallized from ether/hexane, obtained as a mixture of E/Z isomers; IR, see Table I; ^1H NMR ($CDCl_3$) δ 0.95 (3 H, t, J = 7 Hz, $EtCH_3$), 1.13, 1.28 (together 9 H, 2 s, *t*-Bu), 2.4 (2 H, m, $EtCH_2$), 2.9 (6 H, br s, NMe_2), 7.2 (5 H, s, aromatic H); mass spectrum, m/e (relative intensity) 311 (24, M^+), 296 (100, M^+ − Me), 268 (16), 153 (18), 144 (15), 108 (95). Anal. Calcd for $C_{19}H_{25}N_3O$: C, 73.28; H, 8.09; N, 13.49. Found: C, 73.45; H, 8.30; N, 13.43.

N^2-(2-Isopropyl-3,3-dimethylbutyryl)-N^1,N^1-dimethyl-2-phenylcrotonamidine (18). Ketene **2c**[26] (3 mmol), **1b** (0.75 g, 4 mmol), and 10 mL of toluene were mixed and kept at 50 °C for 8 days. Then the solvent was removed at reduced pressure and the residue separated by PTLC (1:1 ethyl acetate/petroleum ether) to give **18** (1:1 mixture of diastereomers): 0.15 g (11%); mp 58–59 °C; IR (KBr) ν_{max} 1650 (C=O), 1545 (C=C, C=N); ^1H NMR ($CDCl_3$) δ 0.74, 0.96 (2 s, 4.5 H each, *t*-Bu), 0.81, 0.90, 1.02, 1.10 (4 d, 1.5 H each, J = 7 Hz, *i*-$PrCH_3$), 1.81, 1.83 (2 d, 1.5 H each, J = 7 Hz, $=CCH_3$), 2.88, 2.93, 3.17 (1.5 + 1.5 + 3 H, 3 s, NMe_2), 6.22, 6.34 (2 q, 0.5 H each, J = 7 Hz, =CH), 7.2–7.4 (5 H, aromatic H). Anal. Calcd for $C_{21}H_{32}N_2O$: C, 76.78; H, 9.82; N, 8.53. Found: C, 76.64; H, 10.13; N, 8.45.

Registry No. **1a**, 54856-83-6; **1b**, 64276-78-4; **1c**, 66206-69-7; **2a**, 525-06-4; **2b**, 29342-22-1; **2c**, 71106-63-3; **3a**, 54856-84-7; **3b**, 72217-67-5; **4a**, 73805-50-2; **4b**, 73816-14-5; **4c**, 73805-51-3; **5a**, 56862-07-8; **5b**, 73805-52-4; **6**, 73805-53-5; **7**, 73805-54-6; **8**, 73805-55-7; **9**, 4233-33-4; **10**, 73816-15-6; **12**, 54856-32-5; **14**, 73805-56-8; (*E*)-**16**, 73805-57-9; (*Z*)-**16**, 73805-58-0; (*E*)-**17**, 73805-59-1; (*Z*)-**17**, 73805-60-4; (*E*)-**18**, 73805-61-5; (*Z*)-**18**, 73805-62-6.

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