and hypervalent sulfur compounds indicate that the STO-3G* basis[19] adequately models geometry and trends in barrier heights. However, an extensive series of calculations with the STO-3G* basis paralleling those reported demonstrated that it is not flexible enough to handle the subtle balance between aromaticity and electronegativity encountered in thiadiazole 1-oxide. Accordingly, the 4-31G split valence basis[20] set was used augmented by a set of six Cartesian d functions on sulfur (denoted by 4-31G+d). The GAUSSIAN exponent, $\alpha = 0.54$, was optimized for pyramidal H_2SO. This basis set overestimates the SO bond length by ca. 0.02 Å but predicts the inversion barrier approximately as well as the 4-31G* basis which contains d orbitals on first and second row atoms. Because of strongly coupled internal coordinates, cyclic structures pose a special problem for geometry optimization. To overcome these difficulties, equilibrium geometries were determined with a conjugate gradient method using analytically calculated energy derivatives. All structures were fully optimized, with the exception that the heterocyclic rings were constrained to be planar, by using the 4-31G+d basis set.

Acknowledgment. We are grateful to Drs. Arthur A. Patchett and G. B. Smith for useful discussions and Mr. Jack Smith for the mass spectra. Special thanks are due to Dr. Raymond Firestone for many helpful suggestions.

Registry No. **4**, 31681-45-5; **5a**, 13534-15-1; **5b**, 79844-63-6; **6a**, 79844-64-7; **6b**, 79844-65-8; **7**, 80028-45-1; **8**, 79844-66-9; **9**, 80028-46-2; **10** isomer 1, 80028-47-3; **10** isomer 2, 80028-48-4; **11**, 4057-61-8; pyrrolidine, 123-75-1; L-ephedrine, 321-98-2; (*S*)-2,3-dihydroxy-1-(*tert*-butylamino)propane, 30315-46-9; H_2SO, 25540-60-7; $(CH_3)_2SO$, 67-68-5; $(NH_2)_2SO$, 36986-61-5.

Supplementary Material Available: The final fractional coordinates and temperature parameters for **6b** from the X-ray experiments (1 page). Ordering information is given on any current masthead page.

(18) J. S. Binkley, R. A. Whiteside, R. Krishnan, R. Seeger, D. J. DeFrees, H. B. Schlegel, S. Topiol, L. R. Kahn, and J. A. Pople, Carnegie-Mellon University, Pittsburgh, PA, 1980.
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A New Thermal Rearrangement in the 4-Isoxazoline System. Some Chemical and Stereochemical Properties of a Benzodiazepine Oxide–Ethyl Propiolate Adduct

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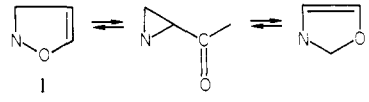
Contribution from the Research Laboratories, The Upjohn Company, Kalamazoo, Michigan 49001, and Department of Chemistry, Wayne State University, Detroit, Michigan 48202. *Received July 22, 1981*

Abstract: Reaction of 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one 4-oxide, **3**, with ethyl propiolate afforded the expected 4-isoxazoline **4** and a rearrangement product **5**. Product **5** and a further rearrangement product, **6**, could be obtained from **4** upon treatment with boiling ethanol which also yielded a dihydroquinoxalone **7**. The structures of isomers **4**, **5**, and **6** were determined by X-ray diffraction analyses. The conformational and configurational properties of these compounds were further studied by NMR. The rearrangement of **4** to **5** represents a new reaction path for 4-isoxazolines.

4-Isoxazolines, **1**, whose isolable members are relatively rare,



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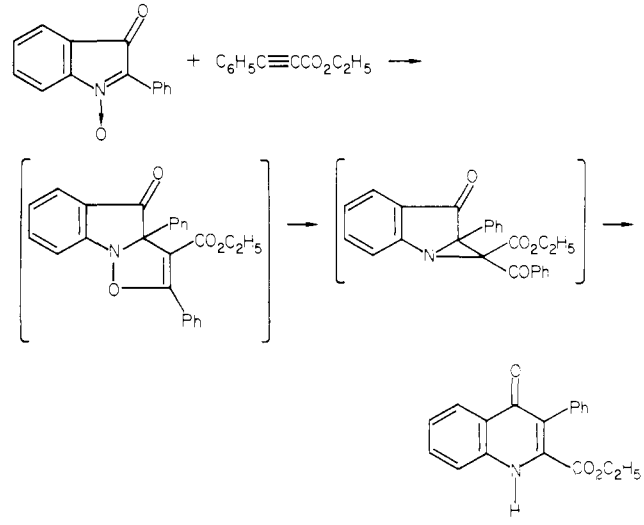
are markable heterocycles because of the number of interesting rearrangements which arise from them. Baldwin[1] has shown that in the simplest case they interconvert with ketoaziridines and 2-oxazolines. Often these primary reactions are masked by subsequent changes. For example, a 4-isoxazoline presumably is an intermediate in the conversion of 2-phenylisatogen and ethyl phenylpropiolate to quinolone **2**; in this case deacylation and ring expansion has occurred.[2] With diazacyclopentadienone *N*-oxides and oxadiazine *N*-oxides, 1,3- and 3,3-sigmatropic shifts after 4-isoxazoline formation were invoked to rationalize the formation of the ultimate products.[3] A more deep seated rearrangement was observed with a pyrrolone *N*-oxide.[4] Extensive rearrangement also was observed with the 4-isoxazolines derived from fervenulin 4-oxides.[5] In most of these cases and others the 4-isoxazolines



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were not isolable and were proposed as transient, first-formed intermediates.

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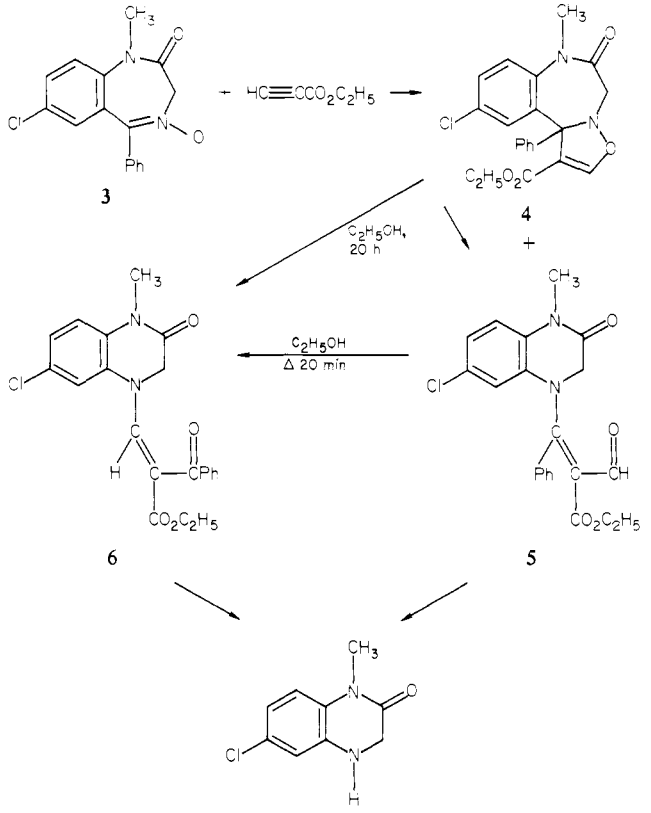
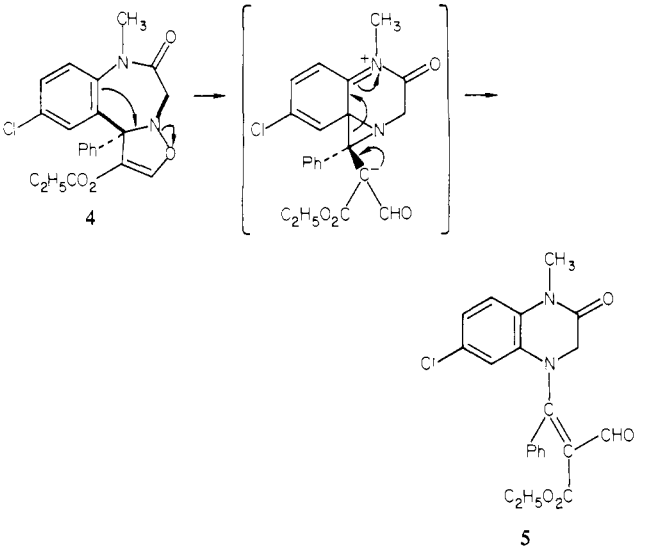
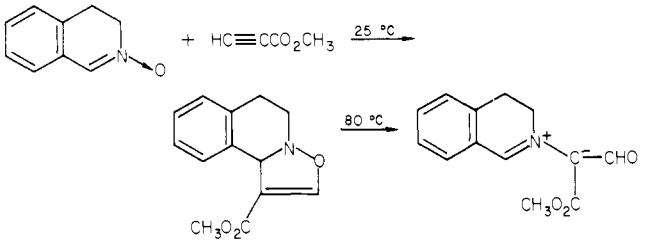
Scheme I



Scheme II



In one case Huisgen was able to isolate the 4-isoxazoline and to observe its conversion to a stable azomethine ylide upon ring opening of the ketoaziridine rearrangement product.[6]

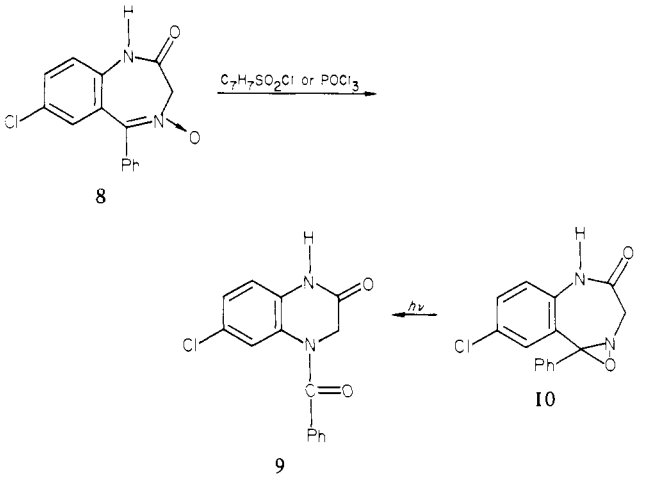


We wish to report a new transformation of the 4-isoxazoline system in which the first example of a 1,2-carbon-to-nitrogen rearrangement accompanied by cleavage of the nitrogen–oxygen bond has been observed. In the course of our general program of study of the cycloaddition reactions of 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one 4-oxides, **3**,[7] we heated this substance with ethyl propiolate in boiling tetrahydrofuran; a mixture of compounds **4** and **5** was obtained. In turn, compound **5** could be converted to **6** by further heating in ethanol. Subsequently, it was found that heating **4** in ethanol yielded a mixture of **5** and **6**, and also **7**. These results are summarized in Scheme I.

The structures of compounds **4**, **5**, and **6** were determined by X-ray diffraction while that of **7** was derived spectroscopically. The NMR spectra of **4**, **5**, and **6** were complex, indicating the presence of two isomers in each case, so further studies of these spectra were undertaken. The barrier to ring inversion in the seven-membered ring was determined and has been reported separately.[8]

Scheme II shows a possible mechanism for the transformation of **4** → **5**. The regiochemistry of compound **4** is consistent with that expected of such a cycloaddition.[6] The stereochemistry of **4** is such (see below) that the torsion angle between the fused aromatic ring containing an electron-releasing, ortho-nitrogen substituent and the N–O bond of the isoxazoline ring is 146°. This stereochemistry is close to ideal (180°) for a 1,2 migration from the backside; the difference may be compensated for by the presence of a good leaving group (enolate ion), a weak N–O bond, and an electron-rich migrating group. (A tricyclic intermediate of the phenonium ion type shown may be involved but is not required.)

Ring contraction reactions of other benzodiazepine derivatives containing N–O bonds are known, and all may be viewed as resulting from the development of and electron-deficient nitrogen by cleavage of the N–O bond. These include the Beckmann-type rearrangement of **8** with *p*-toluenesulfonyl chloride or phosphorus oxychloride[9] to give **9**, photolytic conversion[10] of oxaziridine **10** to **9**, and the Stieglitz-type rearrangement of compounds such as **11** to produce tetrahydroquinoxalines.[11]



(1) Baldwin, J. E.; Pudussery, R. G.; Qureshi, A. K., Sklarz, B. *J. Am. Chem. Soc.* **1968**, *90*, 5325–5326.
(2) Noland, W. E.; Modler, R. F. *J. Am. Chem. Soc.* **1964**, *86*, 2086–2087.
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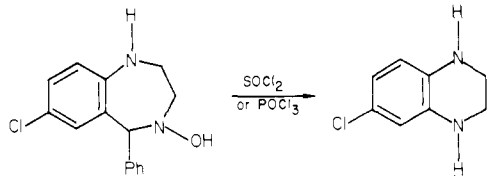

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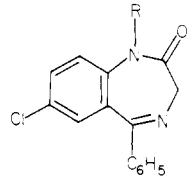
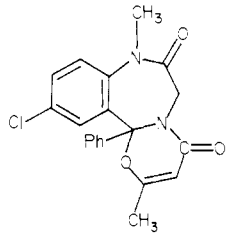
The transformation of **5** to **6** may be rationalized as shown in Scheme III. Compound **7** is seen to be a displacement product of either **5** or **6** in the presence of ethanol. Such amine transfer reactions are known; a particularly elegant one was elucidated by Stork and Landesman in a reaction where no other nucleophile such as ethanol was present.[12]

Structural Features of Isoxazoline 4. The X-ray structure of **4** (detailed in the Experimental Section), the first of a 4-isoxazoline, confirms the features responsible for the reactivity of the ring system: a long N–O bond[13] and a relatively short C–O bond. The observed bond lengths (Figure 1) may indicate a "weak point" in this heterocycle at which the conversion to **5** may begin.

The diazepine ring of **4** is in a boat conformation as expected from the structures of diazepam **12**[14] and ketazolam **13**.[15] The



12a, R = H
b, R = CH_3
c, R = $CH(CH_3)_2$



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torsion angles (Table I) are closer to the tricyclic ketazolam. Any nonboat conformations are completely ruled out.

The sterochemical consequences of a boat–boat interconversion in **4** are complex. While such an interconversion of diazepam gives rise to enantiomers, the presence of two additional chiral centers in **4**, the nitrogen and C-3 of the isoxazoline ring, introduces the possibility of four pairs of diastereomers, **4A**, **4B**, **4C**, and **4D**.

Their sterochemical features are summarized in Table II. Two of the four are characterized by conformations in which the phenyl ring is quasi-axial to the seven-membered ring (**4B** and **4C**); while in the other two diastereomers (**4A** and **4D**), the phenyl is quasi-equatorial. The two axial isomers are nitrogen invertomers distinguished by having either a cis or trans ring junction (cis-axial and trans-axial). The two equatorial isomers may be similarly distinguished (cis-equatorial and trans-equatorial). The pairs of cis isomers are interconverted by fluxion of the seven-membered ring (as are the trans-axial and trans-equatorial isomers). Inversion of the isoxazoline nitrogen interconverts the cis-equatorial:trans-equatorial pair or the cis-axial:trans-axial pair (**4A**:**4D** or **4B**;**4C**). Isomer **4A** is the one found in the crystal.

The room temperature NMR spectrum of compound 4 (chloroform-*d*, 100 MHz) indicated that a 60–40 mixture of two diastereomers was present in solution (see Table III). Large differences[17] were observed in the chemical shifts of the two *N*-methyl signals ($\Delta\delta$ = –0.68) for the two isomers and in the two

Scheme III

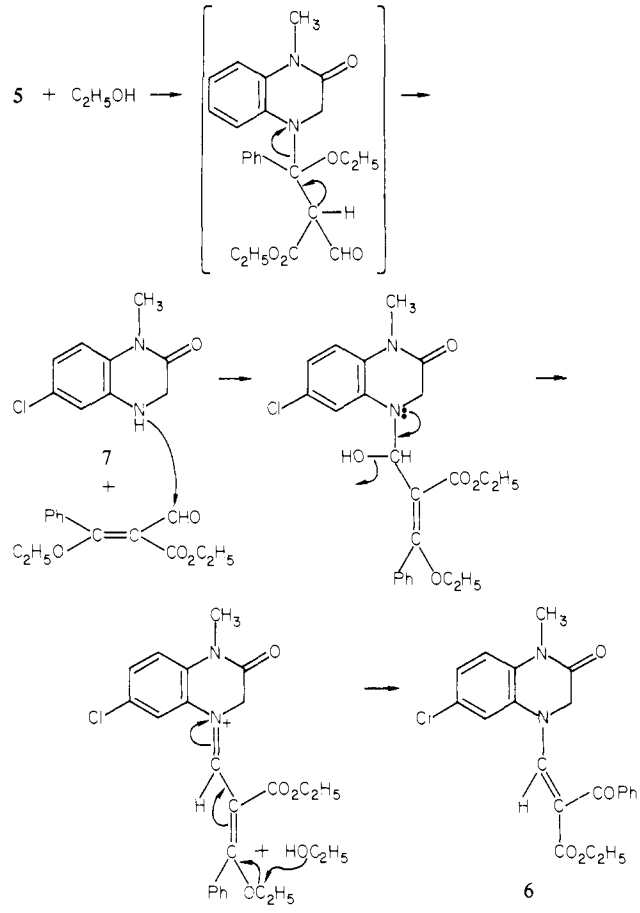

Table I. Torsion Angles in the Seven-Membered Rings (from X-ray Results)

	4	12a[14]	13a[15]
C(11B)–C(11A)–C(7A)–N(7)	3.1	–3.3	3.8
C(11A)–C(7A)–N(7)–C(6)	50.5	51.8	51.3
C(7A)–N(7)–C(6)–C(5)	–5.8	–13.4	–3.1
N(7)–C(6)–C(5)–N(4)	–70.3	–64.9	–72.8
C(6)–C(5)–N(4)–C(11B)	50.3	74.6	50.0
C(5)–N(4)–C(11B)–C(11A)	31.9	–2.9	35.0
N(4)–C(11B)–C(11A)–C(7A)	–64.9	–40.2	–69.8

aromatic 6-hydrogens ($\Delta\delta$ = 0.63). Other differences were apparent in the phenyl region, but they could not be analyzed. Smaller differences were observed in the two vinyl hydrogen signals ($\Delta\delta$ = 0.07), the two cyclic methylene AB multiplets ($\Delta\delta$ = –0.16), the two *O*-methylene quartets ($\Delta\delta$ = –0.05), and the two terminal methyl triplets ($\Delta\delta$ = 0.04).

Of the four possible isomers, **4A**, **4B**, **4C**, and **4D**, the latter two, **4C** and **4D**, appear to have higher strain energies than the former. The trans fusion of the five- and seven-membered rings distorts the seven-membered ring and appears, from examination of molecular models, to impose significant angle strain and nonbonded repulsion. Isomer **4C** exhibits a significant peri-like interaction between the *N*-methyl group and the ortho hydrogen in the chlorophenyl ring. Furthermore, the eclipsing of the peri hydrogen by the amide methyl should destablize **4C** relative to the other conformers.[18] Isomer **4C** also shows some interaction between the phenyl and the methylene of the seven-membered ring.

Inspection of the model of **4D**, the other trans-fused isomer, indicates that the phenyl ring is brought into close proximity to

(11) Walser, H.; Silverman, G.; Fryer, R. I.; Sternbach, L. H.; Hellerbach, J. *J. Org. Chem.* **1971**, *36*, 1248–1251.
(12) Stork, G.; Landesman, H. K. *J. Am. Chem. Soc.* **1956**, *78*, 5129–5130.
(13) The N–O bond length of formaldoxime is 1.41 Å: Levine, I. N. *J. Chem. Phys.* **1963**, *38*, 2326–2328.
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(15) Szmuszkovicz, J.; Chidester, C. G.; Duchamp, D. J. MacKellar, F. A.; Slomp, G. *Tetrahedron Lett.* **1971**, 3665–3668.
(16) The apparently short C(14)–C(15) bond in the ethyl group is an artifact of the thermal motion in the crystal. The temperature factors of C(15) are quite high; a maximum thermally corrected distance of 1.61 Å is calculated for this bond according to the model of Busing, W. R.; Levy, H. A. *Acta Crystallogr.* **1964**, *17*, 142–146.
(17) Differences are expressed as $\Delta\delta = \delta$(minor isomer) – δ(major isomer).

(18) As a rough estimate of the energy involved in this interaction, we may take the difference in the energies of activation for ring reversal for **12a** and **12b**, ca. 6 kcal/mol.

Table II. Stereochemical Account of the Four Possible Diastereoisomers Corresponding to Structure 4 (Three Chiral Elements)[a]

dia-stereo-isomer	stereochemistry of Ph vs :N (ring fusion between 5 and 7 rings)	vs. seven-membered ring	$N-CH_3$ torsion angle with respect to chlorobenzene ring	peri H vs. phenyl	conformation of :N vs. CH_2
4A	cis	quasi-equatorial	48° (good)	eclipsed	gauche gauche
4B	cis	quasi-axial	same as above but opposite direction (good)	far	gauche trans
4C	trans	quasi-axial (severe interaction with CH_2)	0° (intolerable)	far	near gauche near trans
4D	trans	quasi-equatorial 45° (severe interaction with amide)	ca. 45° (good)	far	partially eclipsed eclipsed

[a] Dreiding and CPK models were used. All seven-membered rings are in boat-like conformations.

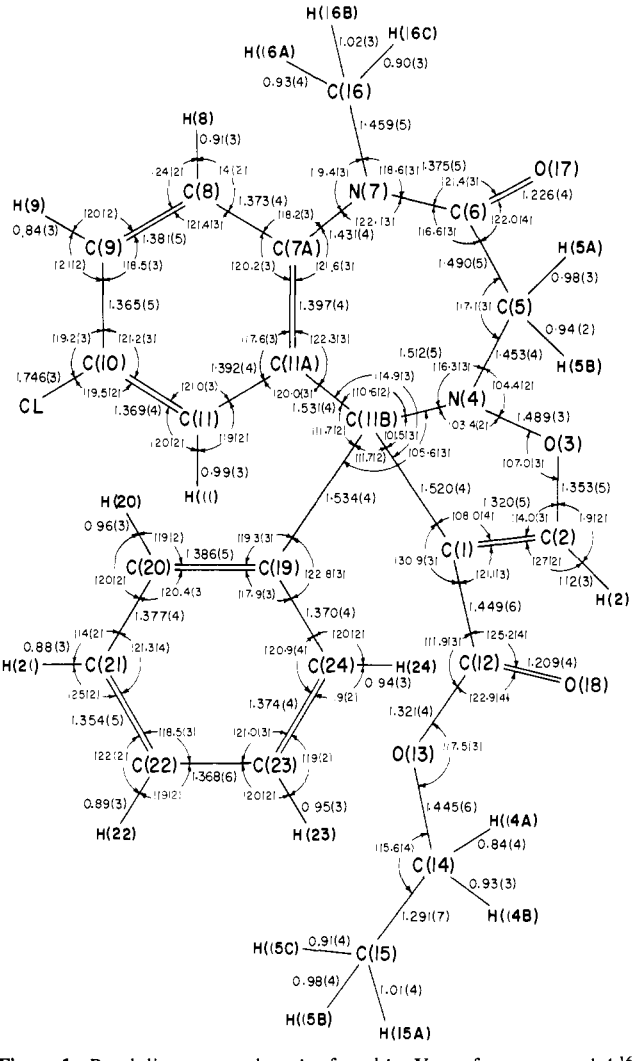


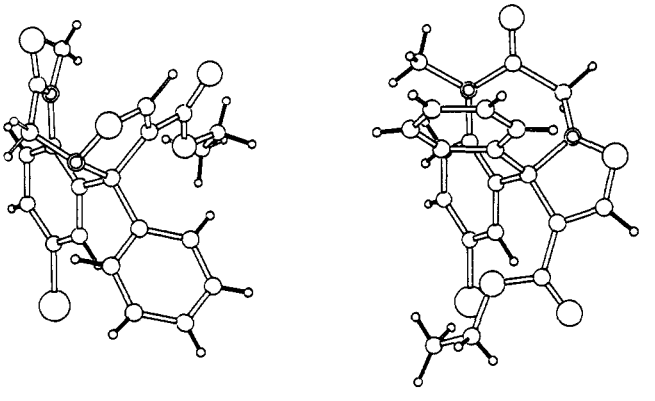
Figure 1. Bond distances and angles found by X-ray for compound **4**.[16] Bond distances are in Angstrom units; bond angles are in degrees. Standard deviations (in parentheses) apply to the last quoted digit.

the amide nitrogen and the carbonyl carbon atom, and a severe repulsive interaction would be expected. On this basis the two diastereomers observed in solution should correspond to **4A** and **4B**, the cis fusion isomers. Figure 2 illustrates these isomers. The **4A** figure is drawn from the X-ray results. The **4B** molecule coordinates were obtained from the **4A** ones by "flipping" the seven-membered ring of the **4A** molecule to the alternate boat conformation by use of a conformational analysis computer program. The chlorobenzene rings in both drawings are in identical orientations. Cis-ring fusion is consistent with a concerted cycloaddition process.

Table III. NMR Data Obtained with a Solution of 4 in $CDCl_3$ (100 MHz)

shift, δ	relative area[a]	multiplicity	assignment[b]
1.15	3	triplet, $J = 7$ Hz	β-H of ester (B)
1.20	3	triplet, $J = 7$ Hz	β-H of ester (A)
2.57	3	singlet	$N-CH_3$ (B)
3.25	3	singlet	$N-CH_3$ (A)
3.54	1	A of AB, $J = 16$ Hz	3-H (B)
3.71	1	B of AB, $J = 16$ Hz	3'-H (B)
3.70	1	A of AB, $J = 15$ Hz	3-H (A)
3.88	1	B of AB, $J = 15$ Hz	3'-H (A)
4.08	2	quartet, $J = 7$ Hz	α-H of ester (B)
4.13	2	quartet, $J = 7$ Hz	α-H of ester (A)
6.69	1	doublet, $J = 2$ Hz	6-H (A)
7.32	1	doublet, $J = 2$ Hz	6-H (B)
7.1–7.7	7	multiplet	8-, 9-H and phenyl
6.91	1	broad singlet	vinyl hydrogen (A)
6.98	1	broad singlet	vinyl hydrogen (B)

[a] Relative to that component. [b] A = major component; B = minor component.



a **b**

Figure 2. (a) Compound **4A** as found in the crystal. (b) Proposed alternate ring-flipped form for **4B** (see Discussion).

Since low-temperature NMR experiments[8] have shown the predominant isomer in solution to be the same as that found in the solid state (**4A**, the cis-equatorial), we would assign **4B** (the cis-axial) to the minor solution isomer. The NMR chemical shifts provide support for this assignment. The chemical shift of the *N*-methyl group in **4A** (δ 3.25) is comparable with that observed for *N*-acetyl-*N*-methyl-*o*-toluidine in which the *N*-methyl group appears at δ 3.2.[19] The *N*-methyl group in the minor isomer **4B**, however, is shifted upfield, relative to that in **4A**, to δ 2.57. Examination of molecular models indicates that while the *N*-methyl group in the cis-equatorial conformer should exhibit a normal chemical shift, that in the cis-axial isomer lies well within

(19) Bhacca, N. S.; Johnson, L. F.; Shoolery, J. N. "NMR Spectra Catalog", Vol. 1, No. 264.

Table IV. NMR Data Obtained with a Solution of 5 in $CDCl_3$

shift, δ	relative area[a]	multiplicity	assignment[b]
0.77	3	triplet, J = 7 Hz	β-H of ester (A)
1.21[c]	3	triplet, J = 7 Hz	β-H of ester (B)
3.42	3	singlet	N-CH_3 (B)
3.48	3	singlet	N-CH_3 (A)
3.85	2	quartet	α-H of ester (A)
3.95	2	quartet	α-H of ester (B)
4.03	2	broad singlet	3-CH_2 (B)
4.34	2	broad singlet	3 CH_2 (A)
6.50	1	broad singlet	5-H of both
6.8–7.6	7	multiplet	7-, 8-H and phenyl
9.12	1	singlet	CHO (B)
9.83	1	singlet	CHO (A)

[a] Relative to that component. [b] A = major component; B = minor component. [c] A small amount of ethanol impurity appears at δ 1.19 (and at δ 3.47) as shoulders on this triplet.

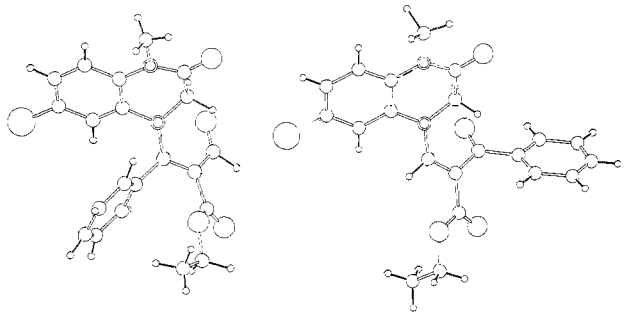


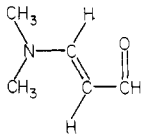
Figure 3. Drawings of **5** (left) and **6A** (right) from crystal structure results.

the shielding cone of the axial phenyl group and a substantial upfield shift would be anticipated. The coplanarity of the phenyl ring with the peri 6-hydrogen in **4A**, but not in **4B**, also explains the large difference in the shielding of this hydrogen (δ 6.69 and 7.32, respectively). The accord between the chemical shifts observed and those deduced provides confirming evidence for the correctness of the assignments made above.

Structure of 5. The structure of **5** was determined by a single-crystal X-ray analysis. As in the case of **4**, a computerized direct-methods procedure gave a trial structure. The N and O atoms in this unusual product were identified by studying the temperature factor shifts when all atoms, except Cl, were assigned a C scattering factor, and by locating the hydrogen atoms. Details are given in the Experimental Section.

In chloroform-*d* solution, **5** exists as a 60–40 mixture of two isomers as evidenced by NMR (see Table IV). That the isomers were interconvertible was shown by collapse of all doubling upon observing the spectrum of **5** at 85 °C, with return to doubling at ambient temperature. Large differences[17] were observed in the chemical shifts of the two aldehyde signals ($\Delta\delta$ = −0.71), the terminal methyls ($\Delta\delta$ = 0.44), and the cyclic methylenes ($\Delta\delta$ = −0.31). The *N*-methyls and the *O*-methylenes were nearly the same.

Since the two cyclic methylene signals were A_2—rather than AB—type spectra, ring inversion of the new six-membered ring was judged to be rapid on the NMR time scale. This is supported by the X-ray results, since the new six-membered ring is only slightly nonplanar (see Figure 3) and would be expected to have a very low barrier to interconversion. Hence the exchange must be between geometric isomers in this vinylogous amide. This type of restricted rotation is not new and has been reported, for example, in **14**.[20]



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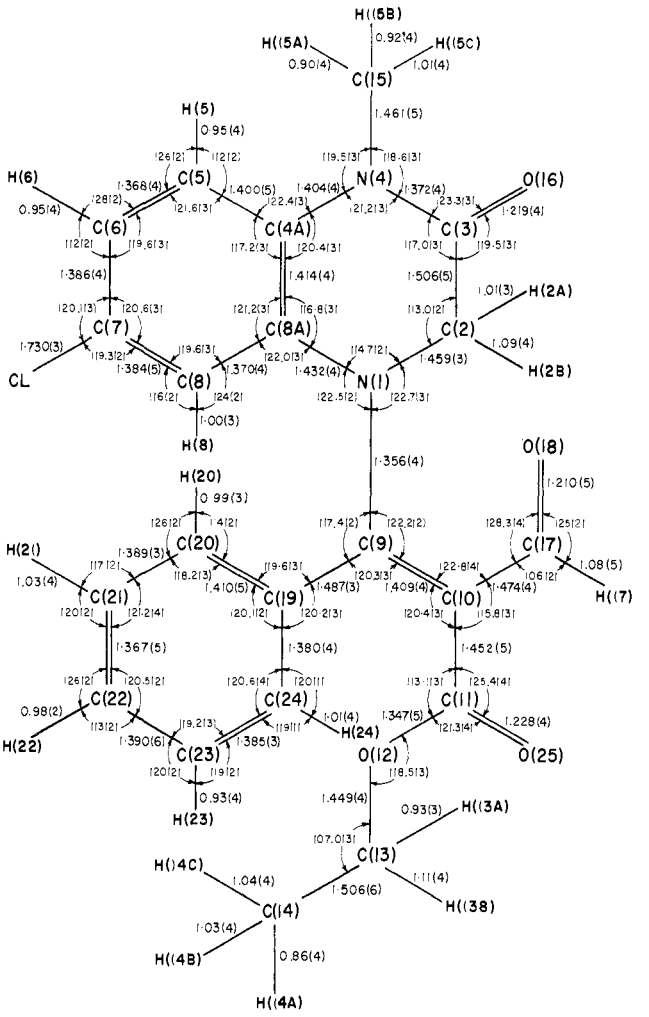


Figure 4. Bond distances and angles found by X-ray for compound **5**.

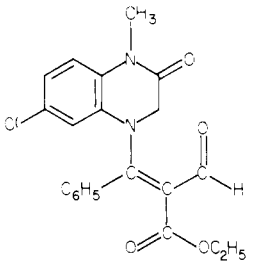
Differentiation of the *N*-methyls ($\Delta\delta$, N-CH_3 = 0.31, $\Delta G^{\ddagger}$ = 14.9 kcal/mol) was attributed to restricted rotation about the C–N bond. The activation energy[21] for this rotation is smaller than that in dimethylformamide[22] as would be expected for consideration of the partial double bond character in the two homologues.

Considerable delocalization in the vinylogous amide-like portion of **5** is evident in the X-ray bond distances shown in Figure 4. In particular, the N(1)–C(9) distance is quite short, as short as the C(3)–N(4) amide bond and much shorter than a normal C–N single bond, 1.472 Å (also compare with the N(1)–C(2) bond). The C(9)–C(10) distance is much longer than the usual double-bond distance and is larger than most of the aromatic C–C distances found here. The C(9)–C(19), C(10)–C(17), and C(10)–C(11) distances are likewise very much shorter than C–C single bonds, for example, the C(2)–C(3) bond. These shortened bonds have considerable double-bond character with bond numbers of 1.08, 1.10, and 1.20, respectively. Therefore, excluding the double-bond itself, there are four bonds with enough double-bond character for hindered rotation to be expected.

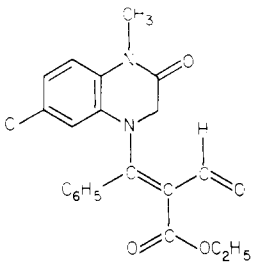
The observed NMR shift differences appear to be in best agreement with the isomers **5A** and **5B**—both of which are different from that found in X-ray, **5C**.

The large $\Delta\delta$ observed for the aldehyde, the terminal methyl group, and the cyclic methylene could be rationalized with the rotation of the aldehyde group, which lies between the other two and is the smallest and least hindered. The major isomer, **5A**,

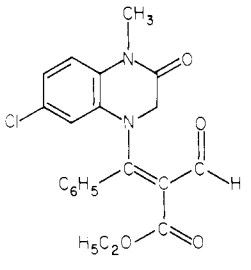
(20) Martin, M.; Martin, G. *C.R. Hebd. Seances Acad. Sci.* **1963**, *256*, 403–405.
(21) Kramer, H. E. A.; Gompper, R. *Tetrahedron Lett.* **1963**, 969–972.
(22) Anet, F. A. L.; Anet, R. In "Determination of Organic Structures by Physical Methods"; Nachod, F. C., Tuckermann, J. J., Ed.; Academic Press: New York, 1971; Vol. 3, p 550.



5A



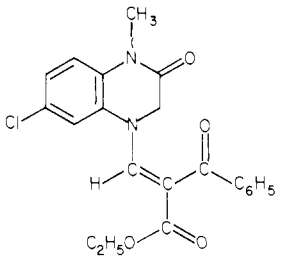
5B



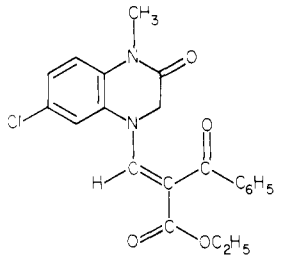
5C

with the ester hydrogens shielded and the cyclic methylene deshielded, has the negative oxygen dipole pointing to the ring methylenes. When the aldehyde rotates to point the dipole in the other direction, see **5B**, the ring methylene hydrogens return to normal shielding and the ester hydrogens, especially the terminal methyl hydrogens, now become deshielded.

Structure of 6. X-ray analysis was likewise required for determination of the structure of **6**. As with **4** and **5**, computerized direct methods were used to determine a trial structure. Here, however, unlike **4** and **5**, the crystal contained two symmetry-independent molecules—each of which was a different conformer **6A** and **6B**.

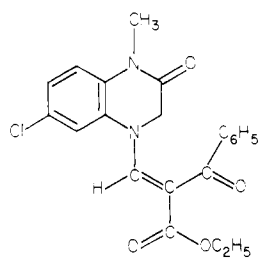


6A



6B

In chloroform solution, the NMR showed an 83–17 mixture of two isomers for **6** (see Table V). Doubling[17] was observed in the signals attributed to the cyclic methylene ($\Delta\delta$ = 0.84), the terminal methyl ($\Delta\delta$ = −0.1), the *O*-methylene ($\Delta\delta$ = −0.08), and the *N*-methyl ($\Delta\delta$ = 0.06). The cyclic methylene signals were again an A_2 singlet due to rapid ring inversion, leading to the conclusion that the isomerism is geometric, similar to that of **5**, except that for **6** the abundances are reversed; i.e., the major component should be with the ketone C=O oriented away from the ring as shown in **6C**, and the minor isomer should be **6B**, the one found in the solid state.



6C

The bond distances in the crystal (see Figure 5) show considerable delocalization in **6**, although not as much as in **5**. The C(9)–C(10) double bond is somewhat lengthened here, but it is 0.05 Å shorter than in **5**. Likewise the C–C single bonds are not shortened as much as in **5**. With the possible exception of the angles at N(1) and C(2), the distances and angles in the bicyclic portions of **5** and the two solid-state conformers of **6** are identical even though the crystal packing in **5** and **6** is considerably different.

Table V. NMR Data Obtained with a Solution of 6 in $CDCl_3$

shift, δ	relative area[a]	multiplicity	assignment[b]
0.91	3	triplet, J = 7 Hz	β-H of ester (B)
1.01	3	triplet, J = 7 Hz	β-H of ester (A)
3.33	3	singlet	N-CH_3 (A)
3.39	3	singlet	N-CH_3 (B)
3.37	2	broad singlet	3-CH_2 (A)
4.21	2	broad singlet	3-CH_2 (B)
4.02	2	quartet	α-H of ester (B)
4.10	2	quartet	α-H of ester (A)
6.8–7.9	9	multiplet	vinyl and aromatic H

[a] Relative for that component. [b] A = major component; B = minor component.

As shown in Figure 3, the conjugated area in **6** is somewhat nonplanar, as in **5**, in order to accommodate the various nonbonded interactions. It is of interest to compare the out of plane twists[23] in **6A** and **6B**, the two crystal conformers. The average out-of-plane twist about the N(1)–C(9) and C(9)–C(10) bonds are almost identical. The average twist about the C(10)–C(11) bond is 9.2° for **6A** and considerably more, 17.1°, for **6B**. Similarly about the C(17)–C(19) bond, **6A** has less twist (14.2°) than **6B** (17.7°). About the C(10)–C(17) bond, however, the situation is reversed with **6B** having less twist (44.5°) than **6A** (52.4°). From the point of view of energy stabilization through conjugation, these out-of-plane twists for **6A** and **6B** should about cancel, suggesting about equal energy for the two.[24]

Experimental Section

Melting points were taken in a capillary tube and are corrected. IR spectra were determined in Nujol by using a Perkin-Elmer Model 421 recording spectrophotometer. UV spectra were determined in 95% EtOH by using a Cary Model 14 spectrophotometer. Mass spectra were recorded by using a CH-4 Atlas mass spectrometer. The silica gel used for chromatography was obtained from E. Merck A.G., Darmstadt, Germany. NMR spectra were recorded on a Varian XL-100 and A-60A spectrometer equipped with a Varian variable-temperature probe; chemical shifts were recorded in parts per million downfield from Me_4Si.

Ethyl 10-Chloro-5,6,7,11b-tetrahydro-7-methyl-6-oxo-11b-phenylisoxazolo[2,3-*d*][1,4]benzodiazepine-1-carboxylate (4) and [α-(7-Chloro-3,4-dihydro-4-methyl-3-oxo-1(2*H*)-quinoxazolinyl)benzylidene]malonaldehydic Acid Ethyl Ester (5). A solution of **3** (1.5 g, 5 mmol) and ethyl propiolate (0.49 g, 5 mmol) in 50 mL of tetrahydrofuran was allowed to stand for 5 h. TLC on silica gel in 50% ethyl acetate-cyclohexane indicated no reaction. It was then refluxed for 18 h. TLC showed some **3** and two faster moving spots. The reaction mixture was evaporated and the residue triturated with ethyl acetate to give 0.564 g of **5** as a yellow solid: mp 194–194.5 °C (1:10 $CHCl_3$–Et_2O); UV max 229 nm (ε 28150), 250 (sh) (18800), 279 (13150), 364 (9800); IR 1690, 1680 (sh), 1645, 1600, 1585, 1575, 1505, 1495 cm^{-1}; NMR Table IV; mass spectrum, m/e 398 (M^+).

Anal. Calcd for $C_{21}H_{19}ClN_2O_4$: C, 63.24; H, 4.80; Cl, 8.89; N, 7.03. Found: C, 63.25; H, 5.24; Cl, 9.15; N, 6.71.

The filtrate was evaporated and the residue chromatographed on 200 g of silica gel by using 50% ethyl acetate–cyclohexane. Fractions 1–2 (100 mL each) and 3–4 (25 mL each) gave no material. Further fractions were all 25 mL. Fractions 5–8 (0.989 g) melted in the range 141–143 °C. Crystallization from ether gave 0.655 g of **4** as colorless prisms: mp 141–142 °C dec; UV max sh 232 nm (ε 15200), 257 (sh) (10350), 264 (sh) (9050), 270 (sh) (7650), 285 (sh) (9900), 350 (610;

(23) The "average out-of-plane twist" was calculated by averaging the magnitude of the differences of the torsion angles from 0° (or 180°, whichever is appropriate) for all torsion angles about a given bond.

(24) For brevity, many of the usually discussed items such as inter- and intramolecular nonbonded contacts and complete torsion angle tables have not been included. These parameters may be readily calculated from Table VI, VII, and VIII using computer programs available at most institutions. If a program is not available, an easy-to-use Fortran program will be supplied by one of the authors (DJD) on request.

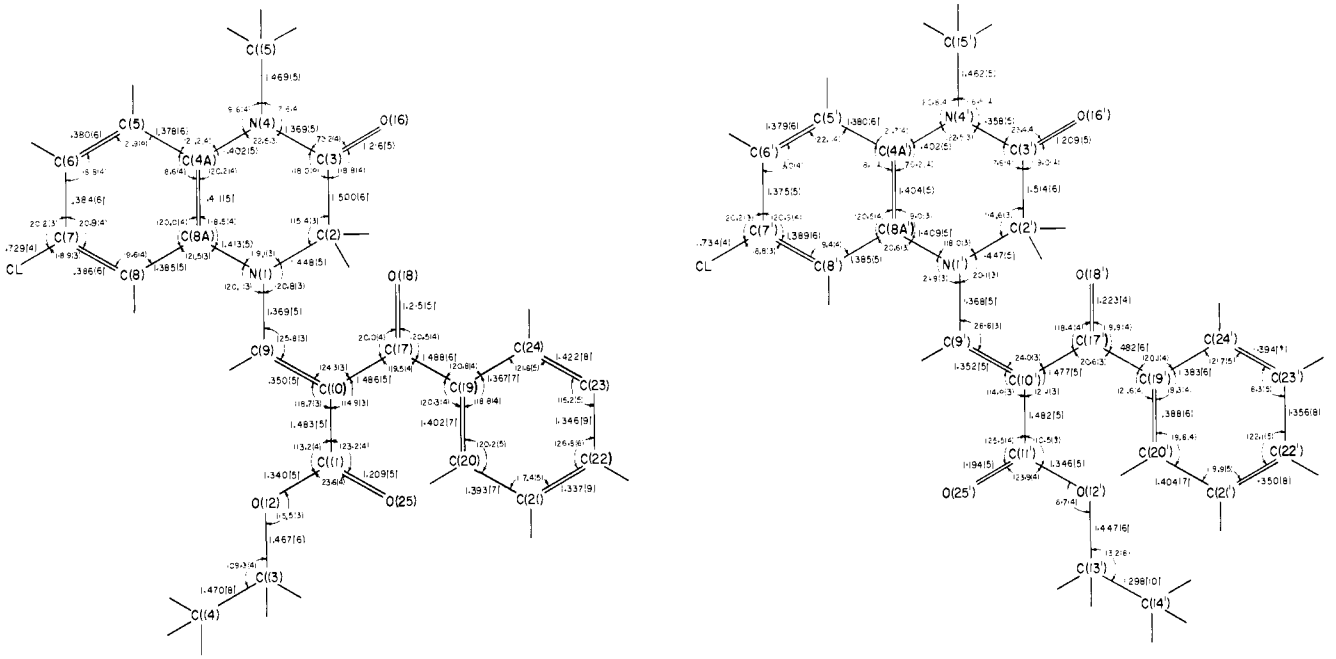


Figure 5. Bond distances and angles for the two symmetry-independent molecules of **6**: left, **6A**; right, **6B**.

IR 3080, 1700, 1675, 1615 (s), 1590, 1585, 1485 cm^{-1}; NMR Table III; mass spectrum, m/e 398 (M^+).

Anal. Calcd for $C_{21}H_{19}ClN_2O_4$: C, 63.24; H, 4.80; Cl, 8.89; N, 7.03. Found: C, 63.31; H, 4.86; Cl, 9.09; N, 6.88.

Fraction 9 (26 mg) was discarded. Fractions 10–13 (0.187 g) melted at 194–195 °C and on crystallization from ether gave additional **5**.

Ethyl α-Benzoyl-7-chloro-3,4-dihydro-4-methyl-3-oxo-1(2*H*)-quinoxalineacrylate (6). Compound **5** (10g) was dissolved in 500 mL of boiling ethanol; the solution was concentrated to ca. 100 mL and allowed to crystallize. The crystalline product proved to be unreacted **5**.

The filtrate from this crystallization was evaporated; the residue was dissolved in 20 mL of methylene chloride and chromatographed on 1 kg of silica gel by using 50% ethyl acetate–cyclohexane and collecting 250-mL fractions. Fractions 14–18 (3.2 g) were crystallized from ether to give 1.9 g of almost colorless prisms of **6**: mp 145–146 °C; UV max 216 nm (ε 25 200), 259 (23 600), 295 (11 900), 339 (12 000), 350 (sh) (11 950); IR 1685, 1650, 1635, 1600, 1575, 1560, 1505 cm^{-1}; NMR, Table V; mass spectrum, m/e 398 (M^+).

Anal. Calcd for $C_{21}H_{19}ClN_2O_4$: C, 63.24; H, 4.80; Cl, 8.89; N, 7.03. Found: C, 63.23; H, 4.67; Cl, 8.89; N, 6.99.

Fractions 19–22 gave no material. Fractions 23–29 (1.1 g) were crystallized from chloroform–ether to give 0.5 g of **5**, mp 198–200 °C.

Reaction of 4 with Hot Ethanol: Compounds 5, 6, and 6-Chloro-3,4-dihydro-1-methyl-2(1*H*)-quinoxazolinone (7). A solution of **4** (1.0 g) in 50 mL of ethanol was refluxed for 21.25 h. It was evaporated and the residue chromatographed on 400 g of silica gel using 40% ethyl acetate–cyclohexane.

Fractions 1–5 (200 mL each) gave no material. Fractions 5–7 (100 mL each) gave some oil (not investigated). Fractions 8–16 (50 mL each) gave a trace. Fractions 17–20 (50 mL each) gave 95 mg which was crystallized from ether to give 70 mg of compound **6**, mp 140–141.5 °C. Fraction 21 (50 mL) gave a trace. Fractions 22–26 (50 mL each) were crystallized from ether to give 106 mg of compound **7**: mp 101–103 °C; UV max 226 nm (ε 39 850), 268 (3150), 312 (5200); IR 3310 (NH); 1665s, 1610 (sh), 1595, 1510 cm^{-1}; NMR δ 6.87–6.65 (m, 3 aromatic H), 4.12 (1, NH, exchanges with D_2O), 3.95 (br, 2, CH_2, sharpens with D_2O), 330 (s, 3, N-CH_3); mass spectrum, m/e 196 (M^+).

Anal. Calcd for $C_9H_9ClN_2O$: C, 54.97; H, 4.61; Cl, 18.03; N, 14.25. Found: C, 54.62; H, 4.56; Cl, 18.09; N, 14.30.

Fraction 27 (150 mL) gave a trace. Fractions 28–31 (70 mg) were crystallized from methylene chloride–ether to give 12 mg of compound **5**, mp 197–199 °C.

X-ray Analysis of 4. Crystal Data: Monoclinic, a = 8.539 (2) Å, b = 14.553 (2) Å, c = 15.811 (2) Å, β = 101.71 (1)°; space group $P2_1/c$; R = 0.089. Table VI gives the final atomic parameters and their standard deviations.[25]

X-ray Analysis of 5. Crystal Data: Monoclinic, a = 13.396 (1) Å, b = 8.513 (2) Å, c = 19.737 (1) Å, β = 122.30 (1)°; space group $P2_1/c$; R = 0.094. Table VII gives the final atomic parameters and their standard deviations.[25]

X-ray Analysis of 6. Crystal Data: Monoclinic, a = 7.235 (1) Å, b = 26.676 (6) Å, c = 20.602 (2) Å, β = 99.279 (9)°; space group: Pd_1/c; R = 0.105. Table VIII gives the final atomic parameters and their standard deviations.[25]

Registry No. 3, 2888-64-4; **4A**, 80513-93-5; **4B**, 80513-94-6; **5**, 80483-98-3; **6**, 80483-99-4; **7**, 80484-00-0; ethyl propiolate, 623-47-2.

Supplementary Material Available: Listings of observed and calculated structure factors, anisotropic temperature factors, hydrogen coordinates, and discussion of experimental details for compounds **4**, **5**, and **6** (85 pages). Ordering information is given on any current masthead page.

(25) Listings of observed and calculated structure factors, anisotropic temperature factors, hydrogen coordinates, and discussion of experimental details for compounds **4**, **5**, and **6** will appear in the microfilm edition of this journal.