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(4) See ref 1, Table I and references cited therein, for a summary of these reactions.
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Carbon-13 Nuclear Magnetic Resonance Study of Representative *trans*- and *cis*-1-Alkyl-2-aryl(alkyl)-3-aroylaziridines

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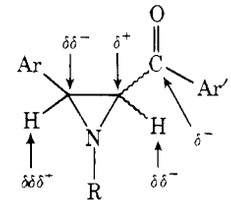
Twenty-two *trans*- and *cis*-1-alkyl-2-aryl(alkyl)-3-aroylaziridines have been studied by use of ^1H and ^{13}C NMR. The ^{13}C chemical shifts of the ring carbons have been tabulated, as well as those for the α-*N*-alkyl carbons (see Table I). Selected coupling constants are reported. The chemical shifts of the ring carbons are correlated with the phenomenon of three-ring to carbonyl hyperconjugation.[2] In addition, the effect of the nitrogen lone pair upon ^1J (^{13}C–H) values and the carbonyl carbon chemical shifts is discussed, while the α-*N*-alkyl carbon values are rationalized in terms of steric compression effects.

A ^{13}C NMR study of representative *trans*- and *cis*-1-alkyl-2-aryl(alkyl)-3-aroylaziridines has been undertaken. While systematic ^{13}C NMR studies of N-unsubstituted alkyl- and phenylaziridines have appeared earlier in the literature,[3,4] no desirable ^{13}C NMR study of the title compounds has been published to date. Work pertaining to the effect of the nitrogen heteroatom in cyclic systems has appeared in the literature,[5–9] as well as that of representative 1-azirines.[10] Here we have studied the effect of three-ring to carbonyl hyperconjugation,[2] the effect of the nitrogen lone pair on selected coupling constants and the carbonyl group, and the steric compression effect (where applicable) in these systems.

The assignments made are based on chemical shift considerations; signal multiplicities from off-resonance decoupling experiments or from coupled spectra; and qualitative considerations of long-range ^{13}C–H couplings; that is to say, the C_2 line width is greater than the line width of C_3 due to three-bond coupling of the C_2 to the adjacent (ortho) protons of the C_2–H aryl substituent (see Table I and the Experimental Section for assignments).

Three-Ring to Carbonyl Hyperconjugation. As revealed in Table I, the ^{13}C NMR studies show that the trans isomers of arylaroylaziridines (except **11a** and **12a**) enjoy substantial conjugation through their three-membered rings. This is borne out by the fact that C_2 appears further downfield than C_3 for **1a–8a** and **10a** by 0.5, 1.2, 0.7, 1.3, 1.2, 1.3, 0.9, 0.9, and 1.0 ppm, respectively. The strength of this statement is not so much the ~1-ppm difference in the values of C_3 and C_2 but the fact that the trend is uniform; i.e., $\Delta\delta$ (C_2–C_3) is always greater than zero. (A similar trend is found in the IR and UV data.[2]) In marked contrast, the opposite trend is found in the ^1H NMR data (see again Table I), such that the ring proton attached to C_3 is always further downfield in both the trans and cis isomers. One plausible explanation for this trend in the trans compounds might be the greater anisotropic effect by the phenyl group upon the hydrogen cis to it.[11a–c] Of course,

Chart I. Bond Polarization along the σ Skeleton of Arylaroylaziridines Assuming Carbonyl to be the Only Electronegative Substituent



an alternating polarization effect, such as was invoked in six-membered N-heterocyclic compounds by Morishima,[11c] appears applicable here (Chart I). That is to say, Pople,[11d] using the CNDO–SCF molecular orbital calculations, suggested that the inductive effect induced by an electronegative substituent (here, carbonyl) alternates and attenuates along to σ skeleton of the arylaroylaziridine three ring. This theory appears to be well correlated with the H_2 and H_3 ring proton values in both the *trans*- and *cis*-aziridines (Table I), wherein H_3 ($\delta\delta^-$) is always further downfield than H_2 ($\delta\delta\delta^+$). Moreover, the fact that the ring hydrogens of trans are further downfield than those of the cis can clearly be attributed to the anisotropic effect of the phenyl and carbonyl groups lying cis to their hydrogens in the *trans*-aziridines.[11a] Finally, one cannot ignore the bond polarization effect of the phenyl group since the *trans*- and *cis*-1-cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)aziridines (**16a,b**) have their C_2 protons significantly upfield, i.e., ~1 ppm, from their respective trans and cis analogues, **11a,b.**[11a,d]

With respect to three-ring to carbonyl hyperconjugation, a brief explanation of the stereochemical requirements is warranted. Basically, following the established corollary[11a,13] that the *N*-alkyl group in the trans series exists preferentially syn to the carbonyl moiety, the following conformer may be drawn to represent **1a–8a, 10a,** and **11a** (see Chart II). In es-

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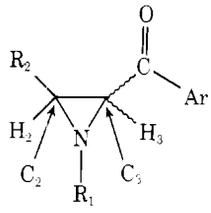
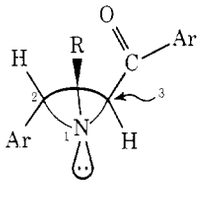
Table I. Proton and Carbon-13 NMR Parameters[d] of Selected *trans*- and *cis*-1-Alkyl-2-aryl(alkyl)-3-aroylaziridines



R_1	R_2	Ar	Trans (cis)	Proton, ppm from Me_4Si[a]			Carbon-13, ppm from Me_4Si			
				H_2	H_3	H_α[b]	C_2	C_3	C_α[b]	Carbonyl C=O
H	Ph	*p*-Ph-C_6H_4	**1a**	3.18	3.55	2.72 (N-H)	43.9	43.4		194.8
Me	Ph	*p*-Ph-C_6H_4	**2a** (**2b**)	3.37 (3.05)	3.55 (3.22)	2.67 (2.60)	49.6 (46.9)	48.4 (49.8)	38.8 (49.8)	193.7 (190.5)
Et	*p*-Ph-C_6H_4	Ph	**3a** (**3b**)	3.52 (3.07)	3.62 (3.23)	2.88 (2.60)	48.7 (49.8)	48.0 (51.2)	45.8 (55.4)	194.2 (193.1)
Bz	Ph	Ph	**4a** (**4b**)	3.62 (3.2)	3.62 (3.32)	4.02 (3.67-3.92)	49.3 (49.6)	48.0 (51.0)	54.8 (63.7)	194.8 (192.8)
i-Pr	*p*-Ph-C_6H_4	Ph	**5a** (**5b**)	3.58 (3.13)	3.67 (3.28)	3.02 (1.85)	48.5 (49.5)	47.3 (50.5)	50.3 (61.6)	194.7 (193.1)
c-C_6H_{11}	Ph	Ph	**6a** (**6b**)	3.57 (3.12)	3.63 (3.28)	2.12 (1-2)	48.4 (49.1)	47.1 (49.8)	57.7 (68.9)	194.5 (193.2)
endo-Norbornyl[c]	Ph	Ph	**7a** (**7b**)	3.50 (3.0)	3.55 (3.07)	3.03 (2.25)	49.0 (49.5)	48.1 (50.6)	60.7 (72.3)	194.6 (193.2)
exo-Norbornyl[c]	Ph	Ph	**8a** (**8b**)	3.35 (3.02)	3.49 (3.06)	2.75 (2.33)	48.3 (49.8)	47.4 (50.5)	64.1 (74.1)	194.6 (193.4)
t-Bu	Ph	Ph	(**9b**)	(3.41)	(3.41)	(-)	(43.2)	(44.3)	(53.7)	(194.0)
c-C_6H_{11}	Ph	*p*-Me-Ph	**10a** (**10b**)	3.57 (3.12)	3.69 (3.28)	2.12 (1-2)	48.1 (49.0)	47.1 (49.8)	57.8 (69.0)	194.0 (192.7)
c-C_6H_{11}	Me	*p*-Ph-C_6H_4	**11a** (**11b**)	2.68 (2.11)	3.32 (2.94)	2.12 (-)	42.1 (42.7)	44.3 (46.5)	58.0 (69.4)	194.9 (194.6)
Me	*p*-NO_2-Ph	Ph	**12a**	3.52	3.60	2.62	48.0	49.3	38.6	193.2
c-C_6H_{11}	H	*p*-Ph-C_6H_4	**13**	2.29	2.93	1.77	35.7	39.8	69.5	195.6

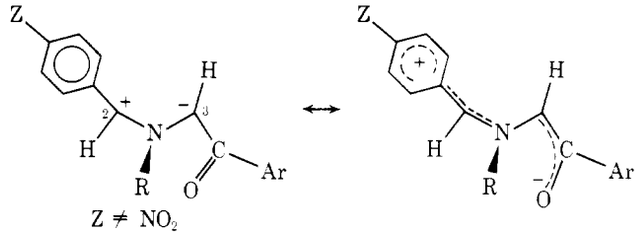
[a] See ref 11a for details on how these compounds were studied by ^1H NMR. [b] The α position refers to either the carbon attached to nitrogen or its hydrogen(s). [c] These newly synthesized[12] isomeric aziridines gave satisfactory microanalysis. [d] Cis values in parentheses.

Chart II. Conformation of Trans Isomers in *N*-Alkylarylaroylaziridines[a]



[a] Ar = Ph or *p*-Ph-C_6H_4; R = H, Me, Et, *i*-Pr, c-C_6H_{11}, etc. (alkyl).

Chart III. Representation of Canonical Structures Which Serve to Resonance Stabilize the C-C Bond Conjugation[a]



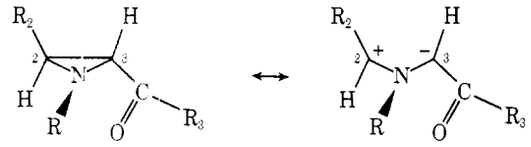
[a] If Z = H, ten structures are possible.

sence the steric requirements demand that the nodal plane of the phenyl and carbonyl groups be orthogonal to the plane of the aziridine ring.[2] Hence, the π orbitals of the attached groups have to be free to orient themselves so that their nodal planes approach a perpendicular relationship to the plane of the three ring and a symmetrical arrangement with respect to the bent bonds.[2,14,15] Furthermore, it appears that the conjugative behavior of the three ring is due to the C-C bond and can well be rationalized by drawing canonical structures of the type shown in Chart III.

It is worth noting that the ability of the aryl ring (attached to C_2) to support a partial positive charge is most crucial. When *trans*-1-methyl-2-(*p*-nitrophenyl)-3-benzoylaziridine (**12a**) was examined by ^{13}C NMR, C_2 was found 1.3 ppm *upfield* from C_3. Another model for comparison in support of three-ring to carbonyl hyperconjugation is to look at the *trans*- and *cis*-methyl 1-isopropyl-2-(*p*-biphenyl)aziridinecarboxylates (**15a,b**) spectroscopically and observe the net change in C_2 and C_3 values in going from trans to cis relative to the ketone analogues **5a,b.**[16a] For the esters the $\delta\Delta\delta$ (C_2-C_3) value was 1.3 ppm vs. a $\delta\Delta\delta$ (C_2-C_3) value of 2.2 ppm for the ketone. As expected, the ketone shows a greater conjugative effect in the trans isomer, owing to its better ability to support a partial negative (δ^-) charge at C_3 (Chart III). The apparent inference from these data is that in **12a** and **15a** the C_2-C_3 bond polarity is significantly diminished (Chart IV)[16b] with a resultant decrease in three-ring to carbonyl hyperconjugation. However, not only must electronic considerations be met, but also steric requirements must be fulfilled in order for three-ring to carbonyl hyperconjugation to occur; here the cis analogues are a prime example of this (see below).

In marked contrast to the trans isomers, the *cis*-1-alkyl-2-aryl-3-aroylaziridines (**2b-10b**) have their C_2 carbons 2.9,

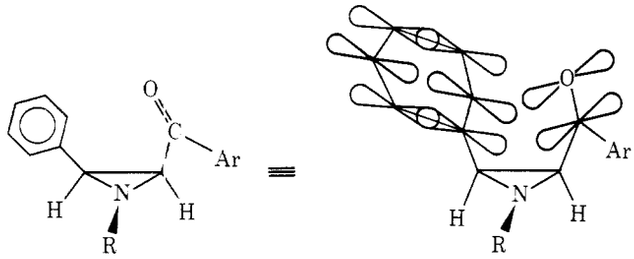
Chart IV. *trans*-Aziridines with Lowered Carbonyl Hyperconjugation



R_1 = *p*-$NO_2C_6H_4$ when R_3 = Ph
R_2 = *p*-PhC_6H_4 when R_3 = OCH_3

relatively minor

Chart V. Gauche Conformer of *cis*-*N*-Alkylarylaroylaziridines



0.4, 1.4, 1.0, 0.7, 1.1, 0.7, 1.1, and 0.8 ppm, respectively, upfield from C_3 (Table I). Again the trend is uniform; however, now $\Delta\delta$ (C_2–C_3) is always less than zero. This trend can be attributed, in part, to diminished three-ring to carbonyl hyperconjugation. Although a cisoid conformer of the cis isomer may be postulated, it is the gauche conformer (Chart V) which has been found to be the main, if not only, conformer present in polar solvent, as revealed by infrared studies,[12,17-19] and it lacks the ability to hyperconjugate. (Note: in the gauche conformer repulsion between the C_2-aryl group and C_3-carbonyl group will not allow for the orbital overlap needed for three-ring to carbonyl hyperconjugation.)

Effect of Nitrogen Lone Pair. An analysis of the chemical shifts of carbonyl carbons in the arylarolyaziridines (Table I) reveals that a consistent, substantial difference exists between the trans and cis isomers. In pairs **2–8** signals of the carbonyl carbons are downfield in the trans isomer compared to the cis by 1–4 ppm. In compounds **11a,b,** which lack an aromatic group at C_2, the carbonyl chemical shifts are rather similar, which suggest that an aromatic group at C_2 is a necessary ingredient to observe a substantial effect. The identity of the N–R substituent does not appear to have a sizable effect (compare **2, 3,** and **6–8**), as long as R is attached to the nitrogen with a primary, secondary, or tertiary carbon. The trans isomers **2a–8a** appear rather similar to their carbocyclic analogue, *trans*-1-(*p*-phenylbenzoyl)-2-phenylcyclopropane (**14**) (Chart VI), except that **14** has an even more downfield carbonyl chemical shift. This similarity suggests that the orientation of the lone pair is not of major importance. In particular, the *trans*-aziridines, which have the lone pair anti to carbonyl, show downfield carbonyl absorptions, compared to the *cis*-aziridines, where carbonyl is syn to the nitrogen lone pair. The shielded nature of the chemical shifts in the cis isomers is presently believed to be due to anisotropic effect, whereby the circulation of electrons in the π system of one substituent shields the other group, and is the case in the *cis*-aziridines because of the shielding effect of the aromatic group at C_2. (In

Chart VI. Carbocyclic Analogue of *trans*-Arylaroylaziridines

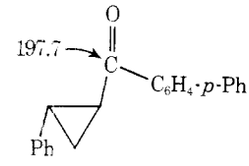
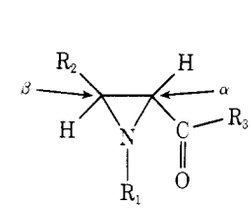
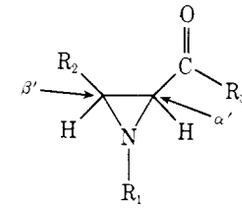


Table II. Stereochemical Dependence of ^{13}C–H Coupling Constants[a] in Selected Aroylaziridines



trans



cis

Compd					
Trans	Cis	J_α	J_β	$J_{\alpha'}$	$J_{\beta'}$
	4b			164	166
5a	**5b**	172	167	162	163
6a	**6b**	177	166	162	164
10a		176	166		
11a		174	164		
12a		171	167		
15a	**15b**	181	167	170	167

[a] *J* values in hertz.

Table III. Calculated vs. Experimental Values[a] for the α-*N*-Alkyl Carbon in *trans*- and *cis*-Arylaroylaziridines

Trans	Cis	N substituent	Exptl	Calcd
2a	2b	-$\overset{*}{C}H_3$	38.8 (49.8)	38.8 (49.2)
3a	3b	-$\overset{*}{C}H_2CH_3$	45.8 (55.4)	45.0 (55.4)
4a	4b	-$\overset{*}{C}H(CH_3)_2$	50.3 (61.6)	51.2 (61.6)
5a	5b	-$\overset{*}{C}H_2Ph$	54.8 (63.7)	52.3 (62.7)
6a	6b		57.7 (68.9)	58.5 (68.9)
7a	7b		60.7 (72.3)	63.2 (73.6)
8a	8b		64.1 (74.1)	63.2 (73.6)

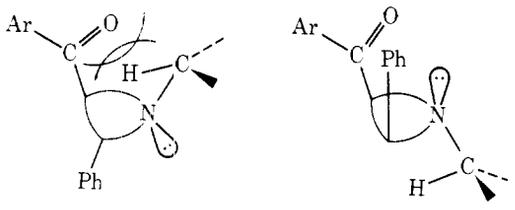
[a] Cis values in parentheses.

^1H NMR, the mutual shielding of aromatic groups near in space is rather common, but in ^{13}C NMR such observations are less frequent.[20-22])

Jennings and co-workers[23] have observed a stereochemical dependence of ^{13}C–H coupling constants in diastereomeric (*Z*)-*cis*- and (*E*)-*trans*-oxaziridines. Similarly, ^1J (^{13}C–H) coupling constants in selected *trans*- and *cis*-*N*-alkylarylaroylaziridines show such a dependence (see Table II) on the orientation of the nitrogen lone pair such that a positive increment is imparted to the coupling constant of nearby ^{13}C–H for a C–H bond cis to the lone pair. For **5a, 6a,** and **10a–12a** (all trans) the difference is in agreement with these findings and the supposition that the preferred conformation is the lone pair syn to phenyl. On the other hand, for **4b–6b** (all cis) the ^1J (^{13}C–H) coupling constants are similar, as expected, and this indicates that the nitrogen lone pair is anti in orientation to both ring protons.

Steric Compression Effect. The value of the chemical shifts of the α-*N*-alkyl carbon increases in both the trans and cis isomers as cited in Table III. Hence, a mean difference of 10.4 ppm is found in the chemical shift between the cis and trans isomers, and looking at the conformations of the isomers (Chart VII) one can postulate that the α-*N*-alkyl carbon in the trans isomer is sterically perturbed by being syn to the carbonyl moiety. In the cis isomer no steric compression shift is

Chart VII. Effect of Steric Compression Shift



observed since the α-*N*-alkyl carbon is anti to the benzoyl group. Since, in this steric perturbation, the carbon to hydrogen bond is shortened and the subsequent carbon electron density increases, it is not surprising that the α-*N*-alkyl carbon in the trans isomer is found (on the average) 10.4 ppm upfield from its unperturbed cis analogue. As the magnitude of the shift is quite large, it appears that the proximity of the α-*N*-alkyl hydrogen(s) and the carbonyl group is an important factor in determining the chemical shift of the α carbon attached to nitrogen.[24]

Of importance also is the order in which the chemical shifts of the α-*N*-alkyl carbon increase (goes downfield) relative to Me_4Si. This trend can be attributed to the fact that the presence of attached and nearby carbons has a profound effect upon ^{13}C NMR chemical shifts. In order that a quantitative grasp of the effect of the attached carbons can be understood, one can derive and employ the following empirical equation (1) for the ^{13}C chemical shift for the *N*-alkyl carbon α to nitrogen

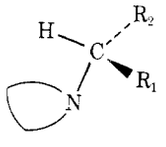
$$\delta^c_{calcd} = Bc\alpha + \alpha N_1 + \beta N_2 + S \quad (1)$$

where $Bc\alpha$ is the base value, taken as 49.2 ppm, N_1 = number of α carbons to carbon α to nitrogen, N_2 = number of β carbons to carbon α to nitrogen, α = 6.2, β = 3.65, and S = steric compression factor = −10.4 ppm (trans isomer only). Hence, by employing this equation one can calculate values for nontertiary α-*N*-alkyl carbons that are quite close to those values found experimentally; in fact, the calculated (δ^c_{calcd}) and experimental (δ^c_{exptl}) values appear in close agreement (see Figure 1).

With respect to the chemical shift of the ring carbons, the *N*-alkyl substituent appears to have *little or no effect* on the chemical shift values of the arylaziridine carbons since all appear within a few parts per million of one another (except in **9b** when the *N*-alkyl group is *tert*-butyl; cf. discussion below). Ordinarily, the effect of a substituent γ to the C_2 and C_3 would be substantial, according to Stothers;[21] however, little effect is observed in this instance. One reason may be that the hydrogen of the α-*N*-alkyl carbon is always extending toward the center of the three ring and impinging on the C_2 and C_3 substituents (Chart VIII). This argument is reinforced by the fact that the small C–N–C angle of the aziridine ring makes it difficult to accommodate any other group than hydrogen "inside" the three ring. Thus, it makes little difference what N–CH–R_1R_2 is because R_1 and R_2 are always extended away from the ring. Moreover, when *tert*-butyl is the *N*-alkyl substituent in the case of **9b**, both ring carbons show an upfield shift owing to a probable steric compression effect by a methyl group which must in this instance lie over the three ring.[20,21]

Another steric compression shift may be found in the

Chart VIII. Conformer of Arylaroylaziridine with the Hydrogen of the *N*-Alkyl Carbon Pointing toward the Center of the Aziridine Ring



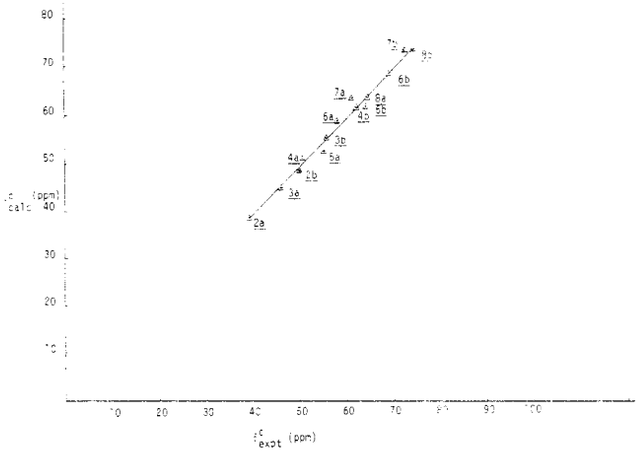


Figure 1. Plot of α-*N*-alkyl carbons [δ^c_{calcd} (ppm) vs. δ^c_{exptl} (ppm)] with regression analysis used to get the best least-squares correlation of all the points, the best straight line of which is found to be δ^c_{calcd} = 1.016, δ^c_{exptl} − 1.021, with the correlation coefficient (r^2) = 0.993.[25]

chemical shifts of the C_2-methyl group in **11a** and **11b**. For **11a** δ = 18.7 ppm, while **11b** has a 13.5-ppm shift. This is another case of a steric substituent shift wherein the C_2-methyl group cis to the carbonyl is shifted 5.2 ppm upfield in the cis isomer, a considerably smaller value than what is observed in the case of the α-*N*-alkyl carbon. The reason may be due to the fact that the C–N bond length in aziridine is considerably shorter than the C–C bond length, in this case approximately 0.10 Å shorter.[2,15] This places the substituent on N in closer proximity to a syn group than a substituent on C_2, creating a worse steric situation for the former and, hence, a greater steric shift.

Experimental Section[26]

These epimeric 1-alkyl-2-aryl(alkyl)-3-aroylaziridines were prepared by known procedures: **1a** and **2a**,[27] **3a,b** and **5a,b**,[11a] **4a,b**, **6a,b**, **9b**, **10a,b**, and **12a**,[28] **7a,b** and **8a,b**,[12,28] **11a,b**,[29] **13**,[30] **14**,[31] and **15a,b**.[11a]

The ^1H noise-decoupled and single-frequency off-resonance decoupled ^{13}C Fourier transform NMR spectra were determined from ca. 1 M $CDCl_3$ solutions on a Varian XL-100-15 spectrometer. Digital resolution is 1.25 Hz/point. Chemical shifts are referenced to internal $CDCl_3$, taken as 76.9 ppm from Me_4Si, and are accurate to 0.1 ppm.[32] Listed below is the complete ^{13}C NMR data for the *trans*- and *cis*-arylaroylaziridine systems.

***trans*-2-Phenyl-3-(*p*-phenylbenzoyl)aziridine (1a):** δ 194.8 (s, C=O), 146.3, 138.1, 134.4 (s, aromatic ipso C's), 126.0–129.0 (m, aromatic C–H's), 43.9 (d, C_2), 43.4 (d, C_3).

***trans*-1-Methyl-2-phenyl-3-(*p*-phenylbenzoyl)aziridine (2a):** δ 193.7 (s, C=O), 145.9, 139.6, 139.5 (s, aromatic ipso C's), 125.9–130.1 (m, aromatic C–H's), 49.6 (d, C_2), 48.4 (d, C_3), 38.8 (q, N–CH_3).

***trans*-1-Ethyl-2-(*p*-biphenyl)-3-benzoylaziridine (3a):** δ 194.2 (s, C=O), 140.6, 137.9, 133.1 (s, aromatic ipso C's), 126.9–128.5 (m, aromatic C–H's), 48.7 (d, C_2), 48.0 (d, C_3), 45.8 (t, N–CH_2), 14.8 (q, CH_3).

***trans*-1-Benzyl-2-phenyl-3-benzoylaziridine (4a):** δ 194.8 (s, C=O), 134.6, 132.9, 132.7 (s, aromatic ipso C's), 126.2–128.1 (m, aromatic C–H's), 54.8 (t, N–CH_2), 49.3 (d, C_2), 48.0 (d, C_3).

***trans*-1-Isopropyl-2-(*p*-biphenyl)-3-benzoylaziridine (5a):** δ 194.7 (s, C=O), 140.7, 140.1, 138.0 (s, aromatic ipso C's), 126.2–132.9 (m, aromatic C–H's), 50.3 (d, N–CH), 48.5 (d, C_2), 47.3 (d, C_3), 22.3 (q, CH_3), 22.1 (q, CH_3).

***trans*-1-Cyclohexyl-2-phenyl-3-benzoylaziridine (6a):** δ 194.5 (s, C=O), 139.2, 138.0 (s, aromatic ipso C's), 126.3–133.0 (m, aromatic C–H's), 57.7 (d, N–CH), 48.4 (d, C_2), 47.1 (d, C_3), 33.0 (t, cyclohexyl C_2), 32.7 (t, cyclohexyl C_6), 26.0 (t, cyclohexyl C_4), 24.5 (t, cyclohexyl C_5), 24.2 (t, cyclohexyl C_3).

***trans*-1-(2-*endo*-Norbornyl)-2-phenyl-3-benzoylaziridine (7a):**[33,34] δ 194.6 (s, C=O), 139.5, 138.0 (s, aromatic ipso C's), 126.2–133.0 (m, aromatic C–H's), 60.7 (d, N–C–H or nb C_2), 49.0 (d, C_2), 48.5 (d, nb C_1), 48.1 (d, C_3), 41.0 (t, nb C_3), 38.4 (t, nb C_7), 37.3 (d, nb C_4), 29.8 (t, nb C_5), 22.1 (t, nb C_6).

***trans*-1-(2-*exo*-Norbornyl)-2-phenyl-3-benzoylaziridine (8a):**[33,34] δ 194.6 (s, C=O), 139.4, 137.9 (s, aromatic ipso C's), 125.9–133.0 (m, aromatic C–H's), 64.1 (d, N–CH or nb C_2), 50.2 (d, nb C_1), 48.3 (d, C_2), 47.4 (d, C_3), 42.8 (t, nb C_3), 36.0 (d, nb C_4), 35.8 (t, nb C_7), 28.7 (t, nb C_5), 26.5 (t, nb C_5).

***trans*-1-Cyclohexyl-2-phenyl-3-(*p*-toluyl)aziridine (10a):** δ 194.0 (s, C=O), 143.8, 139.3, 135.6 (s, aromatic ipso C's), 126.3–129.1 (m, aromatic C–H's), 57.8 (d, N–CH), 48.1 (d, C_2), 47.1 (d, C_3), 33.1 (t, cyclohexyl C_2), 32.7 (t, cyclohexyl C_6), 26.0 (t, cyclohexyl C_4), 24.6 (t, cyclohexyl, C_5), 24.2 (t, cyclohexyl, C_3), 21.6 (q, Ar–CH_3).

***trans*-1-Cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)aziridine (11a):** δ 194.9 (s, C=O), 145.5, 139.5, 136.9 (s, aromatic ipso C's), 127.0–128.7 (m, aromatic C–H's), 58.0 (d, N–CH), 44.3 (d, C_3), 42.1 (d, C_2), 33.2 (t, cyclohexyl C_2), 33.0 (t, cyclohexyl C_6), 25.9 (t, cyclohexyl C_4), 24.8 (t, cyclohexyl C_5), 24.4 (t, cyclohexyl C_3), 18.7 (q, CH_3).

***trans*-1-Methyl-2-(*p*-nitrophenyl)-3-benzoylaziridine (12a):** δ 192.3 (s, C=O), 147.1, 146.3, 137.4 (s, aromatic ipso C's), 123.1–133.5 (m, aromatic C–H's), 49.3 (d, C_3), 48.0 (d, C_2), 38.6 (q, N–CH_3).

1-Cyclohexyl-2-(*p*-phenylbenzoyl)aziridine (13): δ 195.6 (s, C=O), 145.5, 139.6, 135.4 (s, aromatic ipso C's), 127.0–128.7 (m, aromatic C–H's), 69.9 (d, N–CH), 39.8 (t, C_2), 35.7 (d, C_3), 32.7 (t, cyclohexyl C_2), 32.3 (t, cyclohexyl C_6), 25.9 (t, cyclohexyl C_4), 24.7 (t, cyclohexyl C_3 and C_5).

***trans*-1-(*p*-Phenylbenzoyl)-2-phenylcyclopropane (14):**[31] δ 197.7 (s, C=O), 145.4, 140.3, 139.7 (s, aromatic ipso C's), 126.1–128.7 (m, aromatic C–H's), 29.8, 29.3 (both d, C_1, C_2, or C_2, C_1), 19.2 (t, C_3).

Methyl *trans*-1-Isopropyl-2-(*p*-biphenyl)-3-aziridinecarboxylate (15a):[11a] δ 169.2 (s, C=O), 140.6, 140.4 (s, aromatic ipso C's), 126.9–128.5 (m, aromatic C–H's), 51.6 (d, N–CH), 47.6 (d, C_2), 44.1 (d, C_3), 21.8 (q, CH_3), 21.4 (q, CH_3).

***cis*-1-Methyl-2-phenyl-3-(*p*-phenylbenzoyl)aziridine (2b):** δ 190.5 (s, C=O), 146.8, 139.4, 138.1 (s, aromatic ipso C's), 127.2–130.4 (m, aromatic C–H's), 49.8 (q, N–CH_3), 49.8 (d, C_3), 46.9 (d, C_2).

***cis*-1-Ethyl-2-(*p*-biphenyl)-3-benzolaziridine (3b):** δ 193.1 (s, C=O), 140.0, 137.0, 134.3 (s, aromatic ipso C's), 126.6–132.7 (m, aromatic C–H's), 55.4 (t, N–CH_2), 51.2 (d, C_3), 49.8 (d, C_2), 14.1 (q, CH_3).

***cis*-1-Benzyl-2-phenyl-3-benzoylaziridine (4b):** δ 192.8 (s, C=O), 137.6, 136.8, 134.8 (s, aromatic ipso C's), 127.0–132.7 (m, aromatic C–H's), 63.7 (t, N–CH_2), 51.0 (d, C_3), 49.6 (d, C_2).

***cis*-1-Isopropyl-2-(*p*-biphenyl)-3-benzoylaziridine (5b):** δ 193.1 (s, C=O), 134.4–140.6 (s, aromatic ipso C's), 126.4–128.3 (m, aromatic C–H's), 61.6 (d, N–CH), 50.5 (d, C_3), 49.5 (d, C_2), 21.8 (q, CH_3), 21.5 (q, CH_3).

***cis*-1-Cyclohexyl-2-phenyl-3-benzoylaziridine (6b):** δ 193.2 (s, C=O), 137.0, 135.5 (s, aromatic ipso C's), 127.0–135.5 (m, aromatic C–H's), 68.9 (d, N–CH), 49.8 (d, C_3), 49.1 (d, C_2), 32.2 (t, cyclohexyl C_2), 31.8 (t, cyclohexyl C_6), 26.0 (t, cyclohexyl C_4), 24.5 (t, cyclohexyl C_3 and C_5).

***cis*-1-(2-*endo*-Norbornyl)-2-phenyl-3-benzoylaziridine (7b):**[32,33] δ 193.2 (s, C=O), 137.2, 135.3 (s, aromatic ipso C's), 126.9–132.4 (m, aromatic C–H's), 72.3 (d, N–CH or nb C_2), 52.5 (d, nb C_1), 50.6 (d, C_3), 49.5 (d, C_2), 40.9 (t, nb C_3), 38.3 (t, nb C_7), 37.1 (d, nb C_4), 29.8 (t, nb C_5), 22.6 (t, nb C_6).

***cis*-(2-*exo*-Norbornyl)-2-phenyl-3-benzoylaziridine (8b):**[32,33] δ 193.4 (s, C=O), 137.2, 135.5 (s, aromatic ipso C's), 126.9–132.4 (m, aromatic C–H's), 74.1 (d, N–CH or nb C_2), 51.9 (d, nb C_1), 50.5 (d, C_3), 49.8 (d, C_2), 42.2 (t, nb C_3), 35.9 (d, nb C_4), 35.6 (t, nb C_7), 28.9 (t, nb C_5), 26.4 (t, nb C_6).

***cis*-1-*tert*-Butyl-2-phenyl-3-benzoylaziridine (9b):** δ 193.0 (s, C=O), 132.4, 128.3 (s, aromatic ipso C's), 126.9–127.6 (m, aromatic C–H's), 53.7 (s, N–C), 44.2 (d, C_3), 43.2 (d, C_2), 26.5, 26.4, 26.3 (all quartets, CH_3).

***cis*-1-Cyclohexyl-2-phenyl-3-(*p*-toluyl)aziridine (10b):** δ 192.7 (s, C=O), 143.3, 135.7, 134.6 (s, aromatic ipso C's), 126.9–128.8 (m, aromatic C–H's), 69.0 (d, N–CH), 49.8 (d, C_3), 49.0 (d, C_2), 32.3 (t, cyclohexyl C_2), 31.9 (t, cyclohexyl C_6), 26.0 (t, cyclohexyl C_4), 24.5 (t, cyclohexyl C_3 and C_5), 21.6 (q, Ar–CH_3).

***cis*-1-Cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)aziridine (11b):** δ 194.6 (s, C=O), 145.4, 139.6, 136.0 (s, aromatic ipso C's), 127.0–128.7 (m, aromatic C–H's), 69.4 (d, N–CH), 46.5 (d, C_3), 42.7 (d, C_2), 32.3 (t, cyclohexyl C_2), 31.9 (t, cyclohexyl C_6), 25.9 (t, cyclohexyl, C_4), 24.8 (t, cyclohexyl, C_3 and C_5), 13.5 (q, CH_3).

Methyl *cis*-1-Isopropyl-2-(*p*-biphenyl)-3-aziridinecarboxylate (15b):[11a] δ 168.7 (s, C=O), 140.6, 140.4 (s, aromatic ipso C's), 126.5–128.5 (m, aromatic C–H's), 61.2 (d, N–CH), 47.4 (d, C_2), 45.2 (d, C_3), 21.8 (q, CH_3), 21.4 (q, CH_3).

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Registry No. —**1a,** 40208-64-8; **2a,** 6372-52-7; **2b,** 7570-82-3; **3a,** 32044-34-1; **3b,** 32044-33-0; **4a,** 6476-12-6; **4b,** 6372-57-2; **5a,** 32044-36-3; **5b,** 32044-35-2; **6a,** 2211-61-2; **6b,** 2211-65-6; **7/8,** 64600-17-5; **9b,** 20847-26-1; **10a,** 6372-29-8; **10b,** 6476-39-7; **11a,** 32044-50-1; **11b,** 6372-59-4; **12a,** 64611-65-0; **13,** 6372-55-0; **14,** 64600-18-6; **15a,** 23214-22-4; **15b,** 23214-21-3.

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(32) As a check for solvent effects by the $CDCl_3$, selected samples were run with with $CDCl_3$ and Me_4Si; however, the chemical shifts obtained [relative to Me_4Si ($\delta = 0.0$)] were *identical* in all respects with samples run with $CDCl_3$ only.
(33) See ref 20, p 48, for details on how the norbornyl carbons were assigned; for the norbornylaziridines, very close ^{13}C signals were averaged as they were representative of different conformers present in solution.
(34) It is interesting to take note of the fact that when F. M. Menger and T. E.

Thanos, *J. Am. Chem. Soc.*, **98**, 3267 (1976), studied amine quaternization rates in *exo*- and *endo*-2-dimethylaminonorborane, the endo amine quaternized 20 times slower than the exo. However, Menger considered this to be a small factor, which is to say that the *endo*-dimethylamino group is not subjected to unusual steric effects within the endo cavity. The ^{13}C data obtained on **7a,b** and **8a,b** indirectly support Menger's observations because the steric substituent effect, as well as the other chemical shift values for the norbornyl carbons, is about the same in both **7** and **8**. However, a greater "freedom of motion" is observed in the exo case, owing to its greater ability to achieve minimum strain since there is some freedom of motion with respect to the *exo*-norbornyl skeleton. On the other hand, for the endo there is less freedom of motion (its cavity is smaller); hence, the hydrogen on the *endo*-α-*N*-alkyl carbon is more rigidly held in a specific orientation, thereby giving it a larger steric compression shift. Of course, the difference in steric shift of the endo (11.6 ppm) vs. exo (10.0 ppm) is quite moderate.

Synthesis of the 2,3-Dihydro-6*H*-1,4-oxazin-2-ones Chiral at C(3) and Asymmetric Induction in Hydrogenation of the Azomethine Bond

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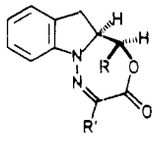
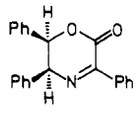
The 2,3-dihydro-6*H*-1,4-oxazin-2-ones **17–26** chiral at C(3) have been prepared, starting from various α-halomethyl aryl ketones and N-protected α-amino acids via intermediary α-(O-α′-N′-protected aminoacyl) hydroxy ketones **1–8** and corresponding hydrobromides **9–16**. 1,3-Asymmetric induction in hydrogeneration of the azomethine bond in **17–24** led to 1,3-disubstituted tetrahydrooxazin-2-ones **27–34**. Their diastereomeric purity was estimated as >98%, based on the analysis of their LIS–NMR spectra, whereas their "3,5-cis" relative configuration was proposed on the grounds of the direction taken by the hydrogenation, based on the conformational analysis of the starting 2,3-dihydro derivatives **17–24**. Heterogeneously catalyzed hydrogenation of the chiral six-membered azomethine derivatives, investigated for the short series of ligands (Me, *i*-Pr, Bz) at the original chiral center, revealed that conformational rigidity around an azomethine bond ensures high diastereoselectivity of the process regardless of the spatial requirements of the larger group on the first center.

Hydrogenation of the azomethine double bond with concurrent asymmetric induction is the most widely used method for preparing chiral compounds with an amino group attached to an asymmetric carbon atom. Knowledge of the greatest significance in this field came mostly from studies by Hiskey and Northrop,[1-3] Harada,[4-6] and Corey.[7,8] Conformational rigidity of the substrate, usually much higher in cyclic than in open-chain azomethine derivatives, significantly enhances the diastereoselectivity of hydrogenation. Thus, reductions of the six- and seven-membered substrates I and II, as carried



I R
a H
b CH_3

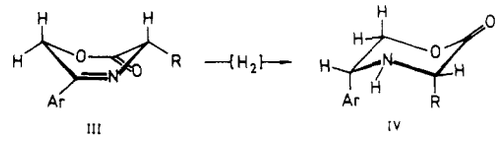


II

out by Corey[6,7] and Kagan,[9] respectively, resulted in nearly 100% stereoselectivity. A recent report[10] of another highly diastereoselective hydrogenation of 2-propyl-5-methyl-$\Delta^{1,2}$-octahydroquinolin in the last step of *d,l*-pumiliotoxin synthesis is also relevant.

Obviously, the high nonequivalence of the diastereotopic faces about the azomethine bond is largely accentuated in cyclic substrates like I and II, which enables a highly stereoselective approach of the reducing agent (diastereoface differentiating reaction[11]). As a part of a wider synthetic program encompassing the preparation of various chiral compounds by diastereoselective azomethine double-bond hydrogenation, we have embarked upon a more detailed study of the diastereoselectivity in 1,3-asymmetric induction obtained with cyclic, six-membered azomethine substrates. Results from this study are the subject of this report.

Scheme I



III IV

Asymmetric hydrogenation of the compounds characterized by the general formulas III, i.e., derivatives of 2,3-dihydro-6*H*-1,4-oxazin-2-ones, has been chosen as an appropriate model reaction (Scheme I).

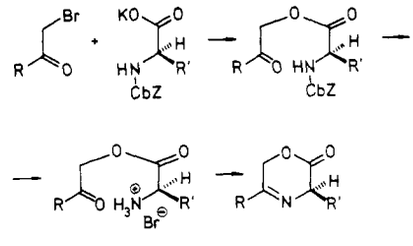
The envisaged route leading to the azomethine substrates III is shown in Scheme II.

It consists of three steps and starts from easily available prochiral compounds, α-halomethyl ketones, and their equally available chiral counterparts, α-amino acids. This route should lead to C(3)-chiral derivatives III possessing various groups at the inducing chiral center. This, in turn, should allow a study on the dependence of the diastereoselectivity of hydrogenation on the steric requirements of the larger groups R′ on the C(3) atom.

Results and Discussion

To start the synthesis of III according to Scheme II, α-halomethyl ketones and potassium salts of N-protected α-

Scheme II



0022-3263/78/1943-1355$01.00/0