Synthesis and Properties of 3-Oxo-1,2-diazetidinium Ylides

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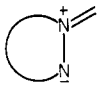
Abstract: Treatment of α-chloroacylhydrazones of diaryl and certain aralkyl and dialkyl ketones with sodium hydride in anhydrous tetrahydrofuran gives 1-(disubstituted methylene)-3-oxo-1,2-diazetidinium inner salts (ylides). The reaction pathway involves formation of the hydrazone anion followed by intramolecular S_N2 halide displacement (with complete inversion at the α carbon) by the sp^2 imine nitrogen. These 1-(disubstituted methylene)-3-oxo-1,2-diazetidinium ylides are reduced by sodium borohydride to give 1-substituted 1,2-diazetidin-3-ones, undergo dipolar cycloaddition reactions to give fused aza-β-lactams, and can be hydrolyzed with *p*-toluenesulfonic acid monohydrate to the *p*-toluenesulfonic acid salt of 1,2-diazetidinone.

Background

Cyclic azomethine imine ylides would appear to be intriguing intermediates for the construction of a variety of novel fused heterocyclic systems possessing two bridgehead nitrogen atoms. Cyclic ylides of type **1** were first described in 1955 by Gotfresden



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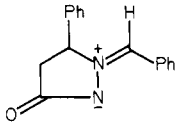
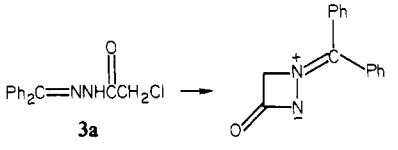
and Vangedal, who prepared the 3-oxo-1,2-pyrazolidinium ylide **2** by condensation of benzaldehyde with 5-phenylpyrazolidin-3-



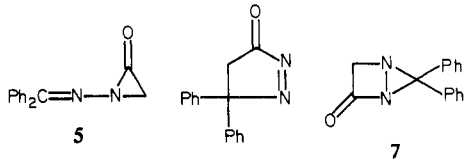
2

one.[3] Ten years later, Howard, Gever, and Wei carried out an analogous reaction with pyrazolidin-3-one itself,[4] but it was not until 1968 that it was realized that these 3-oxo-1,2-pyrazolidinium ylides could function as 1,3-dipoles in cycloaddition reactions.[5]

At approximately the same time, we independently observed that treatment of the chloroacetylhydrazone of benzophenone (**3a**) with strong non-nucleophilic bases such as sodium hydride or potassium *tert*-butoxide in anhydrous THF yielded a sharp melting (mp 199–200 °C) colorless solid with the empirical formula $C_{15}H_{12}N_2O$.[6] This compound has been shown to be 1-(diphenylmethylene)-3-oxo-1,2-diazetidinium ylide (**4a**), the lower



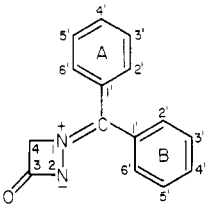
3a **4a**



5 **6** **7**

homolog of the cyclic azomethine ylide system represented by **2**. Evidence for this structural assignment, the chemical and physical properties of this remarkable, highly strained inner salt, and the scope and limitations of this intramolecular dehydrohalogenation reaction are discussed in the present paper.

Table I. Physical Data for 1-(Diphenylmethylene)-3-oxo-1,2-diazetidinium Inner Salt (**4a**)



^{1}H NMR		^{13}C NMR		IR, cm^{-1}
C	5.40 (2 H)	C-3	171.7	1782, 1765, 1750
H (B-2′,6′)	8.02 (2 H)	C-4	74.9	
H (remaining aromatic protons)	7.55 (8 H)	C-5	142.3	
		C-A-1′ and C-B-1′	131.0 and 131.0	

UV, λ_{max}^{EtOH} (log ε)	MS
245 (4.6), 325 (4.4)	236 (M^+), 208, 194, 180, 165, 139, 91, 77

A number of reasonable structures (**4–7**) for the product of intramolecular dehydrohalogenation of the chloroacetylhydrazone of benzophenone (**3a**) can be written, but the spectral characteristics of the product, as summarized in Table I,[7] served to eliminate all structures except **4a**. Thus, although structure **5** possesses a chromophore which might be compatible with the observed UV absorption maximum at 325 nm (ε 25 000), the highest observed IR carbonyl absorption band at 1780 cm^{-1} is too low for an α-lactam.[8] In addition, structure **5** is incompatible with the observation that the resonances of two of the aromatic protons (presumably the ortho protons) are shifted strongly downfield from the remaining eight aromatic hydrogens. A chromophore is also present in compound **6**, but this structure is clearly incompatible with the IR data. Although structure **7** is reasonable in terms of the observed IR spectrum, it does not possess a suitable chromophore and is thus inconsistent with the observed UV spectrum. Only structure **4a** is consistent with all of the above data, and with the remarkable downfield ^{13}C and ^{1}H resonances shown by the C-4 methylene group. That structure **4a** is indeed the correct formulation for this dehydrohalogenation product of

(1) John Simon Guggenheim Memorial Fellow, 1979–1980.
(2) Taken in part from the Ph.D. thesis of N.F. Haley, Princeton University, 1971.
(3) Gotfresden, W. O.; Vangedal, S. *Acta Chem. Scand.* **1955**, *9*, 1498.
(4) Howard, J. C.; Gever, G.; Wei, P. *J. Org. Chem.* **1963**, *28*, 868.
(5) Dorn, H.; Otto, A. *Chem. Ber.* **1968**, *101*, 3287.
(6) Greenwald, R. B.; Taylor, E. C. *J. Am. Chem. Soc.* **1968**, *90*, 5272.
(7) The MS fragmentation pattern for **4a** shows a parent ion, *m/e* 236, which loses CO and a fragment of mass 42. That the latter represents loss of NCO rather than ketene was demonstrated by examination of the C-4 dideuterio derivative **4j**, which gave *m/e* 238 and a fragment of mass 196, again representing loss of NCO; cleavage to dideuterioketene (loss of 44) was not observed. Analogous fragmentation patterns were observed with other C-4 substituted ylides (cf. **4g**).
(8) Dolphin, D.; Wick, A. "Tabulation of Infrared Spectral Data"; Wiley: New York, 1977; p 280.

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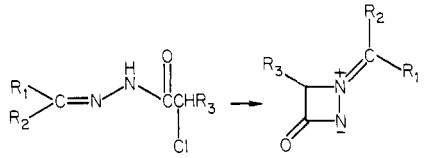
Table II. Synthesis of 3-Oxo-1,2-diazetidinium Inner Salts (Ylides) (4)



3 4

compd	R_1	R_2	R_3	yield, %
a	C_6H_5	C_6H_5	H	88
b	C_6H_5	p-t-BuC_6H_4	H	84
c	C_6H_5	p-$NO_2C_6H_4$	H	75
d	C_6H_5	p-$CH_3OC_6H_4$	H	80
e	C_6H_5	p-BrC_6H_4	H	38
f	C_6H_5	CH_3	H	53[a]
g	C_6H_5	C_6H_5	CH_3	52
h	C_6H_5	C_6H_5	C_6H_5	70
i	C_6H_5	C_6H_5	t-C_4H_9	10
j	C_6H_5	C_6H_5	D_2	97
k	p-$CH_3OC_6H_4$	C_6H_5	H	90
l	p-BrC_6H_4	C_6H_5	H	33
m	p-BrC_6H_4	C_6H_5	D_2	62
n	t-C_4H_9	C_6H_5	H	60
o	i-C_3H_7	C_6H_5	H	65
p	t-C_4H_9	C_6H_5	CH_3	39
q	i-C_3H_7	i-C_3H_7	H	60
r	p-$CH_3OC_6H_4$	p-$CH_3OC_6H_4$	H	70
s	p-ClC_6H_4	p-ClC_6H_4	H	55
t	p-$CH_3OC_6H_4$	t-C_4H_9	H	32
u	adamantylidene		H	43

[a] Cyclized with Dowex-I-X8 ion-exchange resin.

3a was unequivocally established by an X-ray analysis (vide infra).[9]

Synthesis and Mechanism of Formation of 3-Oxo-1,2-diazetidinium Ylides

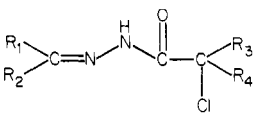
The synthesis of 3-oxo-1,2-diazetidinium ylides as represented by the dehydrohalogenation of **3a** to **4a** is fairly general. Thus, a variety of α-haloacyl ketone hydrazones (**3a–v**), readily prepared by acylation of the appropriate ketone hydrazones with α-halo acid chlorides, have been shown to undergo intramolecular dehydrohalogenation to give 3-oxo-1,2-diazetidinium ylides (**4a–v**). In cases where the use of an unsymmetrical ketone led to the formation of a mixture of syn and anti hydrazones, separation by fractional crystallization followed directly by reaction with the appropriate α-halo acid chloride led to the isolation of *E* and *Z* hydrazides, respectively. This procedure proved to be more satisfactory than attempted isolation and characterization of the thermally less stable hydrazones themselves.

We have summarized in Table II the 3-oxo-1,2-diazetidinium ylides obtained by treatment of a broad variety of α-haloacyl ketone hydrazones with strong bases in inert solvents, usually benzene or THF. The ylides often precipitated directly from the reaction mixture along with sodium chloride after 6–18 h of stirring at room temperature; heating was occasionally required when the α position of the acyl group was substituted. The choice of base for this intramolecular dehydrohalogenation proved to be critical; triethylamine, Triton B, and *n*-butyllithium were ineffective, while pyridine and sodium acetate both acted as nucleophiles to displace the α-halide. However, strong, non-nucleophilic bases such as potassium *tert*-butoxide and sodium hydride effected smooth intramolecular cyclization. Hydrazide **3f** was best cyclized with Dowex-1-X8 (hydroxide form) ion-exchange resin; in this instance, neither sodium hydride nor potassium *tert*-butoxide proved effective.

Certain structural features appear to be critical for a successful intramolecular dehydrohalogenation of the hydrazides (**3**) to give the azomethine ylides (**4**). Of critical importance is the presence of steric bulk at the imine carbon. Thus, R_1 and R_2 could be any

(9) Fritchie, C., Jr.; Wells, J. *J. Chem. Soc., Chem. Commun.* **1968**, 917.

Table III. Acylhydrazones and Acylhydrazides Which Did Not Yield Ylides with NaH



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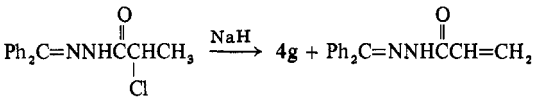
compd	R_1	R_2	R_3	R_4	mp, °C
v	EtO_2C	EtO_2C	H	H	*a*
w	C_4H_9	CH_3	H	H	93–94
x	CH_3	p-$NO_2C_6H_4$	H	H	202–204
y	2-pyridyl	2-pyridyl	H	H	155–156
z	CF_3	C_6H_5	H	H	120–121
aa	6-CH_3O-α-tetralone		H	H	169–170
bb	C_6H_5	C_6H_5	CH_3	CH_3	116–118
cc	C_6H_5	C_6H_5	C_6H_5	C_6H_5	141–143
dd	C_6H_5	C_6H_5	H	Cl	120–121
ee	C_6H_5	H	H	H	161–164
ff	CH_3	CH_3	H	H	95–56
gg	$(C_6H_5)_2C$=NNHCOCH=CH_2				80–82
hh	C_5H_{10}NNHCOCH$_2$Cl				113.0–113.5
ii	$(C_6H_5)_2$NNHCOCH$_2$Cl				163–164
jj	$(C_6H_5)_2C$=NNHSO$_2$CH$_2$Cl				116–118
kk	$(C_6H_5)_2C$=NNHCOCCH$_3$=CH_2				120.2–120.4

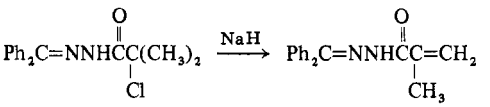
[a] Liquid; bp 138–140 °C (0.3 Torr).

combination of isopropyl, *tert*-butyl, or aryl groups (independent of the presence of electron-donating or electron-withdrawing substituents), but replacement of either R_1 or R_2 by hydrogen, methyl, or trifluoromethyl led either to isolation of unchanged starting material or to polymer formation (see Table III). Conversely, steric hindrance at the α-carbon atom of the acyl group had a predictably deleterious effect upon this intramolecular dehydrohalogenation reaction. Thus, the α-chloropropionyl derivative **3g** yielded both the product of intramolecular dehydrohalogenation (**4g**) and the hydrazide (**8**) resulting from side-chain



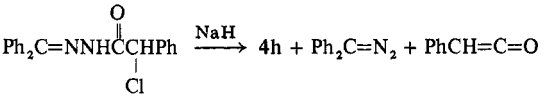
3g 8

dehydrohalogenation. This latter pathway was the only one observed when steric bulk at the α-carbon atom was further increased by addition of a further methyl group (**3bb**).[10] Substitution of



3bb 9

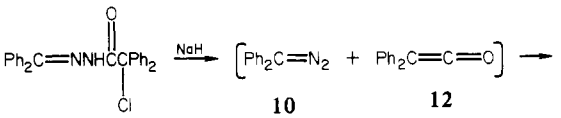
aryl groups on the α carbon led to yet another reaction pathway. Thus, the α-chlorophenacetyl derivative **3h** yielded both the expected ylide **4h** (70%) and a mixture of diphenyldiazomethane (**10**) and phenylketene (**11**), probably from fragmentation of the



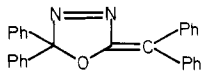
3h 10 11

hydrazide precursor. This latter fragmentation pathway appears to be the only one observed with the α,α-diphenylchloroacetyl derivative **3cc**, which gave 2,2-diphenyl-5-(diphenyl-

(10) This reaction, if successful, would have given a 4,4-dialkyl-3-oxo-1,2-diazetidinium inner salt. Compounds of this specific type have been prepared by an unrelated sequence of reactions terminating in pyrolysis of 2-ylidenehydrazono-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines (Ip, P. C.; Ramakrishnan, K.; Warkentin, J. *Can. J. Chem.* **1974**, *52*, 3671) which is not applicable to the preparation of C-4 monosubstituted or unsubstituted derivatives.



3cc 10 12



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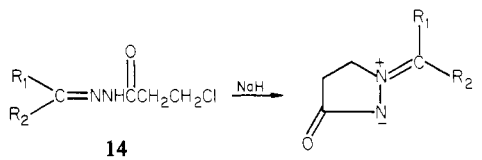
methylene)-1,3,4-oxadiazoline (**13**) as the only isolable product. This latter compound presumably arises by a recombination of the products of initial fragmentation, diphenyldiazomethane (**10**) and diphenylketene (**12**). IR examination of the crude reaction product revealed the probable presence of **10** (a strong IR band at 2050 cm^{-1}).

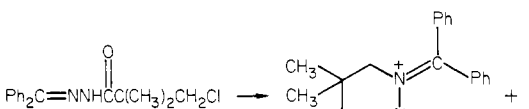
The β-chloropropionylhydrazone of benzophenone (**14a**) underwent an analogous intramolecular dehydrohalogenation when treated in THF solution with sodium hydride to give the 3-oxo-1,2-pyrazolidinium ylide **15a**. Similar cyclizations were achieved



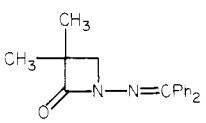
14 15

a, $R_1 = R_2 = Ph$
b, $R_1 = t\text{-Bu}$; $R_2 = Ph$
c, $R_1 = H$; $R_2 = Ph$

with the β-chloropropionyl hydrazones of *tert*-butyl phenyl ketone and of benzaldehyde to give **15b** and **15c**, respectively. This procedure represents a new route to pyrazolidinium ylides and makes available for the first time such ylides possessing two bulky substituents on the exocyclic methylene carbon. Increasing steric bulk at the α-carbon atom diminishes but does not eliminate ylide formation; thus, the 3-chloro-2,2-dimethylpropionylhydrazone of benzophenone (**16**) gave, upon treatment with sodium hydride in



16 17



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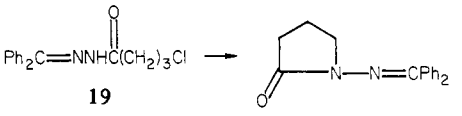
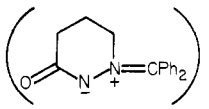
THF, both the expected pyrazolidinium ylide **17** and the N-substituted azetidinone **18** (from intramolecular halide displacement by the amide nitrogen).[11] Attempted extrapolation of this ylide synthesis to the next homolog, however, proved unsuccessful; the 4-chlorobutyryl derivative of benzophenone hydrazone (**19**) provided only the pyrrolidinone derivative **20** and none of the six-membered cyclic azomethine ylide **21**.



19 20



21

not formed

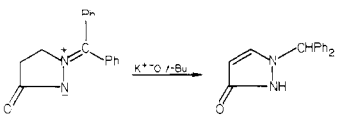
Some additional experimental observations bear upon the mechanism of formation of the above 3-oxo-1,2-diazetidinium ylides (**4**). For example, both the *E* and *Z* isomers of 4-bromobenzophenone hydrazone are known.[12] We converted each of these isomers separately to their respective α-chloroacetyl derivatives, and then subjected each to sodium hydride/THF dehydrohalogenation. Two isomeric, thermally noninterconvertible 3-oxo-1,2-diazetidinium ylides were thus obtained, and an X-ray analysis of the 4-bromophenyl phenylmethylene-3-oxo-1,2-diazetidinium ylide (**41**) prepared from the *Z* hydrazone showed that the geometry of the hydrazone precursor had been retained in the product; i.e., the *Z* hydrazone gave the *Z* ylide with retention of geometry around the imine double bond. The *Z* ylide (**41**) was readily identifiable by NMR, for the two ortho protons of the 4-bromophenyl ring displayed a prominent downfield shift from the remaining aromatic protons owing to anisotropic deshielding by the anionic amide nitrogen. By contrast, the two ortho protons in the unsubstituted phenyl ring were moved downfield in the isomeric *E* ylide (**4e**).

Similarly, sodium hydride/benzene dehydrohalogenation of the pure *E* isomer of the chloroacetylhydrazone of 4-methoxybenzophenone (**3d**) gave a mixture of the *E* ylide **4d** (89%) and the *Z* ylide **4k** (11%).[13] That the formation of this mixture of products was due to isomerization[14] *prior* to ylide formation was shown by subjecting the *E* acetylhydrazone of 4-methoxybenzophenone to the above reaction conditions, which resulted in partial rearrangement to the same mixture of *E* and *Z* isomers (ratio of 90:10). In analogous fashion, the pure *Z* isomer of the chloroacetylhydrazone of 4-methoxybenzophenone (**3k**) under the same dehydrohalogenation conditions gave the *Z* ylide **4k** (98%) contaminated by a small amount of the *E* ylide **4k** (2%). As in the case above, the pure *Z* isomer of the acetylhydrazone of 4-methoxybenzophenone under the same reaction conditions rearranged to give an identical mixture of *Z* and *E* isomers (ratio of 98:2).

Thus, the observation that the ortho protons of the aryl ring adjacent to N-2 in the ylides **4** are shifted strongly downfield provides not only a means of structure assignment for the ylides themselves, but also an unambiguous method for assignment of the *Z* or *E* configuration to the starting hydrazone (provided that the stability of the acetylhydrazones to the reaction conditions is determined independently). In analogous fashion, it was also possible to determine the *E* and *Z* configuration of ylides derived from aralkyl or dialkyl ketones, since aliphatic hydrogens also exhibited a significant downfield shift when adjacent to the anionic nitrogen.

Evidence bearing on the mechanism of halide loss in the intramolecular cyclization reaction leading to the above 3-oxo-1,2-diazetidinium ylides was obtained as follows:

(11) Sodium hydride must be used as the base for the preparation of 3-oxo-1,2-pyrazolidinium ylides, as potassium *tert*-butoxide causes isomerization of the product ylide. This isomerization can be smoothly effected by treatment of ylide **15a** with potassium *tert*-butoxide in refluxing benzene, forming 1-benzhydryl-3(2*H*)-pyrazolone (A). Spectral data were compatible with other 1-substituted-3-hydroxypyrazoles: Katritzky, A. R.; Maine, F. W.; Golding, S. *Tetrahedron* **1965**, *21*, 1693.



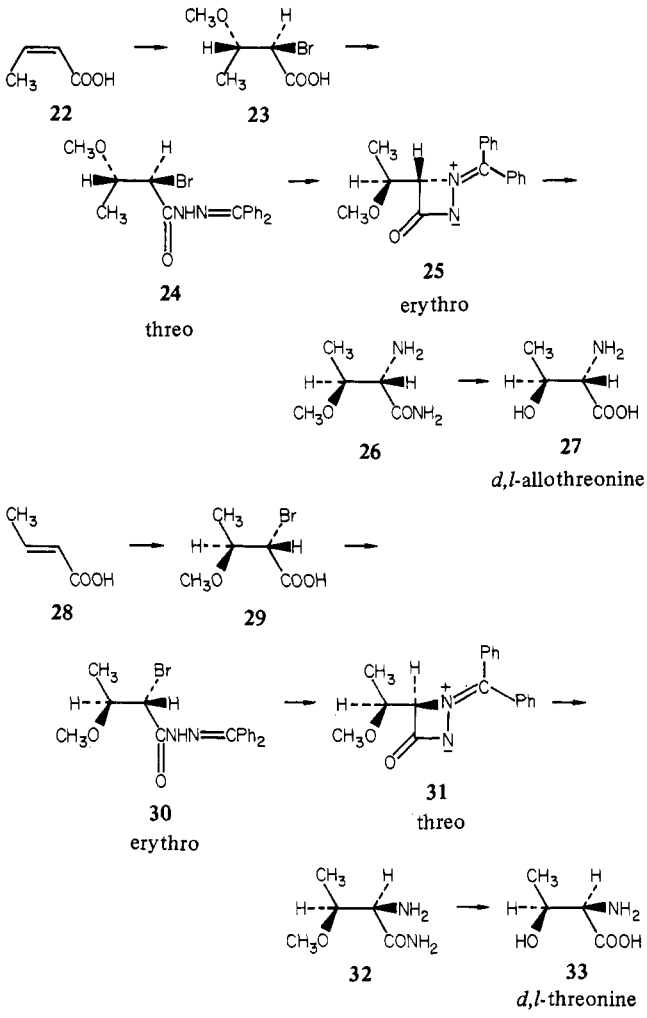
15a A

(12) Hawbecker, B. L. *J. Chem. Educ.* **1970**, *47*, 218.

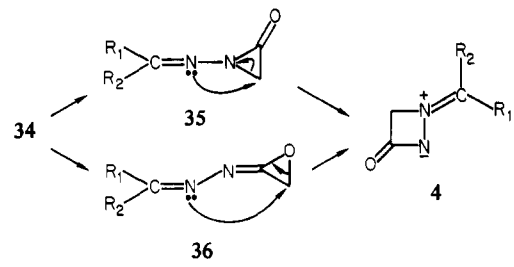
(13) Ylide formation is incomplete after 3 h, but NMR analysis of the crude reaction mixture allowed the resulting *E*:*Z* product ratio to be compared directly with the *E*:*Z* hydrazide isomerization ratio determined under identical reaction conditions (NaH/benzene, 25 °C/3 h).

(14) Pearson, D. E.; Carter, K. N.; Greer, C. M. *J. Am. Chem. Soc.* **1953**, *75*, 5905. For a general discussion of *E*/*Z* isomerization of hydrazones, see: Karabatsos, G. J.; Vane, F. M.; Taller, R. A.; Hsi, N. *J. Am. Chem. Soc.* **1964**, *86*, 3351.

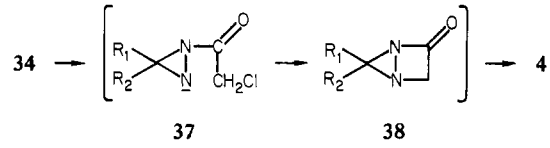
Scheme I



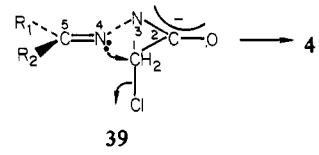
Scheme II



Scheme III



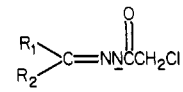
Scheme IV



2. Steric bulk at the imine carbon is required for a successful intramolecular dehydrohalogenation.

3. Cyclization involves S_N2 displacement of halogen at the α position of the acyl moiety.

Since the initial result of treatment of any of the above α-haloacyl hydrazones with strong base must be removal of the amide proton, the anion **34** is considered to be the effective



34

precursor to cyclization in all of the following mechanistic considerations.

One possible mechanism (Scheme II) involving initial formation of an α-lactam (**35**), followed by ring expansion to **4**, was eliminated since it is known that α-lactams carrying substituents on nitrogen which stabilize ring-opened precursors are difficult to form and, in any event, undergo facile cleavage of the acyl–nitrogen bond. It may be relevant that the N-substituted azetidinone **18** (analogous to **35**) is stable under the reaction conditions and does not ring-expand. An alternate pathway proceeding through an oxirane (**36**) was likewise considered unlikely, since similar iminooxiranes are known to undergo either cleavage to aldehydes and isonitriles, or rearrangement to α-lactams.[16]

The pathway outlined in Scheme III, which involves initial intramolecular diaziridine anion formation (**37**), intramolecular S_N2 halide displacement to yield a 5,5-disubstituted 1,4-diazabicyclo[2.1.0]pentan-2-one (**38**), and ring opening[17] to give the observed ylide, is considered unsatisfactory since (a) *E* and *Z* haloacyl hydrazones should give the same ylide (i.e., stereochemical

Cis and trans crotonic acids (**22** and **28**, Scheme I) were separately treated with methyl hypobromite, and the resulting diastereomeric α-bromo-β-methoxybutyric acids **23** and **29** converted to their acid chlorides with thionyl chloride. Addition of benzophenone hydrazone then gave the threo and erythro benzophenone α-bromo-β-methoxybutyrylhydrazones **24** and **30**, respectively. Each of these pure diastereomeric acyl hydrazones was then treated with sodium hydride in anhydrous THF, and *each gave only one diastereomeric 3-oxo-1,2-diazetidinium ylide* (**25** and **31**, respectively) which was judged >98% pure by NMR. The configurations of these ylides were then determined by degradation to *d,l*-allothreonine (**27**) and *d,l*-threonine (**33**), respectively, by hydrogenolysis of the iminium >C=N⁺< and N—N bonds followed by hydrolysis of the resulting diastereomeric α-amino-β-methoxybutyramides (**26** and **32**, respectively) with 47% HBr (it is known that hydrolysis of methoxyaminoamides under these conditions proceeds without racemization).[15] It was thus conclusively demonstrated that the threo hydrazone yields only the erythro ylide, and that the erythro hydrazone gives only the threo ylide. Displacement of halide from the acylated hydrazones therefore occurs exclusively with inversion of stereochemistry at the α-carbon atom.

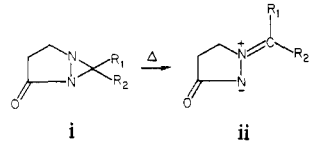
The following experimental observations must therefore be accommodated in any mechanism proposed for the formation of the above cyclic azomethine imine ylides from α-haloacyl ketone hydrazones:

1. The stereochemical integrity of the carbon–nitrogen imine bond in the acyl hydrazone precursor must be retained.

(15) Pfister, K.; Howe, E. E.; Robinson, C. A.; Shabica, A. C.; Pietrusza, E. W.; Tischler, M. *J. Am. Chem. Soc.* **1949**, *71*, 1096.

(16) Lengyel, I.; Sheehan, J. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 25.

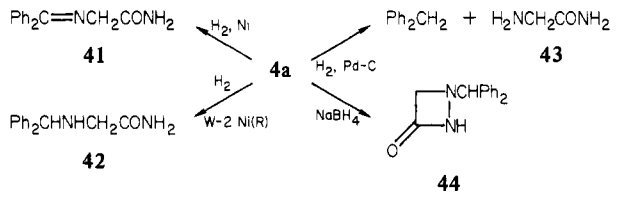
(17) Intermediate **38**, if formed, would be expected to lead to **4**, since the



i ii

homologous fused diaziridine i undergoes facile thermal ring opening to ii (see, for example, Tomaschewski, G.; Geissler, G.; Schauer, G. *J. Prakt. Chem.* **1980**, *322*, 623).

Scheme V

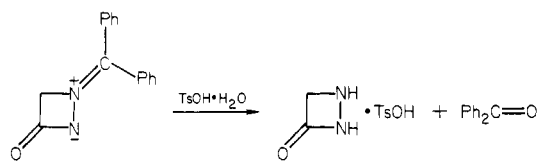


integrity should be lost upon cyclization) and (b) in order to preserve the original hydrazone configuration in the final ylide, intermediate **37** cannot undergo inversion at the amide nitrogen. Although exact models are not available, it does not appear that this latter criterion can be met in view of the known facility with which acylaziridines invert at nitrogen.[18]

The mechanism outlined in Scheme IV involving direct intramolecular nucleophilic displacement of halide by the imine nitrogen is consistent with all experimental observations. Many exceptions are known to the well-known generalization that four-membered rings are formed only with difficulty through intramolecular displacement reactions,[19] and precedents are also available for intramolecular halide displacement by sp^2-hybridized nitrogen.[20] In order to accommodate the observation that the stereochemical integrity of the imine bond is retained in ylide formation, and the effects of substituents at the α-carbon atom, this mechanism requires that cyclization occur through the *E*-amide conformation **39**. Indeed, molecular models suggest a quasiplanar arrangement for C-1 through C-5 when steric bulk is present at the imine carbon; continuous π-orbital overlap hinders rotation around the N–N bond and places the imine lone electron pair directly behind the α-acyl halide substituent.[21] It should be noted that the nucleophilicity of N-4 (the imine nitrogen) is enhanced by amide anion formation, which reduces the electronegativity of N-3.[22]

Chemistry of 3-Oxo-1,2-diazetidinium Ylides

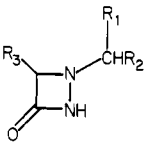
These 1-(diarylmethylene)-3-oxo-1,2-diazetidinium ylides are remarkably stable thermally and can be recovered unchanged after refluxing for 24 h in ethanol or toluene. Furthermore, as mentioned above, *E* and *Z* isomers cannot be interconverted by heating (i.e., there is no thermal rotation around the iminium >C=N⁺< bond). The chemical reactivity of **4a** was investigated in detail as representative of the 1-(diarylmethylene)-3-oxo-1,2-diazetidinium ylides. Thus, **4a** proved to be stable to mild bases such as sodium carbonate or triethylamine, and could be recovered unchanged after prolonged exposure. By contrast, **4a** was much more sensitive to acids. Aqueous hydrochloric acid rapidly destroyed **4a** at room temperature, while ethanolic hydrochloric acid cleaved **4a** to ethyl hydrazinoacetate and benzophenone. Remarkably, however, selective cleavage of the iminium bond with retention of the labile β-lactam group could be achieved by treatment of **4a** with 1 molar equiv of water. Thus, reaction of **4a** with 1 equiv of *p*-toluenesulfonic acid monohydrate in methylene chloride solution resulted in precipitation of 3-oxo-1,2-diazetidinium tosylate (**40**) in excellent yield. The chemistry of this extremely reactive, synthetically versatile, novel small ring heterocycle, and its utilization for the preparation of highly strained aza analogues of the β-lactam antibiotics, will be described independently.



4a **40**

1-(Diphenylmethylene)-3-oxo-1,2-diazetidinium ylide (**4a**) gives a variety of reduction products depending upon the reducing agent or catalyst employed (see Scheme V). For example, reduction with hydrogen in the presence of deactivated Raney nickel[23] gave the benzophenone imine of aminoacetamide (**41**), while hydrogen and W-2 Raney nickel[24] gave α-diphenylmethylaminoacetamide (**42**) by further reduction of the imine bond. In contrast, reduction with hydrogen in the presence of palladium on carbon resulted in the uptake of 3 equiv of hydrogen with the formation of diphenylmethane and aminoacetamide (**43**). Treatment of **4a** with sodium borohydride resulted in selective reduction of the iminium bond, with retention of the diazetidinone ring, to give 1-(diphenylmethyl)diazetidin-3-one (**44**). Further examples of this convenient route to 1-substituted diazetidinones are summarized in Table IV.

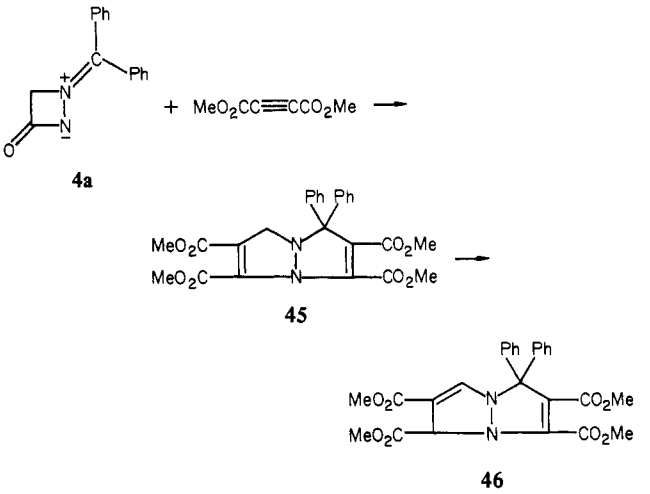
Table IV. 1-Substituted Diazetidin-3-ones (44) Prepared by $NaBH_4$ Reduction of Ylides 4



44

compd	R_1	R_2	R_3
a	Ph	Ph	H
b	Ph	Ph	CH_3
c	Ph	Ph	Ph
d	Ph	*i*-Pr	H
e	*i*-Pr	*i*-Pr	H
f	Ph	*p*-BrC_6H_4	H

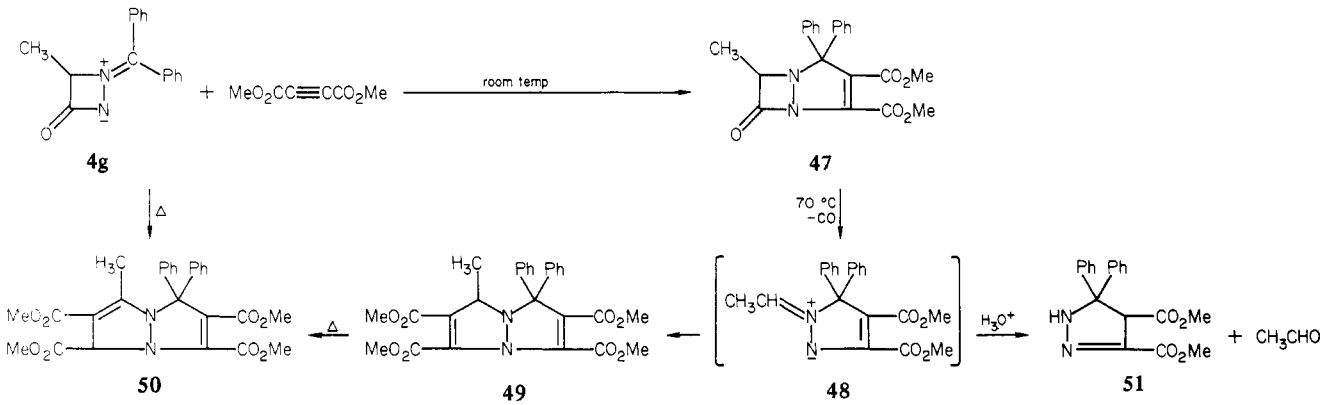
Scheme VI



Although **4a** was unreactive toward norbornene, methyl propiolate, dimethyl maleate, phenyl isocyanate, and diethyl azodicarboxylate, reaction with dimethyl acetylenedicarboxylate in methylene chloride solution resulted in the formation of **45** (a 2:1 cycloadduct with loss of carbon monoxide), which isomerized to **46** upon melting (Scheme VI). We were able to elucidate the pathway leading from **4a** to **45** as follows. Reaction of **4g**, the C-4 methyl derivative of **4a**, with dimethyl acetylenedicarboxylate

(18) Lehn, J. *Fortschr. Chem. Forsch.* **1970**, *15*, 311.
(19) (a) Paquette, L. A. "Principles of Modern Heterocyclic Chemistry"; W. A. Benjamin: New York, 1968; p 77. (b) Bose, A. K.; Mazumdar, B. N. G.; Chattergee, B. G. *J. Am. Chem. Soc.* **1960**, *82*, 2382.
(20) Huisgen, R.; Grashey, R.; Laur, P.; Leitermann, H. *Angew. Chem.* **1960**, *72*, 416.
(21) Room-temperature NMR shows two singlets for the methylene protons and two singlets for the amide proton due to slow rotation about the amide C–N bond. Determination of the relative amount of each conformer was determined by integration. See Experimental Section for shift values.
(22) Pauling, L. "Die Natur der Chemischen Bindung"; Verlag Chemie: Weinheim, 1962; p 85.
(23) Deactivation was effected by boiling commercial Raney nickel in water for 30 min.
(24) Mozingo, R. "Organic Syntheses", Collect. Vol. III; Wiley: New York, 1955; p 181.

Scheme VII



for 5 days at room temperature gave the 1:1 cycloadduct **47**. That this material possessed a fused aza β-lactam grouping was evident not only from its IR spectrum (1840 cm^{-1}), but also from its thermal instability. Thus, warming of this material at 70 °C in an NMR tube (d_6-Me_2SO/1% H_2O) resulted in the gradual disappearance of the aliphatic C-6 methyl group signal with the simultaneous appearance of a new vinyl methyl doublet. Further standing for 30 min at 70 °C resulted in the replacement of this new doublet by resonances corresponding to acetaldehyde, while the remainder of the NMR spectrum matched that of an authentic sample of 5,5-diphenyl-3,4-dicarboethoxy-Δ^2-pyrazoline (**51**).[25] In an independent experiment, both the pyrazoline **51** and acetaldehyde (the latter as its 2,4-DNP derivative) could be isolated from this decomposition reaction of the above 1:1 cycloadduct. It thus appears that the fused aza-β-lactam **47** decomposes by extrusion of carbon monoxide to give a new ylide **48**. This presumed ylide intermediate could be trapped by the addition of a second equivalent of dimethyl acetylenedicarboxylate to afford **49** in quantitative yield. This latter compound isomerized upon recrystallization to give **50**, identical in every respect with the product obtained upon reaction of **4g** with dimethyl acetylenedicarboxylate at 100 °C (see Scheme VII).

We have thus demonstrated that novel 3-oxo-1,2-diazetidinium ylides are readily accessible by intramolecular dehydrohalogenation of α-haloacyl hydrazones of certain diaryl, aralkyl, and dialkyl ketones, and that their formation involves an unusual intramolecular S_N2 displacement involving an sp^2-hybridized imine nitrogen. Furthermore, these readily accessible ylides may be easily converted to substituted diazetidinones, as well as to diazetidinone itself. Subsequent papers will describe the synthetic versatility of these interesting small ring heterocycles.

Experimental Section

All melting and boiling points are uncorrected. Melting points were determined on either a Thomas-Hoover or a Mettler FP-1 capillary melting point apparatus. Infrared spectra were determined on Perkin-Elmer 237B or 467 spectrophotometers, while NMR spectra were recorded on Varian A-60 (60 MHz) or Perkin-Elmer R-32 (90 MHz) spectrometers. Ultraviolet spectra were obtained on a Cary 11 spectrophotometer with 1-cm cells in absolute ethanol (given in mμ (log ϵ)). Mass spectra were determined on an AEI MS-9 spectrometer at 70 eV. Percentage yields were determined after recrystallization and in most cases are unoptimized.

Elemental analyses were performed by Baron Consulting Co., Orange, Conn.; Eli Lilly & Co., Indianapolis, Ind.; or Hoffmann-La Roche, Nutley, N.J.

Synthesis of Haloacyl Hydrazones. General Procedure. To a solution of 0.1 mol of the appropriate hydrazone and 0.1 mol of pyridine in 100 mL of dry methylene chloride was added dropwise 0.1 mol of the acid halide, the rate of addition regulated to afford a gentle reflux. The mixture was heated externally for 15 min following the addition. Extraction with 100 mL of water followed by drying of the methylene chloride layer over $MgSO_4$ and evaporation in vacuo afforded the product, which was then recrystallized or distilled as appropriate. The acyl hydrazones were recrystallized from 2-propanol unless noted otherwise.

(25) Van Alphen, J. *Recl. Trav. Chim. Pays-Bas* **1943**, *62*, 210.

Benzophenone α-chloroacetylhydrazone (3a): mp 101 °C (from ethanol), 89% yield; IR (KBr) 3200, 3100, 3050, 1730, 1695 (s) cm^{-1}; NMR ($CDCl_3$) δ 8.45 (s, 1 H), 7.42 (m, 10 H), 4.65 and 4.05 (singlets from *E* and *Z* amide isomers, 2 H).

Anal. Calcd for $C_{15}H_{13}N_2OCl$: C, 66.06; H, 4.80; N, 10.27. Found: C, 65.90; H, 4.78; N, 10.39.

4-*tert*-Butylbenzophenone α-chloroacetylhydrazone (3b): mp 161.4 °C, 85% yield; IR (KBr) 3340, 3060, 1710 (s), 1615, 1530 cm^{-1}; NMR ($CDCl_3$) δ 7.27 (m, 9 H), 4.70 and 4.06 (s, 2 H), 1.40 and 1.32 (s, 9 H).

Anal. Calcd for $C_{19}H_{21}N_2OCl$: C, 69.39; H, 6.44; N, 8.52; Cl, 10.78. Found: C, 68.77; H, 6.32; N, 8.23; Cl, 10.94.

4-Nitrobenzophenone α-chloroacetylhydrazone (3c): mp 142–144 °C (from ethanol), 30% yield; IR (Nujol) 3220, 1700 (s), 1515 cm^{-1}; NMR ($CDCl_3$) δ 8.28 (AB q, 4 H), 7.60 (m, 5 H), 4.72 (s, 2 H).

Anal. Calcd for $C_{15}H_{12}N_3O_3Cl$: C, 56.70; H, 3.81; N, 13.23. Found: C, 56.50; H, 3.70; N, 13.51.

4-Methoxybenzophenone (*E*)-α-Chloroacetylhydrazone (3d). This material was prepared from the pure *E* hydrazone and recrystallized from methanol: yield 72%, mp 154–155 °C; IR (KBr) 3280, 1735, 1700 (s), 1610, 1250 cm^{-1}; NMR ($CDCl_3$) δ 8.36 (s, 1 H), 7.36 (m, 7 H), 6.82 (d, 2 H), 4.62 (s, 2 H), 3.80 (s, 3 H).

Anal. Calcd for $C_{16}H_{15}N_2O_2Cl$: C, 63.47; H, 4.99; N, 9.25. Found: C, 63.35; H, 5.12; N, 9.38.

4-Bromobenzophenone (*E*)-α-Chloroacetylhydrazone (3e). This material was prepared from the pure *E* hydrazone: mp 123–127 °C, 60% yield; IR (KBr) 3240, 1685, 1535, 1325 cm^{-1}.

Anal. Calcd for $C_{15}H_{12}N_2OBrCl$: C, 51.18; H, 3.44; N, 7.96. Found: C, 51.03; H, 3.75; N, 7.56.

Benzophenone α-chloropropionylhydrazone (3g): mp 114–116 °C, 91% yield; IR (KBr) 3150, 3020, 1690 (s), 1450 cm^{-1}; NMR ($CDCl_3$) δ 7.50 (m, 10 H), 5.60 and 4.45 (q, 1 H), 1.80 and 1.74 (d, 3 H, J = 7.0 Hz).

Anal. Calcd for $C_{16}H_{15}N_2OCl$: C, 67.01; H, 5.27; N, 9.77. Found: C, 67.23; H, 5.36; N, 9.74.

Benzophenone α-chlorophenylacetylhydrazone (3h): mp 118–120 °C (from ethanol), 89% yield; IR (KBr) 3305, 3270, 1695, 700 cm^{-1}; NMR ($CDCl_3$) δ 9.50 and 8.42 (br, NH), 7.7–7.3 (m, 15 H), 6.60 and 5.40 (s, 1 H).

Anal. Calcd for $C_{21}H_{17}N_2OCl$: C, 72.30; H, 4.91; N, 8.03; Cl, 10.17. Found: C, 72.31; H, 5.11; N, 8.12; Cl, 10.41.

Benzophenone α-bromo-β,β-dimethylbutyrylhydrazone (3i): mp 96.6 °C, 55% yield; IR (KBr) 3270, 3060, 1690 (s) cm^{-1}; NMR ($CDCl_3$) δ 8.30 (1 H), 7.40 (m, 10 H), 5.46 and 4.08 (s, 1 H), 1.24 and 1.07 (s, 9 H).

Anal. Calcd for $C_{19}H_{21}N_2OBr$: C, 61.13; H, 5.67; N, 7.50; Br, 21.41. Found: C, 61.30; H, 5.47; N, 7.30; Br, 21.60.

Benzophenone α-bromo-α,α-dideuterioacetylhydrazone (3j): mp 119–120 °C, 77% yield; IR (KBr) 3240, 3060, 3030, 2295 (w), 2200 (w), 1700 (s), 1670 (s).

Anal. Calcd for $C_{15}H_{11}D_2N_2OBr$: C, 56.40; H, 4.10; N, 8.81. Found: C, 56.55; H, 4.01; N, 8.77.

4-Methoxybenzophenone (*Z*)-α-Chloroacetylhydrazone (3k). This material was prepared from the pure *Z* hydrazone and recrystallized from methanol: yield 65%, mp 140–141 °C; IR (KBr) 3200, 3100, 1735, 1700 (s), 1610 cm^{-1}; NMR ($CDCl_3$) δ 8.60 (s, 1 H), 7.38 (m, 9 H), 4.59 (s, 2 H), 3.84 (s, 3 H).

Anal. Calcd for $C_{16}H_{15}N_2O_2Cl$: C, 63.47; H, 4.99; N, 9.25. Found: C, 63.39; H, 5.09; N, 9.29.

4-Bromobenzophenone (*Z*)-α-Chloroacetylhydrazone (3l). This material was prepared from the pure *Z* hydrazone: mp 143–145 °C, 94% yield; IR (KBr) 3190, 3100, 1690, 1670, 1450, 1370, 1220 cm^{-1}; NMR

($CDCl_3$) δ 9.45 and 8.45 (s, NH), 7.80–7.10 (m, 9 H), 4.68 and 4.10 (s, 2 H).

Anal. Calcd for $C_{15}H_{12}N_2OBrCl$: C, 51.18; H, 3.44; N, 7.96. Found: C, 51.31; H, 3.41; N, 8.02.

4-Bromobenzophenone (*Z*)-α-Bromo-α,α-dideuterioacetylhydrazone (3m). This material was prepared from the pure *Z* hydrazone: mp 147.0–147.1 °C, 78% yield; IR (KBr) 3195, 3080, 1680 (s), 1660 (s) cm^{-1}.

***tert*-Butyl phenyl ketone α-chloroacetylhydrazone (4n)**: mp 81–83 °C, 68% yield; IR (KBr) 3200, 3100, 1700 (s) cm^{-1}; NMR ($CDCl_3$) δ 8.00 (1 H), 7.35 (m, 5 H), 4.58 (s, 2 H), 1.18 (s, 9 H).

Anal. Calcd for $C_{13}H_{17}N_2OCl$: C, 61.77; H, 6.78; N, 11.09. Found: C, 61.80; H, 6.71; N, 11.00.

Isobutyrophenone α-chloroacetylhydrazone (3o): mp 75.3 °C (from petroleum ether), 42% yield; IR (KBr) 3250, 3015, 1690 (s), 1620 cm^{-1}; NMR ($CDCl_3$) δ 7.49 (m, 3 H), 7.31 (m, 2 H), 4.60 and 4.02 (s, 2 H), 2.87 (m, 1 H), 1.13 and 1.10 (d, 6 H, J = 7 Hz).

Anal. Calcd for $C_{12}H_{15}N_2OCl$: C, 60.37; H, 6.33; N, 11.74. Found: C, 60.36; H, 6.40; N, 11.86.

***tert*-Butyl phenyl ketone α-chloropropionylhydrazone (3p)**: mp 135.3–135.8 °C, 80% yield; IR (KBr) 3200, 1695 (s), 700 cm^{-1}; NMR ($CDCl_3$) δ 8.95 and 7.90 (1 H), 7.50 (m, 3 H), 7.07 (m, 2 H), 5.35 and 4.30 (q, 1 H, J = 6.5 Hz), 1.71 and 1.65 (d, 3 H, J = 6.5 Hz), 1.22 and 1.18 (s, 9 H).

Anal. Calcd for $C_{14}H_{19}N_2OCl$: C, 63.03; H, 7.18; N, 10.50; Cl, 13.29. Found: C, 62.55; H, 7.05; N, 10.49; Cl, 13.14.

2,4-Dimethyl-3-pentanone α-Chloroacetylhydrazone (3q). This compound distills after a forerun of diisopropyl ketone azine: yield 50%, bp 130–135 °C (0.5 Torr); IR (neat) 3200, 3050, 1675 (s), 1625, 1035 cm^{-1}; NMR ($CDCl_3$) δ 4.51 and 4.22 (s, 2 H), 3.05 (septet, 1 H, J = 7.0 Hz), 2.65 (septet, 1 H, J = 7.0 Hz), 1.12 (d, 6 H, J = 7.0 Hz), 1.08 (d, 6 H, J = 7.0 Hz).

Anal. Calcd for $C_9H_{17}N_2OCl$: C, 52.99; H, 8.40; N, 13.74. Found: C, 53.19; H, 8.35; N, 13.50.

4,4′-Dimethoxybenzophenone α-chloroacetylhydrazone (3r): mp 93.1–94.5 °C, 93% yield; IR (Nujol) 3150, 1725, 1680 (s), 1605, 1460 cm^{-1}; NMR ($CDCl_3$) δ 7.25 (m, 8 H), 4.80 (s, 2 H), 3.90 (s, 3 H), 3.83 (s, 3 H).

Anal. Calcd for $C_{17}H_{13}N_2O_3Cl$: C, 61.35; H, 5.15; N, 8.42. Found: C, 61.50; H, 5.10; N, 8.56.

4,4′-Dichlorobenzophenone α-chloroacetylhydrazone (3s): mp 175–177 °C (from acetone), 88% yield; IR (KBr) 3200, 3000, 1725, 1690 (s), 1608 cm^{-1}; NMR ($CDCl_3$) δ 8.47 (1 H), 7.46 (m, 8 H), 4.57 and 4.08 (s, 2 H).

Anal. Calcd for $C_{15}H_{11}N_2OCl_3$: C, 52.73; H, 3.25; N, 8.20. Found: C, 53.01; H, 3.29; N, 8.07.

4-Anisyl *tert*-butyl ketone α-chloroacetylhydrazone (3t): mp 121.1 °C, 92% yield; IR (KBr) 3200, 1690 (s), 1610 cm^{-1}; NMR ($CDCl_3$) δ 6.99 (m, 4 H), 4.52 (s, 2 H), 3.83 (s, 3 H), 1.17 (s, 9 H).

Anal. Calcd for $C_{14}H_{19}N_2O$: C, 59.46; H, 6.77; N, 9.90; Cl, 12.54. Found: C, 59.33; H, 6.76; N, 9.87; Cl, 12.88.

Acetophenone α-chloroacetylhydrazone (3f): mp 137.5–138.5 °C (from methanol), 80% yield.[26]

2-Adamantone α-chloroacetylhydrazone (3u): mp 155.1–155.2 °C, 75% yield;[26] IR (KBr) 3220, 3010, 1675 (s), 1645 cm^{-1}; NMR (d_6-Me_2SO) 10.5 (br, 1 H), 4.50 and 4.13 (s, 2 H), 3.30 (s, 2 H), 1.89 (s, 12 H).

Anal. Calcd for $C_{12}H_{17}N_2OCl$: C, 59.87; H, 7.12; N, 11.64. Found: C, 60.02; H, 7.06; N, 11.50.

Benzophenone (±)-*erythro*-α-bromo-β-methoxybutyrylhydrazone (30): mp 90.5–90.8 °C, 85% yield; IR (KBr) 3330, 3060, 1700 (s), 1510 cm^{-1}; NMR ($CDCl_3$) (isomer 1) δ 8.50 (br, NH), 7.50 (m, aromatic), 5.40 (d, J = 8.5 Hz, CHBr) 3.85 (m, C*H*CH_3), 3.44 (s, OCH_3), 1.45 (d, J = 6.5 Hz, CHC*H*$_3$); (isomer 2) 9.65 (br, NH), 7.50 (m, aromatic), 4.34 (d, J = 3.0 Hz, CHBr), 3.85 (s, C*H*CH_3), 3.14 (s, OCH_3), 1.25 (d, J = 6.0 Hz, CHC*H*$_3$).

Anal. Calcd for $C_{18}H_{19}N_2O_2Br$: C, 57.61; H, 5.10; N, 7.46; Br, 21.29. Found: C, 57.64; H, 5.04; N, 7.47; Br, 21.94.

Benzophenone (±)-*threo*-α-bromo-β-methoxybutyrylhydrazone (24): mp 90.3–90.4 °C, 74% yield; IR (KBr) 3300, 3060, 1705 (s), 1515 cm^{-1}; NMR ($CDCl_3$) (isomer 1) δ 9.73 (br, NH), 7.48 (m, aromatic), 4.28 (d, J = 2.5 Hz, CHBr), 3.83 (m, C*H*CH_3), 3.03 (s, OCH_3), 1.22 (d, J = 7.0 Hz, CHC*H*$_3$); (isomer 2) 8.46 (br, NH), 7.48 (m, aromatic), 5.45 (d, J = 7.0 Hz, CHBr), 3.83 (m, C*H*CH_3), 3.48 (s, OCH_3), 1.33 (d, J = 7.0 Hz, CHC*H*$_3$).

Anal. Calcd for $C_{18}H_{19}N_2O_2Br$: C, 57.61; H, 5.10; N, 7.46. Found: C, 57.45; H, 4.99; N, 7.40.

(26) Ito, S.; Narusawa, T. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 2257.

Benzophenone β-chloropropionylhydrazone (14a): mp 130–131 °C, 83% yield; IR (Nujol) 3200, 1675 (s), 700 cm^{-1}; NMR ($CDCl_3$) δ 8.60 (br, 1 H), 7.50 (m, 10 H), 3.86 (t, J = 7 Hz, 2 H), 3.30 (t, J = 7 Hz, 2 H).

Anal. Calcd for $C_{16}H_{15}N_2OCl$: C, 67.01; H, 5.27; N, 9.77. Found: C, 66.92; H, 5.27; N, 9.77.

Benzaldehyde β-chloropropionylhydrazone (14c): mp 129–129.5 °C (from ethyl acetate), 30% yield; IR (KBr) 3190, 3080, 1675 (s), 1420 cm^{-1}; NMR ($CDCl_3$) δ 10.04 (br, 1 H), 7.92 (s, 1 H), 7.56 (m, 5 H), 3.95 (t, J = 7 Hz, 2 H), 3.30 (t, J = 7 Hz, 2 H).

Anal. Calcd for $C_{10}H_{11}N_2OCl$: C, 57.20; H, 5.28; N, 13.50; Cl, 16.92. Found: C, 57.16; H, 5.41; N, 13.41; Cl, 17.07.

2,2-Dimethylpropiophenone β-chloropropionylhydrazone (14b): mp 125.7 °C, 81% yield; IR (KBr) 3195, 3100, 1680 (s), 1625 cm^{-1}; NMR ($CDCl_3$) δ 7.85 (br, 1 H), 7.45 (m, 3 H), 7.05 (m, 2 H), 3.85 (t, J = 6.5 Hz, 2 H), 3.18 (t, J = 6.5 Hz, 2 H), 1.19 (s, 9 H).

Anal. Calcd for $C_{14}H_{19}N_2OCl$: C, 63.03; H, 7.18; N, 10.50. Found: C, 63.05; H, 7.01; N, 10.66.

Benzophenone β-chloro-α,α-dimethylpropionylhydrazone (16): mp 112–113 °C, 60% yield; IR (KBr) 3380, 3050, 1683 (s), 1505 cm^{-1}; NMR ($CDCl_3$) δ 8.75 (br, 1 H), 7.44 (m, 10 H), 3.62 (s, 2 H), 1.18 (s, 6 H).

Anal. Calcd for $C_{18}H_{19}N_2OCl$: C, 68.67; H, 6.08; N, 8.90; Cl, 11.26. Found: C, 70.23; H, 6.22; N, 8.94; Cl, 10.81.

Benzophenone δ-chlorobutyrylhydrazone (19): mp 112–113 °C, 84% yield; IR (KBr) 3200, 1675 (s), 1445, 1210 cm^{-1}; NMR ($CDCl_3$) δ 8.40 (br, 1 H), 7.40 (m, 10 H), 3.64 (t, J = 7 Hz, 2 H), 3.00 (t, J = 7.5 Hz, 2 H), 2.16 (pentuplet, 2 H).

Anal. Calcd for $C_{17}H_{17}N_2OCl$: C, 67.83; H, 5.69; N, 9.31. Found: C, 67.53; H, 5.70; N, 9.43.

Benzophenone α-Acetoxyacetylhydrazone. Sodium acetate (3.0 g) and benzophenone α-chloroacetylhydrazone (1.0 g) were fused at 150 °C for 3 h. Upon cooling, the mixture was partitioned between 50 mL of water and 50 mL of chloroform, the organic layer dried ($MgSO_4$), and the solvent evaporated. The resulting solid was recrystallized from 2-propanol to give 0.9 g (83%), mp 124.8 °C: IR (KBr) 3390, 1750 (s), 1715 (s), 1530 cm^{-1}; NMR ($CDCl_3$) 8.35 (br, 1 H), 7.40 (m, 10 H), 5.21 (s, 2 H), 2.20 (s, 3 H).

Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.90; H, 5.44; N, 9.45. Found: C, 68.97; H, 5.28; N, 9.30.

Preparation of Diazetidinium and Pyrazolinium Ylides. General Procedure. To a solution of 0.01 mol of the appropriate haloacyl hydrazone in 30 mL of dry benzene or tetrahydrofuran was added 0.01 mol of 53% sodium hydride (in mineral oil) in small portions. After the addition was complete, the solution was stirred at room temperature for 24 h. Following the addition of 20 mL of 50% ammonium chloride solution, the organic layer was separated, dried ($MgSO_4$), and evaporated under reduced pressure. The residue was recrystallized from an appropriate solvent.

1-(Diphenylmethylene)-3-oxo-1,2-diazetidinium inner salt (4a): mp 199–200 °C (from ethanol); yields on this reaction varied from 40 to 98%; IR (Nujol), 1782 (s), 1765 (s), 1750 (s), 1608 cm^{-1}; NMR ($CDCl_3$) δ 8.02 (m, 2 H), 7.55 (m, 8 H), 5.40 (s, 2 H); mass spectrum m/e 236 (M^+), 208, 194.

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.34; H, 5.26; N, 11.66. Found: C, 76.25; H, 5.12; N, 11.86.

1-(4-*tert*-Butylphenyl)phenylmethylene-3-oxo-1,2-diazetidinium inner salt (4b): mp ~125 °C (from ethyl acetate–petroleum ether), 83.5% yield (1:1 mixture of *E* and *Z* isomers); IR (KBr) 3080, 1780 (s), 1595 cm^{-1}; NMR ($CDCl_3$) (*Z* isomer) δ 8.00 (m, 2 H), 7.51 (m, 7 H), 5.36 (s, 2 H), 1.40 (s, 9 H); (*E* isomer) 8.00 (m, 2 H), 7.51 (m, 7 H), 5.28 (s, 2 H), 1.32 (s, 9 H).

Anal. Calcd for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.90; N, 9.58. Found: C, 78.10; H, 6.78; N, 9.54.

(*E*)-1-(4-Nitrophenyl)phenylmethylene-3-oxo-1,2-diazetidinium inner salt (4c): recrystallized from ethanol; first crop pure *E* isomer, mp 196 °C dec, second crop 1:1 mixture of *E*:*Z* isomers, mp 155–165 °C; total yield 75%; IR (Nujol) 3090, 1780 (s), 1600 cm^{-1}; NMR (d_6-Me_2SO) δ 8.42 (d, 2 H), 7.92 (m, 4 H), 7.50 (m, 3 H), 5.70 (s, 2 H).

Anal. Calcd for $C_{15}H_{11}N_3O_3$: C, 64.05; H, 3.94; N, 14.94. Found: C, 64.13; H, 4.10; N, 14.68.

(*E*)-1-[4-(Methoxyphenyl)phenylmethylene]-3-oxo-1,2-diazetidinium inner salt (4d): starting from the pure *E*-acylated hydrazone: mp 152.4–152.9 °C (from ethyl acetate), 80% yield; IR (KBr) 3070, 1785 (s), 1765 (s), 1610 cm^{-1}; NMR ($CDCl_3$) δ 7.88 (m, 2 H), 7.17 (m, 7 H), 5.34 (s, 2 H), 3.86 (s, 3 H).

Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.30; H, 5.48; N, 10.36.

(*E*)-1-(*p*-Bromophenyl)phenylmethylene-3-oxo-1,2-diazetidinium inner salt (4e): starting with pure *E*-acylated hydrazone: mp 174–175 °C

(from ethanol), 38% yield; IR (KBr) 3060, 1785 (s), 1765 (s), 1590 cm^{-1}; NMR ($CDCl_3$) δ 8.02 (m, 2 H), 7.88–7.20 (m, 7 H), 5.36 (s, 2 H); UV/vis 258 (4.09), 328 (4.26).

Anal. Calcd for $C_{15}H_{11}N_2OBr$: C, 57.19; H, 3.52; N, 8.89. Found: C, 57.29; H, 3.37; N, 8.91.

(*Z*)-1-(Methylphenylmethylene)-3-oxo-1,2-diazetidinium Inner Salt (4f). Acetophenone α-chloroacetylhydrazone (2.1 g, 10 mmol) and 200 mL of Dowex 1-X-8 (OH) ion-exchange resin were stirred for 24 h at 25 °C in 200 mL of methanol. The resin was filtered and the methanol evaporated to afford a solid which was recrystallized from ether to afford 0.6 g of the *Z* isomer (a second crop contained 0.3 g as a mixture of isomers): yield 53%, mp 119.7–120.1 °C; IR (KBr) 3060, 1805, 1770 (s), 1765 (s), 1610 cm^{-1}; NMR ($CDCl_3$) (*Z* isomer) δ 8.20 (m, 2 H), 7.50 (m, 3 H), 5.55 (s, 2 H), 2.45 (s, 3 H); (*E* isomer) 7.50 (m, 5 H), 5.40 (q, 2 H), 2.62 (t, 3 H).

Anal. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08. Found: C, 69.10; H, 5.81; N, 15.95.

1-(Diphenylmethylene)-4-methyl-3-oxo-1,2-diazetidinium Inner Salt (4g). This reaction mixture was refluxed at 80 °C for 4 h instead of being stirred at room temperature: mp 151.0–151.5 °C (from ethyl acetate), 63% yield; IR (KBr) 3050, 1785 (s), 1770 (s), 1560 cm^{-1}; NMR ($CDCl_3$) δ 8.01 (m, 2 H), 7.50 (m, 8 H), 5.95 (q, *J* = 7.0 Hz, 1 H), 1.15 (d, 3 H); mass spectrum *m/e* 250 (M^+), 208; UV/vis 244 (4.6), 352 (4.27).

Evaporation of the ethyl acetate filtrate afforded $Ph_2C{=}NNHCOCH{=}CH_2$, mp 80–82 °C.

Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.87; H, 5.85; N, 11.16.

1-(Diphenylmethylene)-4,4-dideuterio-3-oxo-1,2-diazetidinium inner salt (4j): mp 198–199 °C (from ethanol), yield 97%; IR (KBr) 1790 (s), 1775 (s), 1765 (s), 1612 cm^{-1}; NMR ($CDCl_3$) δ 7.96 (m, 2 H), 7.46 (m, 8 H); mass spectrum *m/e* 238 (M^+), 196.

Anal. Calcd for $C_{15}H_{10}D_2N_2O$: C, 75.61; H, 5.08; N, 11.76. Found: C, 75.51; H, 5.17; N, 11.81.

1-(Diphenylmethylene)-3-oxo-4-*tert*-butyl-1,2-diazetidinium inner salt (4i): prepared by the general method except that the reaction mixture was refluxed 3 h instead of being stirred at room temperature, and the residue remaining after solvent evaporation was washed with petroleum ether to remove diphenyldiazomethane: mp 181–184 °C (from ethyl acetate), yield 10%; IR (KBr) 3070, 1770 (s), 1565 cm^{-1}; NMR ($CDCl_3$) δ 7.35 (m, 10 H), 5.86 (s, 1 H), 0.80 (s, 9 H).

Anal. Calcd for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.90; N, 9.58. Found: C, 78.27; H, 6.92; N, 9.64.

(*Z*)-1-(4-Methoxyphenylphenylmethylene)-3-oxo-1,2-diazetidinium inner salt (4k): prepared from the pure *Z* acylated hydrazone (**3k**): mp 145.2–145.6 °C, 90% yield; IR (KBr) 3060, 1785 (s), 1760 (s), 1610 cm^{-1}; NMR ($CDCl_3$) δ 7.40 (ABq, *J* = 8 Hz, 4 H), 7.40 (m, 5 H), 5.23 (s, 2 H), 3.83 (s, 3 H).

Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.13; H, 5.56; N, 10.34.

(*Z*)-1-(*p*-Bromophenylphenylmethylene)-3-oxo-1,2-diazetidinium inner salt (41): prepared from the pure *Z* acylated hydrazone: mp 167.3–167.5 °C (from ethanol), 32% yield; IR (KBr) 3070, 1785 (s), 1760 (s), 1605 cm^{-1}; NMR ($CDCl_3$) δ 8.05–7.25 (m, 9 H), 5.33 (s, 2 H); UV/vis 255 (4.19), 331 (4.32).

Anal. Calcd for $C_{15}H_{11}N_2OBr$: C, 57.19; H, 3.52; N, 8.89. Found: C, 56.83; H, 3.12; N, 8.75.

(*Z*)-1-(*p*-Bromophenylphenylmethylene)-4,4-dideuterio-3-oxo-1,2-diazetidinium inner salt (4m): prepared from the pure *Z* acylated hydrazone: mp 167.3 °C (from ethanol), 62% yield; IR (KBr), 3060, 2290 (w), 1780 (s), 1770 (s), 1590 cm^{-1}; mass spectrum *m/e* 318, 316 (M^+), 276, 274.

Anal. Calcd for $C_{15}H_9D_2N_2OBr$: C, 56.80; H, 3.50; N, 8.83; Br, 25.19. Found: C, 56.92; H, 3.75; N, 8.62; Br, 25.58.

(*E*)-1-(*tert*-Butylphenylmethylene)-3-oxo-1,2-diazetidinium inner salt (4n): mp 199.6 °C (from ethyl acetate–petroleum ether), 60% yield; IR (KBr) 3060, 1795 (s), 1620 cm^{-1}; NMR ($CDCl_3$) δ 7.35 (m, 5 H), 5.00 (s, 2 H), 1.40 (s, 9 H); UV/vis 275 (4.22).

Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 71.99; H, 7.49; N, 12.92.

1-(Isopropylphenylmethylene)-3-oxo-1,2-diazetidinium inner salt (4o). Recrystallization from ethyl acetate afforded a 92.5/7.5 ratio of *E*/*Z* isomers: mp ~151 °C, 65% yield; IR (KBr) 3060, 1790 (s), 1645 cm^{-1}; NMR ($CDCl_3$) δ 7.50 (m, 5 H), 5.60 (s, *Z* isomer), 5.15 (s, *E* isomer), 3.68 (septet, *J* = 7 Hz, 1 H), 1.26 (d, *J* = 7 Hz, 6 H); mass spectrum *m/e* 202 (M^+), 160; UV/vis 275 (4.22).

Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 71.20; H, 6.85; N, 13.59.

1-(*tert*-Butylphenylmethylene)-4-methyl-3-oxo-1,2-diazetidinium Inner Salt (4p). Recrystallization from ether/petroleum ether afforded an 85/15 ratio of *E*/*Z* isomers: mp 145.8–147 °C, 39% yield; IR (KBr) 3040, 1775 (s), 1600, 1090 cm^{-1}; NMR ($CDCl_3$) (*Z* isomer) δ 7.45 (m, 5 H), 5.85 (q, *J* = 7.0 Hz, 1 H), 1.33 (s, 9 H), 1.13 (d, *J* = 7.0 Hz, 3 H); (*E* isomer) 7.45 (m, 5 H), 5.40 (q, *J* = 7.0 Hz, 1 H), 1.37 (s, 9 H), 1.05 (d, *J* = 7.0 Hz, 3 H).

Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 73.17; H, 7.87; N, 12.21.

1-(Diisopropylmethylene)-3-oxo-1,2-diazetidinium inner salt (4q): mp 103.0 °C (from ether), 60% yield; IR (KBr) 2980, 2940, 2880, 1780 (s), 1645 (s), 1225, 995 cm^{-1}; NMR ($CDCl_3$) δ 5.35 (s, 2 H), 3.06 (septet, *J* = 7.0 Hz, 1 H), 2.75 (septet, *J* = 7.0 Hz, 1 H), 1.36 (d, *J* = 7.0 Hz, 6 H), and 1.25 (d, *J* = 7.0 Hz, 6 H).

Anal. Calcd for $C_9H_{16}N_2O$: C, 64.25; H, 9.59; N, 16.65. Found: C, 64.23; H, 9.68; N, 16.62.

1-(4,4′-Dianisylmethylene)-3-oxo-1,2-diazetidinium inner salt (4r): mp 139–140 °C (from ethyl acetate), 70% yield; IR (KBr) 3030, 2850, 1750 (s), 1615 cm^{-1}; NMR ($CDCl_3$) δ 7.41 (q, $\Delta\nu_{AB}$ = 62.8 Hz, *J* = 9.5 Hz, 4 H), 7.23 (q, $\Delta\nu_{AB}$ = 15.6 Hz, *J* = 9.0 Hz, 4 H), 5.27 (s, 2 H), 3.88 (s, 3 H), 3.83 (s, 3 H); UV/vis 242 (4.07), 293 (4.19), 335 (4.39).

Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.90; H, 5.44; N, 9.45. Found: C, 68.73; H, 5.45; N, 9.21.

1-(4,4′-Dichlorodiphenylmethylene)-3-oxo-1,2-diazetidinium inner salt (4s): mp 203–204 °C (from ethanol), 55% yield; IR (Nujol) 1785 (s), 1760 (s), 1590 cm^{-1}; NMR ($CDCl_3$) δ 7.86 (d, *J* = 9.0 Hz, 2 H), 7.46 (m, 6 H), 5.35 (s, 2 H).

Anal. Calcd for $C_{15}H_{10}Cl_2N_2O$: C, 59.03; H, 3.30; N, 9.18; Cl, 23.24. Found: C, 59.11; H, 3.40; N, 8.92; Cl, 23.36.

1-(*tert*-Butyl-*p*-methoxyphenylmethylene)-3-oxo-1,2-diazetidinium Inner Salt (4t). Recrystallization from 2-propanol yielded 0.6 g of the *Z* isomer; evaporation of the filtrate afforded 0.2 g of the *E* isomer: total yield 32%, mp (*E*) 150.5 °C, (*Z*) 132.2 °C; IR (KBr) (*E*) 3080, 2840, 1790 (s), 1770 (s), 1612, 1595 cm^{-1}; (*Z*) 1765 (s), 1600 cm^{-1}; NMR ($CDCl_3$) (*E*) δ 7.10 (m, 4 H), 5.02 (s, 2 H), 3.85 (s, 3 H), 1.38 (s, 9 H); (*Z*) 7.10 (q, 4 H, *J* = 9.0 Hz), 5.65 (s, 2 H), 3.82 (s, 3 H), 1.31 (s, 9 H); mass spectrum *m/e* 246 (M^+), 231, 218, 204; UV/vis (*E*) 274 (4.24); (*Z*) 270 (4.19).

Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.01; H, 7.31; N, 11.14.

1-(Adamantylidene)-3-oxo-1,2-diazetidinium inner salt (4u): mp 188.6 °C (from ether), 43% yield; IR (KBr) 2900, 1805, 1785 (s), 1765, 1675 (s) cm^{-1}; NMR ($CDCl_3$) δ 5.26 (s, 2 H), 3.52 (m, 1 H), 2.75 (m, 1 H), 2.05 (m, 12 H).

Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.72. Found: C, 70.79; H, 7.95; N, 13.82.

(±)-*erythro*-1-(Diphenylmethylene)-4-(1-methoxyethyl)-3-oxo-1,2-diazetidinium inner salt (25): starting with the threo acylated hydrazone (**24**): mp 125.0–125.4 °C (from ether), 88% yield; IR (KBr) 3080, 3000, 1775 (s), 1600 cm^{-1}; NMR ($CDCl_3$) δ 8.00 (m, 2 H), 7.50 (m, 8 H), 5.94 (d, *J* = 2.5 Hz, 1 H), 3.10 (s, 3 H), 2.85 (m, 1 H), 1.18 (d, *J* = 6.5 Hz, 3 H).

Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.32; H, 6.04; N, 9.61.

(±)-*threo*-1-(Diphenylmethylene)-4-(1-methoxyethyl)-3-oxo-1,2-diazetidinium inner salt (31): starting with the erythro acylated hydrazone (**30**); mp 125.7–126.9 °C (from ether), 71% yield; IR (KBr) 3070, 3000, 1780 (s), 1600 cm^{-1}; NMR ($CDCl_3$) δ 8.00 (m, 2 H), 7.53 (m, 8 H), 6.10 (d, *J* = 5.0 Hz, 1 H), 3.26 (m, 1 H), 3.02 (s, 3 H), 1.05 (d, *J* = 7.0 Hz, 3 H).

Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.15; H, 6.00; N, 9.45.

1-(Diphenylmethylene)-3-oxo-1,2-pyrazolinium inner salt (15a): mp 230–231 °C (from ethanol), 56% yield; IR (KBr) 1665 (s), 1530, 1290 cm^{-1}; NMR ($CDCl_3$) δ 8.05 (m, 2 H), 7.50 (m, 8 H), 4.18 (t, *J* = 7.5 Hz, 2 H), 2.65 (t, *J* = 7.5 Hz, 2 H); UV/vis 240 (4.13), 335 (4.37).

Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.76; H, 5.64; N, 11.19. Found: C, 76.83; H, 5.31; N, 11.50.

1-(*tert*-Butylphenylmethylene)-3-oxo-1,2-pyrazolinium inner salt (15b): mp 192.1 °C (from ethyl acetate–hexane), 82% yield; IR (KBr) 3020, 1655 (s), 1560 cm^{-1}; NMR ($CDCl_3$) δ 7.45 (m, 3 H), 7.16 (m, 2 H), 3.86 (t, *J* = 8.0 Hz, 2 H), 2.55 (t, *J* = 8.0 Hz, 2 H), 1.37 (s, 9 H); mass spectrum *m/e* 230 (M^+), 215, 175, 173, 172.

Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 72.79; H, 7.75; N, 12.33.

1-Benzylidene-3-oxo-1,2-pyrazolidinium inner salt (15c): mp 208–210 °C (from 2-propanol), 55% yield; IR (KBr) 3060, 1670 (s), 1645 (s), 1600, 1590 cm^{-1}; NMR ($CDCl_3$) δ 8.23 (m, 2 H), 7.37 (m, 3 H), 7.16 (br s, 1 H), 4.50 (t, 2 H), 2.78 (t, 2 H); UV/vis 327 (4.47), 342 (4.45).

Anal. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08. Found: C, 68.70; H, 5.97; N, 16.22.

1-(Diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-pyrazolidinium Inner Salt (17) and 1-[(Diphenylmethylene)amino]-3,3-dimethylazetidin-2-one (18). The solid obtained from the reaction workup was chromatographed on 30 g of silica gel eluting first with benzene and then with ethyl acetate. The benzene fractions contained **18**: mp 152–155 °C (from 2-propanol), 76% yield; IR (KBr) 3060, 1765 (s), 1440 cm^{-1}; NMR ($CDCl_3$) δ 7.41 (m, 10 H), 2.78 (s, 2 H), 1.20 (s, 6 H).

Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.07. Found: C, 77.71; H, 6.42; N, 9.80.

The ethyl acetate fractions afforded **17** (13%): mp 207–209 °C (from ethyl acetate); IR (KBr) 3050, 1660 (s), 1290 cm^{-1}; NMR ($CDCl_3$) δ 8.10 (m, 2 H), 7.41 (m, 8 H), 3.93 (s, 2 H), 1.29 (s, 6 H).

Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.07. Found: C, 77.65; H, 6.68; N, 10.23.

1-[(Diphenylmethylene)amino]pyrrolidin-2-one (20): mp 132–134 °C (from 2-propanol), 57% yield; IR (KBr) 3060, 1725 (s), 1385 cm^{-1}; NMR ($CDCl_3$) δ 7.42 (m, 10 H), 3.26 (t, 2 H), 2.00 (m, 4 H).

Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.24; H, 6.10; N, 10.60. Found: C, 77.16; H, 6.32; N, 10.54.

2,2-Diphenyl-5-diphenylmethylene-1,3,4-oxadiazoline (13). To a solution of 4.24 g (10 mmol) of benzophenone α-chlorodiphenylacetylhydrazone in 40 mL of dry benzene was added in small portions 10 mmol of 53% NaH dispersion in mineral oil. After the addition was complete, the red solution was stirred for an additional 15 min, washed with water and dried ($MgSO_4$). Evaporation left a dark red oil (IR 2050 cm^{-1}) that was allowed to stand overnight. The residue was then dissolved in boiling ethanol which upon cooling deposited 1.65 g of yellow crystals, mp 138–140 °C, identical with an authentic sample.[27]

(±)-Threonine (33) from Ylide 31. A mixture of 0.50 g (1.7 mmol) of **31** and 0.01 g of 10% Pd/C in 50 mL of ethanol was hydrogenated at 50 psi of hydrogen until uptake was complete. The catalyst was removed by filtration and the solvent evaporated under reduced pressure. The residual semisolid material was washed with 25 mL of ether and converted to (±)-threonine according to the procedure of Pfister:[28] mp 233–235 °C dec (lit. mp 234–235 °C dec[29]), 46% yield.

(±)-Allothreonine (27) from Ylide 25. This material was prepared from **25** as described above: mp 251–252 °C dec (lit. mp 252–253 °C dec[29]).

Acidic Hydrolysis of 4a. A. Formation of Ethyl Hydrazinoacetate. A solution of 2.4 g (0.01 mol) of **4a** and 5 mL of 30% HCl in 20 mL of ethanol was heated under reflux for 1 h and then cooled; the solvent was evaporated. The residue was extracted twice with ether and the ether extracts were dried ($MgSO_4$) and evaporated to give benzophenone (93%), mp 47–49 °C. The ether-insoluble syrup was dissolved in 10 mL of ethanol which was saturated with dry HCl and heated under reflux for 2 h. Cooling resulted in the separation of a small quantity of ethyl hydrazinoacetate, mp 152 °C (lit. mp 153 °C[30]).

B. Formation of 3-Oxo-1,2-diazetidinium Tosylate (40). To 2.36 g (0.01 mol) of **4a** in 50 mL of dry CH_2Cl_2 was added 1.90 g (0.01 mol) of p-TSA·H_2O, and the solution was stirred at room temperature for 1 h. The solid which formed was collected by filtration and washed with ether to give 2.20 g (90%) of **40**, mp 147–149 °C dec. IR (KBr) 3115, 1820 (s), 1605, 1125, 1030, 1005, 680 cm^{-1}; NMR (TFA) δ 1820 (q, J = 8.5 Hz, 4 H), 5.46 (s, 2 H), 2.45 (s, 3 H).

Anal. Calcd for $C_9H_{12}N_2SO_4$: C, 44.25; H, 4.95; N, 11.47. Found: C, 43.96; H, 5.11; N, 11.73.

4-Methyl-3-oxo-1,2-diazetidinium Tosylate. This material was prepared from **4g** as described above: mp >160 °C dec (from methanol/ether), 99% yield; IR (KBr) 3115, 1820 (s), 1230, 1140, 1120, 1030, 1005, 680 cm^{-1}; NMR (TFA) δ 7.56 (q, J = 8.5 Hz, 4 H), 5.83 (q, J = 7.0 Hz, 2 H), 2.46 (s, 3 H), 1.97 (d, J = 7.0 Hz, 3 H).

Anal. Calcd for $C_{10}H_{14}N_2SO_4$: C, 46.50; H, 5.46; N, 10.85. Found: C, 46.30; H, 5.65; N, 10.86.

Benzophenone Imine of Aminoacetamide (41). A. From Benzophenone and Aminoacetamide. A mixture of 1.82 g (0.01 mol) of benzophenone and 0.74 g (0.01 mol) of aminoacetamide (glycinamide) was heated with ethyl acetate, and filtered. Cooling of the filtrate resulted in the separation of 1.40 g (59%) of white crystals: mp 162–163 °C; NMR (d_6-Me_2SO) δ 7.50 (m, 12 H), 3.89 (s, 2 H), (d_6-Me_2SO + H_2O) 7.50 (m, 10 H), 3.89 (s, 2 H); mass spectrum m/e 238 (M^+); UV/vis 248 (4.25).

Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.92; N, 11.76. Found: C, 75.33; H, 6.08; N, 11.67.

B. From 4a. A solution of 2.36 g (0.01 mol) of **4a** in 50 mL of ethanol was hydrogenated at 45 psi with 2.0 g of Raney nickel (deactivated by refluxing in water for 45 min). When hydrogen uptake had ceased, the catalyst was removed by filtration, the filtrate evaporated, and the residue recrystallized from ethyl acetate, yield 1.57 g (66%), mp 162–163 °C. The compound was identical in every respect with the material formed by method A.

α-Diphenylmethylaminoacetamide (42). A solution of 2.36 g (0.01 mol) of **4a** in 50 mL of ethanol was hydrogenated at 60 psi in the presence of 2.0 g of W-2 Raney nickel until hydrogen uptake ceased. The catalyst was removed by filtration and the filtrate evaporated. The residual oil was dissolved in benzene and hexane was added to the cloud point; standing then resulted in the separation of 1.73 g (72%) of α-diphenylmethylaminoacetamide, mp 109–110 °C, identical with an authentic sample prepared from ethyl diphenylmethylaminoacetate and alcoholic ammonia.

Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.44; H, 6.66; N, 11.58. Found: C, 74.70; H, 6.75; N, 11.46.

Sodium Borohydride Reduction of 3-Oxo-1,2-diazetidinium and 3-Oxo-1,2-pyrazolidinium Ylides. General Procedure. To a solution or slurry of 0.01 mol of the ylide in 25 mL of methanol at 0 °C was added, in small portions, 0.01 mol of sodium borohydride. After addition was complete, the reaction mixture was stirred for 1 h and poured over 10 g of ice; the mixture was either filtered (if the reduction product separated) or extracted with ether and the extracts were evaporated to dryness. The N-1 inversion barrier constants were determined at the coalescence temperature.[31]

1-Benzhydryldiazetidin-3-one (44a): mp 173.4 °C (from methanol), 84% yield; IR (KBr) 1760 (s), 1735 (s), 1450, 1400, 760, 700 cm^{-1}; NMR (d_6-Me_2SO) δ 7.40 (m, 10 H), 4.67 (s, 1 H), 4.00 (q, $\Delta\nu_{AB}$ = 25.4 Hz, J = 14.0 Hz, 1 H); mass spectrum m/e 238 (M^+), 194, 167, 152, 139, 128, 77; metastable peaks at 42.8, 138.3. Inversion barrier constants $\Delta G^{\ddagger}$ = 18.6 ± 0.2 kcal/mol; t(°C) = 100, k = 94.7 s^{-1}.

Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.69; H, 5.93; N, 11.77. Found: C, 75.47; H, 5.99; N, 11.47.

1-Benzhydryl-4-methyldiazetidin-3-one (44b): mp 163–165 °C (from ethyl acetate/hexane), 55% yield; IR (Nujol) 3175, 1750 (s), 1730 (s) cm^{-1}; NMR (d_6-Me_2SO) δ 7.36 (m, 10 H), 4.60 (s, 1 H), 3.92 (q, J = 7.0 Hz, 1 H), 1.17 (d, J = 7.0 Hz, 3 H).

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.25; H, 6.40; N, 11.12. Found: C, 76.07; H, 6.35; N, 11.09.

1-Benzhydryl-4-phenyldiazetidin-3-one (44c): mp 158–159 °C (from ethyl acetate), 83% yield; IR (Nujol) 3175, 1760 cm^{-1}; NMR (d_6-Me_2SO) δ 7.7–6.9 (m, 15 H), 4.92 (s, 1 H), 4.62 (s, 1 H).

Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.32; H, 5.78; N, 8.92. Found: C, 80.20; H, 5.78; N, 8.92.

1-(p-Bromobenzhydryl)diazetidin-3-one (44f). This material could be prepared from either the E or Z ylides **4e** or **41**: mp 154.2–154.5 °C (from ethanol), 89% yield; IR (KBr) 3180, 1765 (s), 1735 (s), 1485, 1070, 1010, 805, 720, 700 cm^{-1}; NMR (d_6-Me_2SO) δ 9.90 (s, 1 H), 7.34 (m, 9 H), 4.68 (s, 1 H), 4.03 (q, $\Delta\nu_{AB}$ = 26.5 Hz, J_{AB} = 14.0 Hz, 2 H).

Anal. Calcd for $C_{15}H_{13}BrN_2O$: C, 56.78; H, 4.13; N, 8.83. Found: C, 56.51; H, 4.01; N, 8.63.

1-(2-Methyl-1-phenylpropyl)diazetidin-3-one (44d): mp 82.1 °C (from ether/hexane), 69% yield; IR (KBr) 3160, 1775 (s), 1735, 750, 700 cm^{-1}; NMR ($CDCl_3$) δ 7.30 (s, 5 H), 2 AB quartets of unequal population, 4.16 (q, $\Delta\nu_{AB}$ = 29.9 Hz, J_{AB} = 14.0 Hz), 3.85 (q, $\Delta\nu_{AB}$ = 31.3 Hz, J_{AB} = 14.5 Hz, 2 H), 3.35 (d, J = 4.0 Hz, 1 H), 2.05 (septet with finer splitting, 1 H), 0.83 (m, 6 H); partial coalescence at 70 °C.

Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71. Found: C, 70.30; H, 8.00; N, 13.82.

1-(2,4-Dimethyl-3-pentyl)diazetidin-3-one (44e): mp 75.6 °C (from ether–petroleum ether), 91% yield; IR (KBr) 3170, 2970, 1780 (s), 1745 (s), 1465, 1370, 1260 cm^{-1}; NMR ($CDCl_3$) δ 7.90 (br, 1 H), 4.10 (br, 2 H) [at −20 °C 4.10, q, J = 14.0 Hz, $\Delta\nu_{AB}$ = 31.0 Hz, 2 H], 2.15 (t,

(27) Kirmse, W. *Chem. Ber.* **1960**, *93*, 2357.
(28) See footnote 15.
(29) Beilstein's "Handbuch der Organischen Chemie", 4th ed.; Springer Verlag: Berlin, 1963; Vol. 4, pp 1625–1630.
(30) Knobloch, W.; Niedrich, H. *J. Prakt. Chem.* **1962**, *17*, 273.

(31) An approximate evaluation of $\Delta G^{\ddagger}_{act}$ for N-1 inversion was obtained at the coalescence temperature (T_c) of the C-4 ^1H AB quartet via the Eyring equation (eq 1): Gunther, H. "NMR Spectroscopy An Introduction"; Wiley: New York, 1980; p 243. These data are consistent with other diazetidinone N-1 inversion barriers. For example: see Fahr, E.; Fischer, W.; Jung, A.; Sauer, L.; Mannschrek, A. *Tetrahedron Lett.* **1967**, 161.

$$\Delta G_c^{\ddagger}\ (\text{kcal/mol}^{-1}) = 4.57T_c[9.97 + \log T_c/(\Delta\nu_{AB}^2 + J_{AB}^6)^{1/2}]$$

$\Delta\nu_{AB}$ = frequency difference between resonances of H_A and H_B

J_{AB} = observed coupling constant

J = 2.5 Hz, 1 H), 1.72 (m, 2 H), 0.97 (d, J = 6.5 Hz, 6 H), 0.93 (d, J = 6.5 Hz, 6 H); mass spectrum m/e 170 (M^+), 127, 99, 84, 57, 55, 43, 41; metastable peaks at 94.8, 77.2, 53.4. Inversion barrier constants $\Delta G^{\ddagger}$ =15.1 ± 0.2 kcal/mol, t(°C) = 32.0 ± 1, k = 102.6 s^{-1}.

Anal. Calcd for $C_9H_{18}N_2O$: C, 63.49; H, 10.66; N, 16.45. Found: C, 63.71; H, 10.30; N, 16.37.

2,2-Diphenyl-3,4,6,7-tetracarbomethoxy-1,5-diazabicyclo[3.3.0]octa-3,6-diene (45). A mixture of 2.5 g (10.5 mmol) of **4a** and 3.0 g (21.0 mmol) of dimethyl acetylenedicarboxylate in 20 mL of dry CH_2Cl_2 was heated at 100 °C for 2 h in a sealed bomb. After the mixture was cooled to room temperature, the solvent was removed and the residue chromatographed on Florisil and eluted with benzene. The red-orange fractions were collected and evaporated to afford 4.65 g (90%): mp 135.2–136 °C (from ethyl acetate/petroleum ether); IR (KBr) 1760 (s), 1750 (s), 1705 (s), 1590, 1435, 1345, 1250, 760 cm^{-1}; NMR ($CDCl_3$) δ 7.39 (m, 10 H), 3.89 (s, 3 H), 3.85 (s, 3 H), 3.77 (s, 2 H), 3.60 (s, 3 H), 3.53 (s, 3 H); mass spectrum m/e 492.15333 (M^+), 461, 433, 415, 402, 308, 276, 249, 233, 219, 218, 189, 178, 165, 153, 129, 121, 115, 105, 91, 77, 59; metastable peaks at 381, 370.5, 166.5, 143.4.

Anal. Calcd for $C_{26}H_{24}N_2O_8$: C, 63.41; H, 4.91; N, 5.69. Found: C, 63.40; H, 5.02; N, 5.85.

2,2-Diphenyl-3,4,6,7-tetracarbomethoxy-1,5-diazabicyclo[3.3.0]octa-3,7-diene (46). 2,2-Diphenyl-3,4,6,7-tetracarbomethoxy-1,5-diazabicyclo[3.3.0]octa-3,6-diene (**45**) (500 mg) was heated to 190 °C for 10 min, during which time its color changed from red-orange to yellow. Cooling provided 490 mg of **46**: mp 117.4–117.5 °C (from ethyl acetate/petroleum ether), 98% yield; IR (KBr) 2950, 2840, 1770 (s), 1725 (s), 1450, 1260, 705 cm^{-1}; NMR ($CDCl_3$) δ 7.90 (s, 1 H), 7.17 (s, 10 H), 6.20 (s, 1 H), 3.82 (s, 3 H), 3.77 (s, 3 H), 3.73 (s, 3 H), 3.45 (s, 3 H); mass spectrum m/e 492 (M^+), 461, 433, 402, 374, 373, 314, 308, 276, 249, 235, 219, 191, 189, 165, 153, 105, 91, 77.

Anal. Calcd for $C_{26}H_{24}N_2O_8$: C, 63.41; H, 4.91; N, 5.69. Found: C, 63.32; H, 4.80; N, 5.73.

2,3-Dicarbomethoxy-4,4-diphenyl-6-methyl-7-oxo-1,5-diazabicyclo-[3.2.0]hept-2-ene (47). A solution of 0.50 g (2 mmol) of **4g** and 0.28 g (2 mmol) of dimethyl acetylenedicarboxylate in 20 mL of CH_2Cl_2 was stirred 5 days at 20 °C. The solvent was removed in vacuo at 20 °C and the residue triturated and cooled in 5 mL of dry ethanol to afford 0.43 g of yellow crystals: mp 138 °C dec, 56% yield; IR (KBr) 1840 (s), 1750, 1725 (s), 1612 cm^{-1}; NMR ($CDCl_3$) δ 7.50 (m, 10 H), 4.16 (q, J = 7 Hz, 1 H), 3.90 (s, 3 H), 3.60 (s, 3 H), 1.13 (d, J = 7 Hz, 3 H); mass spectrum m/e 392 (M^+), 364.

Anal. Calcd for $C_{22}H_{20}N_2O_5$: C, 67.34; H, 5.14; N, 7.14. Found: C, 67.46; H, 5.18; N, 6.91.

2,2-Diphenyl-8-methyl-3,4,6,7-tetracarbomethoxy-1,5-diazabicyclo-[3.3.0]octa-3,7-diene (50). A mixture of 1.0 g (4 mmol) of **4g** and 1.14 g (8 mmol) of dimethyl acetylenedicarboxylate in 25 mL of CH_2Cl_2 was heated at 100 °C for 16 h in a 45-mL stainless steel bomb. The mixture was then cooled, evaporated under reduced pressure, and chromatographed on 100 g of silica gel ($CHCl_3$) to give 1.56 g (77%) of white crystals: mp 127–128 °C (from ethyl acetate/petroleum ether); IR (KBr) 3030, 2960, 1770 (s), 1725 (s), 1545, 1450, 1435, 1260, 754, 700 cm^{-1}; NMR ($CDCl_3$) δ 7.31 (m, 10 H), 6.19 (s, 1 H), 3.86 (s, 3 H), 3.83 (s, 3 H), 3.73 (s, 3 H), 3.53 (s, 3 H), 2.39 (s, 3 H); mass spectrum m/e 506 (M^+), 475, 447, 415, 388, 276, 249, 219, 218, 191, 189, 167; metastable peaks at 396.1, 385.1.

Anal. Calcd for $C_{27}H_{26}N_2O_8$: C, 64.02; H, 5.17; N, 5.53. Found: C, 64.28; H, 5.06; N, 5.45.

Compound **50** could also be prepared in ~80% yield by heating a mixture of **47** and a slight excess of dimethyl acetylenedicarboxylate in CH_2Cl_2 under reflux for 3 h followed by solvent evaporation. The NMR spectrum of the crude product indicated the presence of **49** (C-methyl doublet), but recrystallization of the crude product from ethyl acetate/petroleum ether resulted in complete conversion to **50**, mp 127–128 °C.

5,5-Diphenyl-3,4-dicarbomethoxy-Δ²-pyrazoline (51). A mixture of 390 mg (1 mmol) of **47** in 10 mL of ethanol was heated under reflux for 15 min; 3 mL of 5 N HCl was added, and the solution was warmed for 5 min, diluted with 10 mL of water, and then neutralized with aqueous $NaHCO_3$. The neutral solution was extracted with ether, the ether extracts were evaporated, and the residual semisolid was triturated with petroleum ether to give 203 mg (60%) of **51**, mp 142–142.5 °C (from ethanol). The compound was identical in every respect with an authentic sample of **51**.[25]

1-Benzhydryl-3(2*H*)-pyrazolone (A). A mixture of 1.5 g (6.0 mmol) of **15a**, 2.0 g (17.7 mmol) of potassium *tert*-butoxide, and 50 mL of benzene was warmed on a steam bath for 2 h and then poured into 100 mL of water. The aqueous phase was separated and neutralized with dilute HCl; the product which precipitated was collected by filtration, dried, and recrystallized from ethanol to give 1.13 g (75%): mp 179–180 °C; IR (KBr) 1545 (s), 1300, 1210, 1050, 1030, 740, 700 cm^{-1}; NMR ($CDCl_3$) δ 11.4 (br, 1 H), 7.25 (m, 10 H), 6.94 (d, J = 2.5 Hz, 1 H), 6.54 (br s, 1 H), 5.60 (d, J = 2.5 Hz, 1 H).

Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.70; H, 5.57; N, 10.98.