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Regiochemical Control of the Ring Opening of Aziridines by Means of Chelating Processes. 2. Synthesis and Ring-Opening Reactions of Aziridines Derived from 5,6-Dihydro-2*H*-pyran and of the Diastereoisomeric cis- and trans-Aziridines Derived from 3-(Benzyloxy)cyclohexene, 2-(Benzyloxy)-3,6-dihydro-, and 2-(Benzyloxy)-6-methyl-3,6-dihydro-2*H*-pyran

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Abstract: The regiochemical outcome of the ring opening of the activated and unactivated title aziridines was examined. In some cases a nice degree of regiocontrol can be obtained depending on the opening reaction conditions (standard, metal-assisted, or under acid-proton catalysis). The results have been rationalized by admitting the incursion, under appropriate reaction conditions, of chelated bidentate structures in which the metal or, in some cases, the proton is coordinated between the aziridine nitrogen and the *O*-heterofunctionality.
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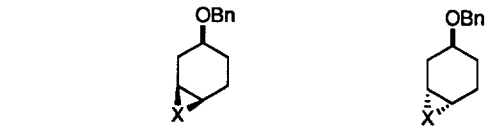
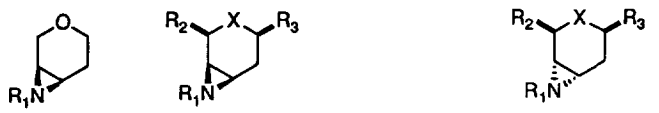
The regio- and stereochemical control of the ring-opening reactions of small-membered heterocycles such as oxiranes and aziridines can be useful in the synthesis of polyfunctionalized complex molecules such as natural compounds. Whereas the stereochemistry of the ring-opening process of these heterocycles is usually anti,[1-3] the control of the regioselectivity of the ring-opening of non-symmetrical systems is sometimes not easy to obtain. The presence of a remote polar group turned out to be effective to obtain in some cases a nice regiochemical control of the ring-opening of oxiranes by metal-assisted chelation processes.[4] The best results were observed with the conformationally semirigid cis epoxide **1** in which the appropriate use of chelating or non-chelating conditions (metal salt-promoted or standard reaction conditions, respectively) led to a rigid control of the regioselectivity.[5] More recently, a regiochemical study of the corresponding aziridines (**3-4**) showed that the cis diastereoisomers **3** were able to determine a nice regioalternating process depending on the reaction conditions.[6] Unlike the corresponding reactions of the cis epoxide **1**,[5] the incursion of chelating processes into the reactions of aziridines **3** is highly effective also under protic acid catalysis.[6]

In consideration of the attractive results obtained with aziridines **3**,[6] we have now extended our examination to other aziridine systems whose corresponding epoxides have previously been studied in our laboratories with satisfactory results,[4,7-9] that is to say the activated and non-activated aziridines **5-8**, **9-12**, **13-18**, and **19-23** derived from the olefins **24**, **26-28**, respectively. Cis and trans aziridines **9-12**, which can be considered as regioisomers of the previously studied aziridines **3-4**,[6] have the polar group (OBn) linked to the cyclohexane ring, whereas in the aziridines **5-8** the polar group (the pyranosidic oxygen) is inserted into



1 X=O **2**
3 X= NH, NCOOEt, NTs **4**



5, R_1=H
6, R_1=COOEt
7, R_1=COOBn
8, R_1=Ts

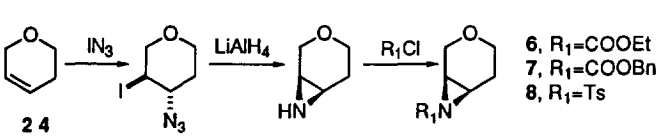
9	R_1=R_3=H; R_2=OBn; X=CH_2	**10**
11	R_1=COOEt; R_3=H; R_2=OBn; X=CH_2	**12**
13	R_1=R_2=H; R_3=OBn; X=O	**14**
15	R_1=COOEt; R_2=H; R_3=OBn; X=O	**16**
17	R_1=Ts; R_2=H; R_3=OBn; X=O	**18**
19	R_1=H; R_2=Me; R_3=OBn; X=O	**20**
21	R_1=COOEt; R_2=Me; R_3=OBn; X=O	**22**
	R_1=Ts; R_2=Me; R_3=OBn; X=O	**23**

the cyclic system. As for the aziridines **13-18** and **19-23**, the polar functionality is both directly inserted into the cyclic system (the pyranosidic oxygen) and present on the cyclic system itself (the OBn group). Our interest in aziridines **5-23**, and in particular in the pyranosidic ones (**5-8**, **13-23**), was also due to the fact that these systems, structurally related to deoxy aminosugars, can profitably be utilized for the synthesis of natural compounds or some their fragments. In this sense, when this work was in progress, the preliminary results obtained with cis aziridines **15** and **17** showed us the possibility of carrying out a new completely stereoselective synthesis of the enantiopure amino sugar component (E ring) of Calicheamicin γ_1^I.[10]

Results

The synthesis of aziridines **5-8** started from the reaction of olefin **24** with IN_3 to give the iodo azide **25**.[11a] Reduction of **25** with $LiAlH_4$ afforded the unsubstituted aziridine **5**[11b] which was then transformed into the corresponding *N*-substituted aziridines **6-8** by usual procedures (Scheme 1).

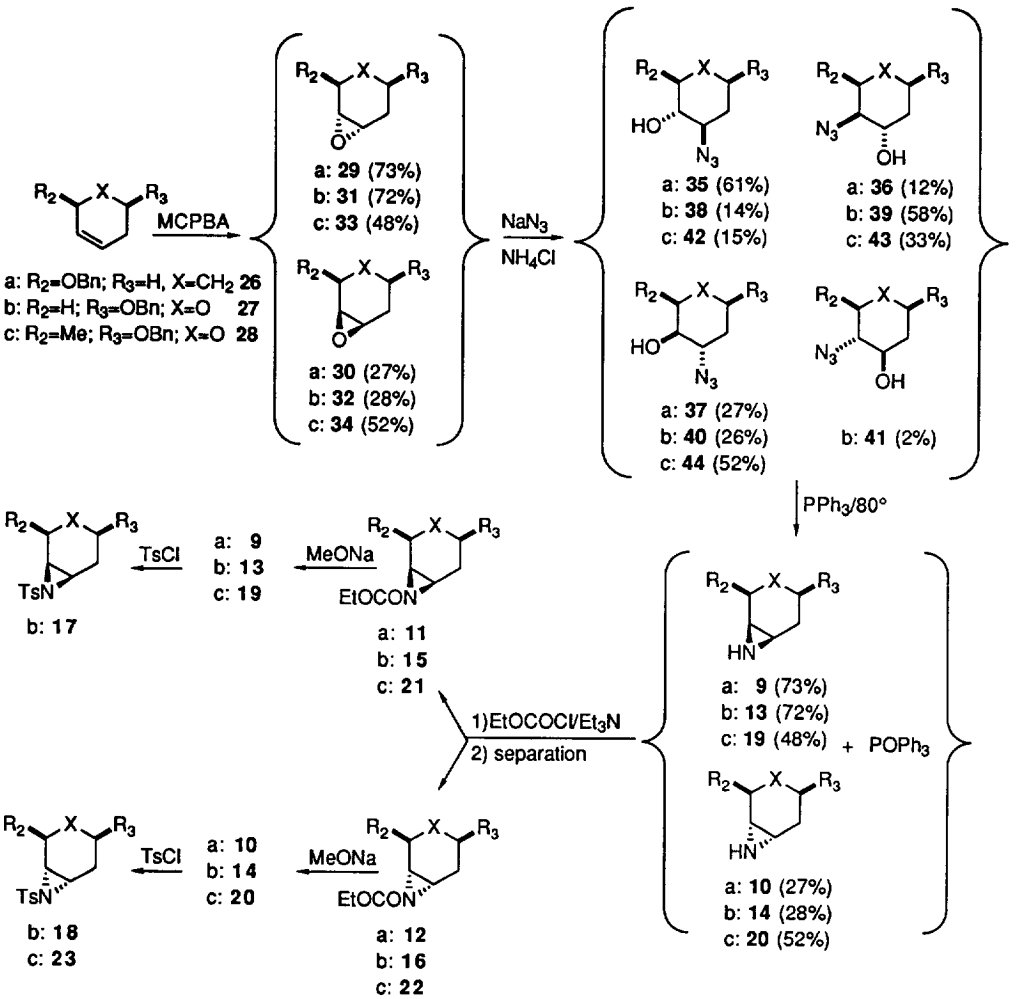
Scheme 1



24 **25** **5**

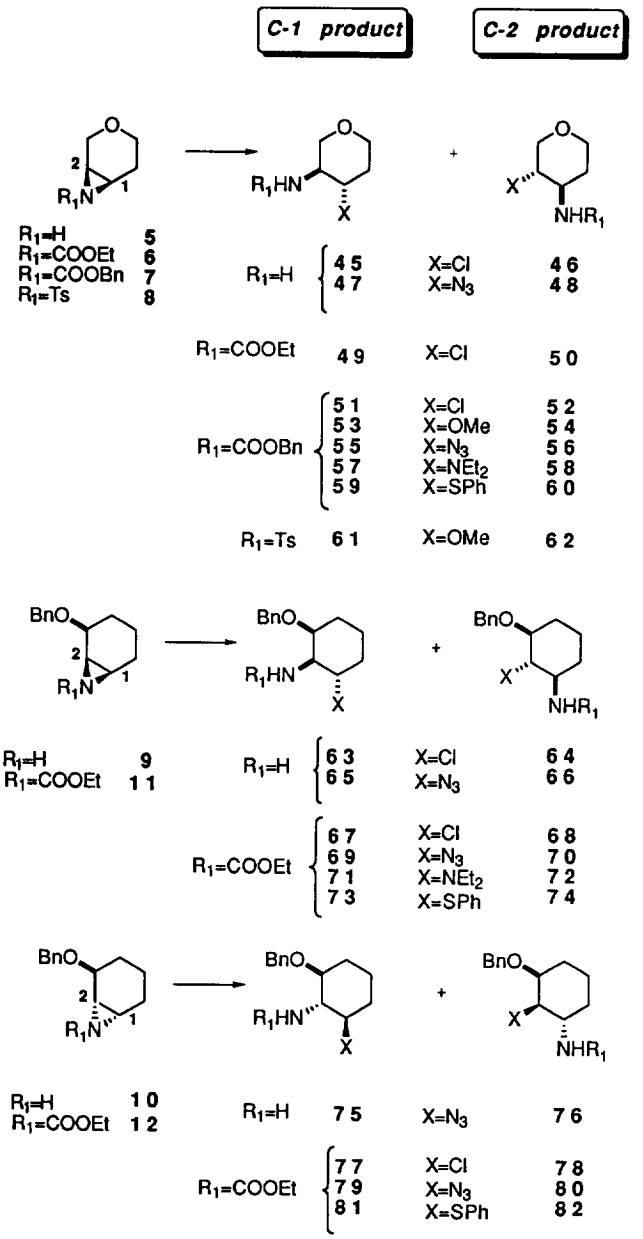
Aziridines **9-10** were prepared by treatment of the 73:27 mixture of epoxides trans **29** and cis **30**, obtained by reaction of olefin **26** with *m*-CPBA,[4] with NaN_3 in aqueous methanol in the presence of NH_4Cl to give a 61:12:27 mixture of the azido alcohols **35-37**.[4] Treatment of this mixture with Ph_3P[12] yielded a 73:27

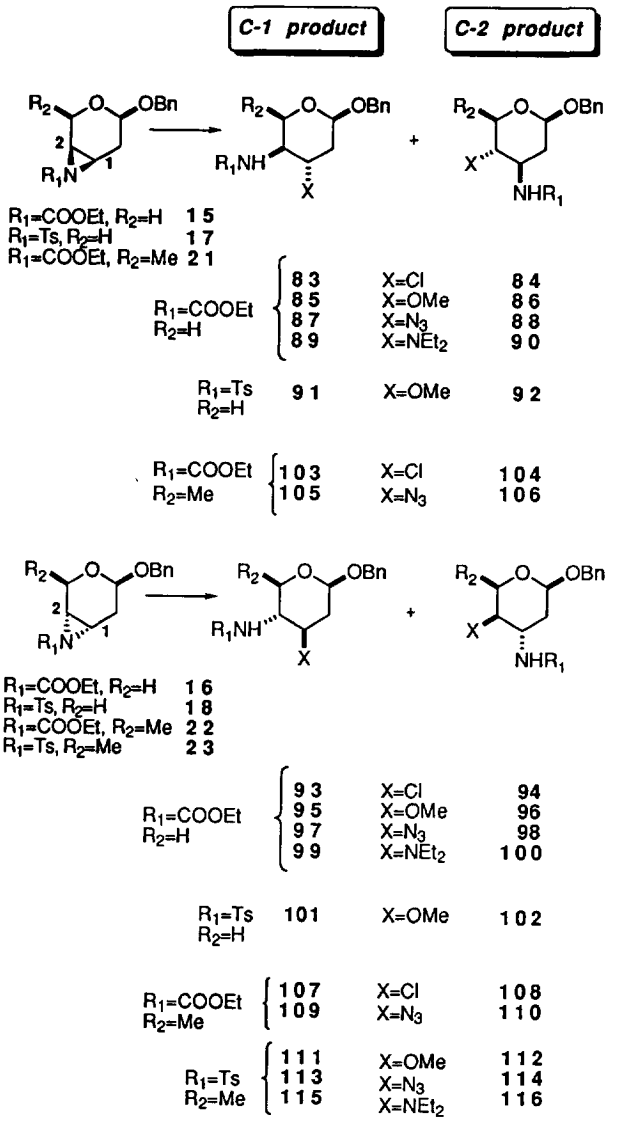
Scheme 2



mixture of the *N*-unsubstituted aziridines cis **9** and trans **10** contaminated with a consistent amount of triphenylphosphine oxide (Ph_3PO). In order to avoid the somewhat difficult chromatographic separation between aziridines **9** and **10** and Ph_3PO, the crude reaction mixture was treated with ethyl chloroformate (EtOCOCl), which transformed **9** and **10** into the corresponding *N*-COOEt substituted aziridines **11** and **12.** Aziridines **11** and **12** were easily separated from Ph_3PO and obtained in a pure state by flash chromatography. Treatment of aziridines **11** and **12** with MeONa in methanol at rt afforded pure aziridines **9** and **10** (Scheme 2). Aziridines **13-16** and **19-22** were prepared by similar synthetic procedures, starting from the known olefins **27**[8] and **28**,[9] respectively. The *N*-tosyl aziridines **17**, **18** and **23** were prepared by reaction of the corresponding *N*-unsubstituted aziridines **13**, **14**, and **20**, with TsCl in anhydrous pyridine (Scheme 2).

Scheme 3


C-1 product
C-2 product
R1=H 5
R1=COOEt 6
R1=COOBn 7
R1=Ts 8
R1=H 45 47 X=Cl X=N3 46 48
R1=COOEt 49 X=Cl 50
R1=COOBn 51 53 55 57 59 X=Cl X=OMe X=N3 X=NEt2 X=SPh 52 54 56 58 60
R1=Ts 61 X=OMe 62
R1=H 9
R1=COOEt 11
R1=H 63 65 X=Cl X=N3 64 66
R1=COOEt 67 69 71 73 X=Cl X=N3 X=NEt2 X=SPh 68 70 72 74
R1=H 10
R1=COOEt 12
R1=H 75 X=N3 76
R1=COOEt 77 79 81 X=Cl X=N3 X=SPh 78 80 82

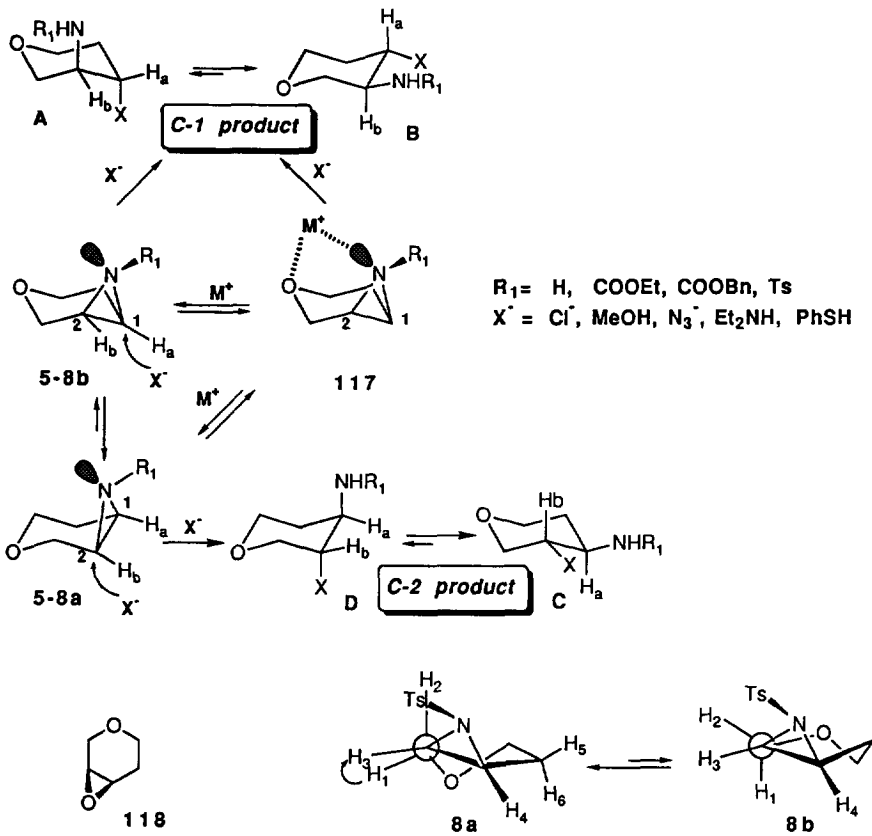


Some of the aziridines prepared (**5-8**, **9-12**, **15-18**, and **21-23**) were subjected to ring-opening reactions with nucleophiles carried out under conditions (standard, proton acid-catalyzed, and metal salt-promoted)[13] which, in the case of the previously studied epoxides **1-2**, and **29-34**[5a,7-9] and aziridines **3-4**,[6] have given clear evidence of the incursion of chelated species into the opening processes. The results obtained are reported in the Tables 1-3. The relative amounts of the regioisomeric products (*C-1* and *C-2 products*, Scheme 3)[14] obtained in the addition reactions were determined by integration of the easily detectable signals of protons H_a, H_b and H_c of the two regioisomers (when present) in the ^1H NMR spectra of the crude reaction mixtures (Schemes 4-7).

Discussion

The regiochemical results obtained in the ring-opening reactions of the cis and trans aziridines **5-8**, **9-12**, **15-18**, and **21-23** showed a close correlation with the results observed in the corresponding reactions of the previously examined epoxides[4,7-9] apart from some differences in the case of the reactions carried out under protic acid catalysis.

Scheme 4



The opening reactions of the tetrahydropyranyl aziridines **5-8**, carried out under standard conditions,[13] showed a high C-1 selectivity (entries 3, 12, 13, 17-19, and 22, Table 1), with the only exception of the aminolysis of **7** in which an opposite C-2 selectivity was observed (entry 15, Table 1) and the Cl^- addition reactions to **6** and **7** which were not selective (entries 6 and 8, Table 1). Evidently, the electron-withdrawing effect of the pyranosidic oxygen, disfavoring the nucleophilic attack on the nearby C-(2) aziridine carbon, largely forces aziridines **5-8** to react at the C-(1) aziridine carbon by a diaxial ring opening[15] of its less stable conformation **b** (Scheme 4). On the contrary, the formation of *C-2 products* in the aminolysis should

reasonably arise from an axial attack of the nucleophile on the more stable conformation **a**. However, as already pointed out for the corresponding reaction of the epoxide **118** (Scheme 4) where a similar behavior was observed,[7] it is not easy to rationalize the different regiochemical behavior of the aminolysis compared with the other opening reactions.

Table 1. Regioselectivity of the Ring Opening Reactions of the Aziridines 5-8 Under Standard and Chelating Conditions.

entry	aziridine	reagents	solvent	reaction time and temperature	*C-1 product*		*C-2 product*		yield %
1	**5**	HCl	Et_2O	1h (0°C)	>99	**45**	**46**	<1	87
2	**5**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	18h (60°C)	>99	**47**	**48**	<1	92
3	**5**	NaN_3	DMSO	48h (100°C)	>99			<1	28
4	**5**	$NaN_3/Mg(ClO_4)_2$ 0.5M	THF	18h (60°C)	>99			<1	86
5	**6**	HCl	$CHCl_3$	10 min (rt)	>99	**49**	**50**	<1	99
6	**6**	NaCl	DMF	7 days (100°C)	50			50	96
7	**7**	HCl	$CHCl_3$	10 min (rt)	>99	**51**	**52**	<1	98
8	**7**	NaCl	DMF	7 days (100°C)	50			50	50[a]
9	**7**	$MeOH/H_2SO_4$	MeOH	2h (rt)	>99	**53**	**54**	<1	99
10	**7**	$MeOH/LiClO_4$ 17M	MeOH	2h (80°C)	complex mixture				
11	**7**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	3h (80°C)	70	**55**	**56**	30	98
12	**7**	NaN_3	DMSO	5h (80°C)	84			16	44
13	**7**	NaN_3	DMF	24h (rt)	70			30	80
14	**7**	$NaN_3/LiClO_4$ 2M	MeCN	1h (80°C)	>99			<1	85
15	**7**	$NHEt_2$	EtOH	48h (80°C)	26	**57**	**58**	74	88
16	**7**	$NHEt_2/LiClO_4$ 2M	MeCN	2h (80°C)	80			20	86
17	**7**	$PhSH/NEt_3$	MeOH	18 h (rt)	>99	**59**	**60**	<1	99
18	**7**	PhSH	DMF	2h (80°C)	>99			<1	88
19	**7**	PhSNa	DMF	1h (rt)	>99			<1	86
20	**7**	$PhSH/LiClO_4$ 2M	MeCN	3h (80°C)	>99			<1	98
21	**8**	$MeOH/H_2SO_4$	MeOH	1h (rt)	>99	**61**	**62**	<1	98
22	**8**	MeONa	MeOH	1h (rt)	85			15	93
23	**8**	$MeOH/LiClO_4$ 17M	MeOH	4 days (80°C)	>99			<1	85

[a] The low yield is the consequence of the deprotection of the starting aziridine **7**.

When the reactions of aziridines **5-8** were carried out under metal-salt promoted reaction conditions (chelating conditions),[13] an increase in the C-1 selectivity was always found (entries 14, 16, and 23, Table 1), apart, obviously, from the reactions which were already completely C-1 selective under standard conditions.

These results can be explained by proposing the intermediacy of chelated-bidentate structures mediated by the metal ion (Li^+), such as **117**, in which aziridines **5-8** are forced to adopt the less stable conformation **b**: the usual axial attack of the nucleophile necessarily leads to *C-1 products*. A marked increase in C-1 selectivity was observed also on passing from standard reaction conditions to reactions carried out under protic acid catalysis[13] (entries 5, 7, 9, 11 and 21, Table 1), indicating that in the case of aziridines **5-8**, the incursion of the chelated intermediate structure of type **117** (with $M^+=H^+$) can be mediated also by the proton (Scheme 4).

The complete or high C-1 selectivity observed in the reactions of the cis aziridines **11**, **15**, **17**, and **21** under standard conditions (entries 5, 7, 9, 11, 15, 19, 21, 24, 27, and 28, Table 2) can be rationalized on the basis of a preferential reactivity of these aziridines in their respective more stable conformation a (Schemes 5

Scheme 5

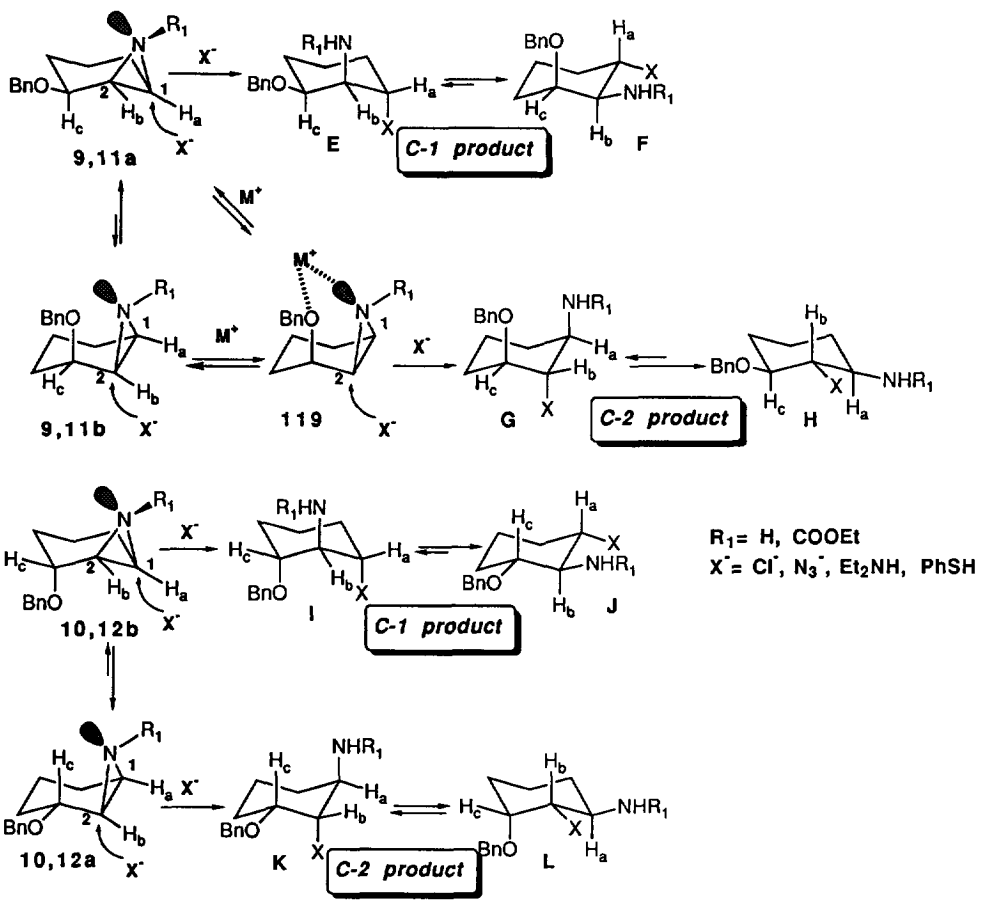


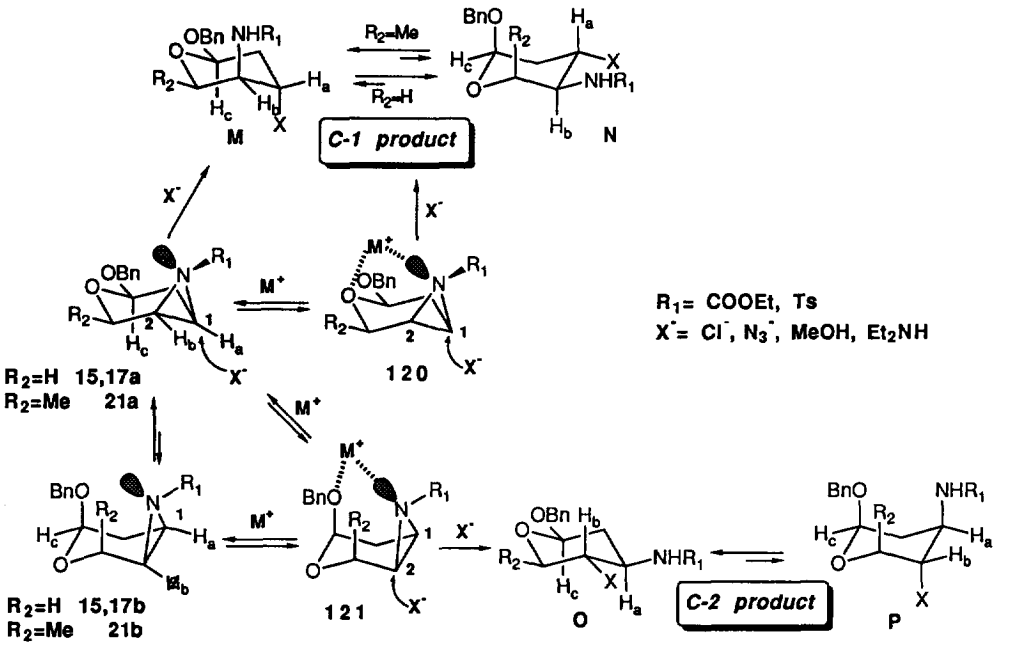
Table 2. Regioselectivity of the Ring Opening Reactions of the Cis Aziridines 9, 11, 15, 17, and 21 Under Standard and Chelating Conditions.

entry	aziridine	reagents	solvent	reaction time and temperature	*C-1*	*product*	*C-2*	*product*	yield %
1	**9**	HCl	Et_2O	1h (0°C)	>99	**63**	**64**	<1	85
2	**9**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	6h (60°C)	>99	**65**	**66**	<1	99
3	**9**	$NaN_3/Mg(ClO_4)_2$ 0.5 M	THF	6h (60°C)	>99			<1	80
4	**11**	HCl	$CHCl_3$	10 min (rt)	>99	**67**	**68**	<1	98
5	**11**	NaCl	DMF	48h (120°C)	>99			<1	30
6	**11**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	4h (80°C)	>99	**69**	**70**	< 1	98
7	**11**	NaN_3	DMF	6h (80°C)	>99			<1	82
8	**11**	$NaN_3/LiClO_4$ 2M	MeCN	4h (80°C)	>99			<1	75
9	**11**	$NHEt_2$	EtOH	4 days (80°C)	>99	**71**	**72**	<1	85
10	**11**	$NHEt_2/LiClO_4$ 2M	MeCN	6h (80°C)	>99			<1	20[a]
11	**11**	$PhSH/NEt_3$	MeOH	3 days (rt)	>99	**73**	**74**	< 1	99
12	**11**	$PhSH/LiClO_4$ 2M	MeCN	5h (80°C)	66			3 4	95
13	**15**	HCl	$CHCl_3$	10 min (rt)	75	**83**	**84**	25	92
14	**15**	HCl	CCl_4	10 min (rt)	89			11	98
15	**15**	NaCl	DMF	3 days (110°C)	76			24	85
16	**15**	$MeOH/H_2SO_4$	MeOH	10 min (rt)	>99	**85**	**86**	< 1	94
17	**15**	$MeOH/LiClO_4$17M	MeOH	4h (80°C)	>86			*b*	74
18	**15**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	2h (80°C)	>99	**87**	**88**	< 1	84
19	**15**	NaN_3	DMF	2h (80°C)	>99			<1	90
20	**15**	$NaN_3/LiClO_4$ 5M	MeCN	2h (80°C)	28			72	94
21	**15**	$NHEt_2$	EtOH	24h (80°C)	84	**89**	**90**	16	75
22	**15**	$NHEt_2/LiClO_4$ 2M	MeCN	2h (80°C)	16			84	94
23	**17**	$MeOH/H_2SO_4$	MeOH	30 min (rt)	>99	**91**	**92**	< 1	98
24	**17**	MeONa	MeOH	1h (rt)	>99			<1	98
25	**17**	$MeOH/LiClO_4$17M	MeOH	4 days (80°C)	26			74	98
26	**21**	HCl	$CHCl_3$	10 min (rt)	>99	**103**	**104**	<1	99
27	**21**	NaCl	DMF	4 days (110°C)	>99			<1	30
28	**21**	NaN_3	DMF	4 days (rt)	>99	**105**	**106**	<1	92
29	**21**	$NaN_3/LiClO_4$ 2M	MeCN	4h (80°C)	>99			<1	96

[a] The low yields are the consequence of a partial deprotection of the starting aziridine **11**. [b] A complex mixture was obtained containing ether **85** (70%0 and two other inseparable, unidentified compounds (30%).

and 6), the electron-withdrawing inductive effect of the *O*-heterofunctionality being a possible further favoring factor.[7,8] When the same reactions of cis aziridines **15** and **17** were carried out under metal salt-promoted conditions in a polar aprotic solvent ($LiClO_4$ in MeCN), a satisfactory reverse of selectivity (from

Scheme 6



C-1 to C-2 selectivity) was observed and consistent amounts (72-84%) of *C-2 products* are obtained in some cases (entries 20, 22, and 25, Table 2). These results can be explained by admitting the incursion of chelated bidentate species such as **121** (R_2=H) in which the coordination through the metal of the aziridine nitrogen with the oxygen of the OBn functionality forces the aziridine to adopt the less stable conformation **b**. The axial attack of the nucleophile on **121** (R_2=H) necessarily affords *C-2 products* (Scheme 6). The C-2 selectivity observed in the reactions of the cis aziridine **11** under chelating conditions is only partial (34%) and limited to the opening reaction with PhSH (entry 12, Table 2). This behavior is reasonable, considering that the reactivity on the C-(2) carbon of the corresponding intermediate chelated structure **119** (Scheme 5) appears to be decidedly diminished by the combination of two unfavorable effects: *i*) the electron-withdrawing effects of the nearby benzyloxy group, and *ii*) all the stereoelectronic factors implied in the chelation-controlled ring-opening of these systems.[16] In this situation only a strong nucleophile such as PhSH can attack the C-(2) aziridine carbon, as previously observed in the case of the corresponding epoxide **30**.[4]

The complete C-1 selectivity observed in the opening reactions of the cis aziridine **21** under standard conditions was not modified when the same reactions were carried out under chelating conditions. This could mean that a chelated bidentate structure such as **121** (R_2=Me) involving the exocyclic OBn functionality is not formed in this case, with the alternative chelated bidentate structure **120** (R_2=Me) involving the endocyclic

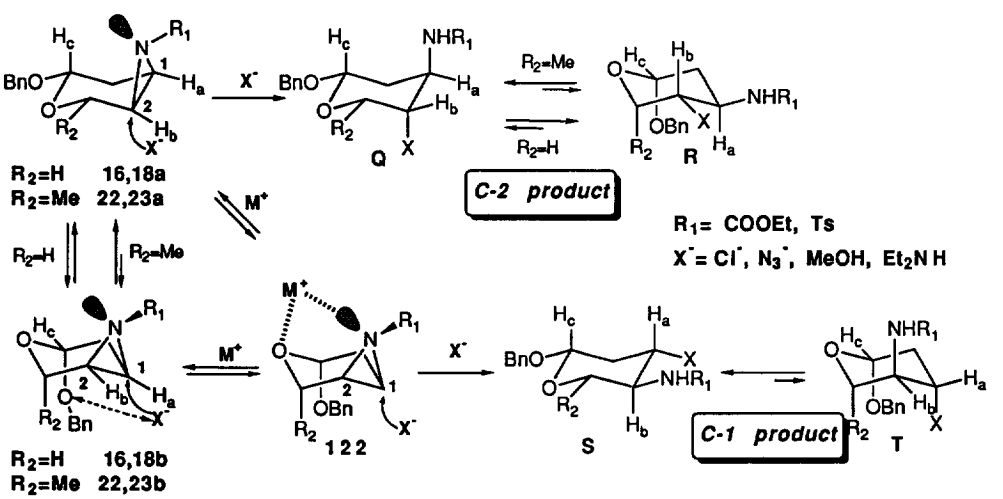
pyranosidic oxygen being largely favored. The reason for this preference should lie in the fact that in **121** (R_2=Me), the particular axial disposition of the methyl group can sterically hinder the insertion of the metal between the two heterofunctionalities (the aziridine nitrogen and the OBn group) to the point that such a species cannot be formed at all (Scheme 6).

No change in selectivity was observed on passing from standard non-chelating conditions to protic acid catalysis (entries 4, 6, 13, 14, 16, 18, 23, and 26, Table 2), suggesting that in the case of **11**, **15**, **17** and **21** a chelated bidentate structure such as **119**, from **11**, or **121** (R_2=H or Me), from **15**, **17** and **21**, in which M^+=H^+, is not operative (Schemes 5 and 6). In the case of **15**, **17**, and **21**, an alternative explanation could be found in a preference of the proton to coordinate the aziridine nitrogen and the endocyclic oxygen, as shown in structure **120** (M^+=H^+, Scheme 6), thus forcing the aziridines to react in their more stable conformation **a**, as under standard conditions, leading necessarily to similar results.

As for the trans aziridines **10** and **12**, where no chelation process is possible, a clear prevalence of the C-1 selectivity was observed in all operating conditions, in agreement with the dependence of the regioselectivity exclusively on the inductive effect of the substituent (OBn) (Table 3). As a consequence, aziridines **10** and **12** preferentially react through their less stable conformation **b**, having the benzyloxy group axial, in order to allow the axial nucleophilic attack[15] on the aziridine C-(1) carbon (Scheme 5).

The results obtained in the opening reactions of the trans aziridines **16**, **18**, **22** and **23** under standard conditions, show that the regioselectivity depends on the type of the nucleophile (Table 3). The C-2 selectivity observed with negatively charged nucleophiles (Cl^-, N_3^-, and MeO^-, entries 10, 14, 19, 23, 28 and 29, Table 3)

Scheme 7



was rationalized by the negative electrostatic interaction between the attacking nucleophile and the axial OBn group of the aziridine which determines a preferential reactivity of these aziridines in their more stable conformation **a**, in spite of the unfavorable electron-withdrawing inductive effect of the pyranosidic oxygen

Table 3. Regioselectivity of the Ring Opening Reactions of the Trans Aziridines 10, 12, 16, 18, 22 and 23 Under Standard and Chelating Conditions.

entry	aziridine	reagents	solvent	reaction time and temperature	*C-1*	*product*	*C-2*	*product*	yield %
1	**10**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	4h (80°C)	>99	**75**	**76**	<1	99
2	**10**	$NaN_3/Mg(ClO4)_2$ 0.5 M	THF	6h (60°C)	complex		mixture		
3	**12**	HCl	$CHCl_3$	10 min (rt)	85	**77**	**78**	15	99
4	**12**	NaCl	DMF	48h (120°C)	50			50	30
5	**12**	NaN_3	DMF	6h (80°C)	87	**79**	**80**	13	85
6	**12**	$NaN_3/LiClO_4$ 2M	MeCN	6h (80°C)	87			13	86
7	**12**	$PhSH/NEt_3$	MeOH	4h (80°C)	87	**81**	**82**	13	90
8	**12**	$PhSH/LiClO_4$ 2M	MeCN	3 days (80°C)	87			13	90
9	**16**	HCl	CCl_4	10 min (rt)	85	**93**	**94**	15	98
10	**16**	NaCl	DMF	7 days (110°C)	13			87	89
11	**16**	$MeOH/H_2SO_4$	MeOH	10 min (rt)	>99	**95**	**96**	<1	94
12	**16**	$MeOH/LiClO_4$17M	MeOH	4h (80°C)	>99			<1	94
13	**16**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	4 days (80°C)	72	**97**	**98**	28	82
14	**16**	NaN_3	DMF	2h (80°C)	8			92	88
15	**16**	$NaN_3/LiClO_4$ 2M	MeCN	2h (80°C)	71			29	94
16	**16**	$NHEt_2$	EtOH	24h (80°C)	73	**99**	**100**	27	97
17	**16**	$NHEt_2/LiClO_4$ 2M	MeCN	48h (80°C)	88			12	98
18	**18**	$MeOH/H_2SO_4$	MeOH	1h (rt)	>99	**101**	**102**	<1	57
19	**18**	MeONa	MeOH	20 min (80°C)	20			80	98
20	**18**	$MeOH/LiClO_4$17M	MeOH	4 h (80°C)	>99			<1	98
21	**22**	HCl	$CHCl_3$	10 min (rt)	80	**107**	**108**	20	98
22	**22**	NaCl	DMF	8 days (110°C)	>99			<1	26
23	**22**	NaN_3	DMF	24h (80°C)	35	**109**	**110**	65	92
24	**22**	$NaN_3/LiClO_4$ 2M	MeCN	48h (80°C)	39			61	89
25	**23**	$MeOH/H_2SO_4$	MeOH	42h (rt)		no	reaction		
26	**23**	$MeOH/H_2SO_4$	MeOH	30 min (50°C)		no	products		*a*
27	**23**	$MeOH/LiClO_4$17M	MeOH	4 days (80°C)		no	reaction		
28	**23**	MeONa	MeOH	1h (rt)	44	**111**	**112**	56	43
29	**23**	NaN_3	DMF	24h (80°C)	32	**113**	**114**	68	94
30	**23**	$NaN_3/LiClO_4$ 2M	MeCN	24h (80°C)	35			65	96
31	**23**	$NHEt_2$	EtOH	48h (80°C)	71	**115**	**116**	29	96
32	**23**	$NHEt_2/LiClO_4$ 2M	MeCN	48h (80°C)	74			26	97

[a] Reaction products without the OBn group are present.

(Scheme 7).[7,8] When a non-charged nucleophile ($NHEt_2$) is used under standard conditions, no similar negative electrostatic interactions are present, and aziridines **16**, **18**, **22** and **23** can react through their less stable conformation **b** at the electronically more favorable C-(1) carbon (entries 16 and 31, Table 3). An increase in the nucleophilic attack on the aziridine C-(1) carbon of trans aziridines **16** and **18** was always observed on passing from standard (non-chelating) to either metal- or proton-promoted opening conditions (chelating conditions) (entries 9, 13, 15, and 17, Table 3), and in some cases a complete C-1 selectivity was obtained (entries 11, 12, 18, and 20, Table 3). This points to the incursion of a chelated bidentate structure such as **122** (R_2= H, M^+=Li^+ or H^+) in which the aziridines are forced to react in their conformation **b**, leading to *C-1 products*. Nothing like this can be observed in the corresponding reactions of aziridines **22** and **23**. Evidently in these systems, chelated species such as **122** (R_2=Me) cannot be formed, probably due to the unfavorable presence of an axial methyl group (Scheme 7 and Table 3).

In conclusion, the aziridines examined show, under appropriate opening reaction conditions, the intervention of chelated bidentate structures which, in some cases, make it possible to achieve a synthetically useful regioselection similar to that found in the corresponding reactions of the related epoxides.

Structures, Configurations and Conformations

The structure of aziridine **5** was assigned on the basis of its method of synthesis starting from the known olefin **24**. The relative configurations of the aziridines cis **9**, **13**, and **19** and trans **10**, **14**, and **20** were unequivocally demonstrated by their method of synthesis from the known epoxides trans **29**, **31**, and **33** and cis **30**, **32**, and **34**, respectively.[6] The configurations of all the *N*-substituted aziridines were clearly defined by their preparation from the corresponding *N*-unsubstituted ones.

The conformational equilibrium inside the tetrahydropyranyl aziridines **5-8** was determined by means of the nOe of protons H_1, H_2, H_3, and H_4 in aziridine **8** (Scheme 4), whose ^1H NMR spectrum appeared to be the most appropriate for such a determination. Saturation of proton H_1 (δ=3.90 Hz) gives an intense nOe on vicinal aziridine proton H_3 (δ=2.96 Hz) and on the geminal proton H_2 (δ=3.72 Hz). Moreover, saturation of protons H_2 and H_3 gives an intense nOe only on proton H_1, and saturation of proton H_4 (δ=3.10) gives a nOe on both H_5 and H_6 (see Scheme 4). All these data point to a preference for conformation **8a**. In particular, in the alternative conformation **8b**, saturation of both H_1 and H_2 should give an equivalent nOe on the vicinal H_3 proton, contrary to observations. This result is confirmed by the vicinal coupling constant values of protons H_1 and H_2: H_1 shows a $J_{H1,H3}$ value (4.0 Hz) larger than the corresponding $J_{H2,H3}$ (0.7 Hz) for H_2, in accordance with a preference for conformation **8a** (Scheme 4). This clear preference for conformation **8a**, in which the pyranoid oxygen is furthest from the aziridine nitrogen, appears to be reasonably determined by the repulsion between the dipoles associated with the two heteroatoms (oxygen and aziridine nitrogen), an effect favoring conformer **8a** in which this negative effect is minimized.[17] Similar considerations can be reasonably extended to the other aziridines **5-7**.

The conformational equilibrium inside the aziridines **9-23** were determined by examination of the H_c proton α to the OBn group in the ^1H NMR spectra of these compounds. In the cis aziridines **9**, **11**, **13**, **15**, **17**, **19**, and **21** and in the trans aziridines **10**, **12**, **20**, **22**, and **23** the $W_{1/2}$ value (17.2 Hz)[18] or the J value (7.2-9.4 Hz) for proton H_c indicate the corresponding conformer **a**, with the OBn group equatorial, as the more stable

Table 4. ^{1}H NMR and Physical Data for Aziridines 9-23 and Ring Opening Products 45-116.

compd	^{1}H NMR δ			m.p.,°C
	H_a ($W_{1/2}$, Hz)[a,b]	H_b ($W_{1/2}$, Hz)[a,b]	H_c ($W_{1/2}$ or J, Hz)[c]	
9	2.30 (8,6)[a,d]	2.39 (7.8)[a,e]	3.87 (17.3)[f]	liquid
10	[g]	[g]	3.71 (J = 7.5 and 5.0)[e]	liquid
11	2.80 (13.0)[a,d]	2.92 (13.0)[a,e]	3.76 (17.4)[g]	liquid
12	[g]	[g]	3.77 (J = 7.7 and 5.2)[e]	liquid
13	[g]	[g]	4.49 (J = 7.4 and 4.5)[e]	56-58
14	[g]	[g]	[g]	60-62
15	2.72 (15.1)[a,d]	2.55 (8.6)[a,d]	4.37 (J = 7.2 and 5.4)[e]	47.5-48.5
16	2.80 (12.9)[a,e]	2.70 (8.6)[a,e]	4.68 (J = 5.2 and 2.8)[e]	55-56.5
17	3.08 (17.3)[a,d]	2.95 (12.1)[a,e]	4.39 (J = 8.2 and 4.2)[e]	129-130.5
18	3.16 (15.5)[a,d]	3.04 (11.6)[a,e]	4.68 (J = 4.5 and 3.1)[e]	97-99
19	[g]	1.95 (J = 4.7)[a,h]	4.44 (J = 9.2 and 4.0)[e]	liquid
20	2.52 (12.9)[a,f]	[g]	4.89 (J = 8.9 and 3.0)[e]	liquid
21	2.52(12.9)[a,d]	2.45 (8.6)[a,e]	4.40 (J = 9.0 and 4.5)[e]	liquid
22	2.92 (12.9)[a,d]	2.52 (8.6)[a,e]	4.52 (J = 8.6 and 3.1)[e]	liquid
23	3.20 (13.0)[a,d]	2.85 (8.7)[a,e]	4.48 (J = 8.8 and 2.9)[e]	101-102
45	4.40 (23.0)[a,d]	3.16 (20.3)[b,d]		(·HCl) 183-185
47	3.20 (24.0)[b,d]	2.74 (23.5)[a,d]		liquid
49	[g]	3.65 (20.0)[a,f]		83-84.5
51	[g]	3.72 (18.0)[a,f]		89-91.5
52	4.11 (20.0)[a,e]	[g]		121-123
53	[g]	3.66 (17.5)[a,f]		72-74
55	3.37 (25.5)[b,f]	[g]		53-55
57	[g]	3.53 (21.5)[a,f]		52-54
58	3.54 (20.0)[a,f]	[g]		53-55
59	[g]	3.62 (19.5)[a,f]		103-105
61	3.17 (17.5)[b,f]	3.05 (16.0)[a,f]		78-80.5
62	[g]	[g]		116-117
63	4.20 (11.8)[b,f]	[g]	[g]	(·HCl) 191-194
65	3.44 (26.1)[b,d]	2.47 (15.2)[a,e]	3.78 (8.6)[f]	liquid
67	[g]	[g]	[g]	91-93
69	3.50 (25.8)[b,d]	3.65 (25.8)[a,d]	3.80 (8.6)[f]	99-100
71	2.92 (28.1)[b,d]	3.43 (23.7)[a,f]	[g]	liquid
73	3.26 (25.9)[b,d]	3.66 (25.1)[a,d]	3.76 (8.6)[f]	89-91
74	3.89 (23.7)[a,f]	3.30 (17.0)[b,h]	3.64 (15.6)[f]	liquid
75	[g]	2.65 (21.7)[a,h]	[g]	liquid
77	3.97 (27.8)[b,f]	[g]	[g]	127-129
78	[g]	[g]	3.87 (12.9)[f]	liquid
79	[g]	3.27 (23.4)[a,i]	[g]	106-107
81	3.14 (31.6)[b,f]	[g]	[g]	114-116
83	[g]	3.80 (21.6)[a,f]	4.91 (J = 3.0)[j]	101-102
84	[g]	[g]	4.93 (7.4)[f]	115-116
85	[g]	[g]	4.90 (J = 4.5 and 3.1)[e]	liquid
87	[g]	[g]	4.94 (J = 2.8)[j]	46-48
88	3.88 (19.4)[a,f]	3.54 (10.8)[b,f]	4.88 (6.5)[f]	91-92
89	3.12 (25.9)[b,f]	[g]	5.01 (J = 2.8 and 1.0)[e]	liquid

90	3.75 (17.3)[a,i]	*g*	4.69 (*J* = 5.9 and 2.8)[e]	liquid
91	3.47 (20.7)[b,d]	3.08 (12.9)[a,f]	4.86 (*J* = 3.7)[j]	112-113
92	3.54 (13.3)[a,f]	3.24 (6.7)[b,f]	4.81 (6.7)[f]	70-71
93	3.99 (23.7)[b,f]	3.71 (23.7)[a,d]	4.61 (*J* = 6.7 and 3.0)[e]	101-103
94	*g*	*g*	4.95 (*J* = 3.2 and 1.0)[e]	127-129
95	*g*	3.66 (17.3)[a,f]	4.62 (*J* = 4.7 and 3.8)[e]	106-108
97	3.71 (19.4)[b,f]	3.55 (17.3)[a,f]	4.69 (*J* = 4.9 and 3.4)[e]	81-82
98	4.51 (25.9)[a,f]	3.47 (25.9)[b,f]	4.91 (*J* = 3.2 and 1.2)[e]	81-83
99	*g*	3.41 (24.6)[a,f]	4.47 (*J* = 9.3 and 2.1)[e]	88-89
100	3.99 (25.9)[a,f]	*g*	4.87 (*J* = 4.9)[h]	66-68
101	*g*	*g*	4.54 (*J* = 6.3 and 3.2)[e]	126-127
102	*g*	3.11 (26.7)[b,d]	4.82 (*J* = 3.1 and 1.5)[e]	112-114
103	*g*	3.68 (15.1)[a,f]	4.92 (*J* = 6.9 and 4.4)[e]	liquid
105	*g*	3.54 (17.1)[a,f]	4.76 (*J* = 9.1 and 2.8)[e]	liquid
107	*g*	3.28 (23.1)[a,i]	4.50 (*J* = 9.5 and 1.6)[e]	151-153
108	*g*	3.91 (6.7)[b,f]	4.97 (*J* = 3.6)[h]	liquid
111	*g*	*g*	4.42 (*J* = 9.7 and 1.8)[e]	154-156
112	3.60 (13.2)[a,f]	2.97 (8.1)[b,f]	4.60 (*J* = 9.0 and 2.2)[e]	120-121
113	3.19 (28.5)[b,d]	2.95 (25.9)[b,k]	4.48 (*J* = 9.7 and 1.7)[e]	132-133
114	3.56 (12.9)[a,f]	3.36 (6.5)[b,f]	4.65 (*J* = 9.4 and 2.0)[e]	123-125
115	*g*	2.95 (20.5)[a,i]	4.38 (*J* = 9.4 and 1.9)[e]	120-122
116	3.62 (18.7)[a,d]	2.79 (16.4)[b,e]	4.73 (*J* = 3.4)[j]	93-95

Compounds **46, 48, 50, 54, 56, 60, 64, 66, 68, 70, 72, 76, 80, 82, 86, 96, 104, 106, 109,** and **110,** which are not present or present in an insufficient amount in the opening reactions of the corresponding aziridines, are not included. [a] *CH*NHR$_1$ (*CH*NR$_1$ in the case of aziridines **9-23**). [b] *CH*X. [c] *CH*OBn. [d] Doublet of doublets of doublets. [e] Doublet of doublets. [f] Multiplet. [g] The signal overlaps with other signals. [h] Doublet. [i] Quintet. [j] Unresolved triplet. [k] Quartet.

conformer. The low *J* values (4.5-5.2 Hz) observed for proton H_c in the trans aziridines **16** and **18** suggest for these compounds an almost equimolar conformational equilibrium between the corresponding conformers **a** and **b** (Table 4 and Schemes 5-7).

The relative structure of all the regioisomeric pairs (*C-1* and *C-2 products*) from aziridines **5-8** and from the cis and trans aziridines **9-23** was unequivocally assigned on the basis of the ^{1}H NMR spectra of these compounds by means of: *i*) appropriate double resonance experiments on the protons α to the NHR, X, and (only in the case of aziridines **9-23**) OBn groups (protons H_a, H_b, and H_c, respectively, Schemes 4-7), *ii*) examination of the $W_{1/2}$ or *J* value[6,18] of the same protons (Table 4) and *iii*) simple conformational considerations. The relative $W_{1/2}$ or *J* values of the signals of protons H_a, H_b, and H_c for all the opening products indicate the conformational equilibrium within each regioisomer, in which the following conformer should reasonably prevail: **B** (*C-1 products*) and **C** (*C-2 products*) from **5-8**, **F** (*C-1 products*) and **H** (*C-2 products*) from **9** and **11** , **J** (*C-1 products*) from **10** and **12**, **N** (R_2=H, *C-1 products*) and **O** (R_2=H, *C-2 products*) from **15** and **17**, **S** (R_2=H, *C-1 products*) and **R** (R_2=H, *C-2 products*) from **16** and **18**, **M** (R_2=Me, *C-1 products*) from **21**, **S** (R_2=Me, *C-1 products*), and **Q** (R_2=Me, *C-2 products*), from **22** and **23**. In the case of compound **78** (*C-2 product* from **12**) and of compound **116** (*C-2 product* from **23**) an almost equimolar equilibrium between the two conformers **K** and **L** and a prevalence of conformer **R** was observed, respectively.

Experimental Section

For general experimental details, see ref. 5a. Olefin **24**,[17] and the mixtures of epoxides **29** and **30**,[4] **31** and **32**,[8] **33** and **34**[9] were prepared as previously described.

4-Azido-3-iodotetrahydropyran (25). Following a previously described procedure[11a] a suspension of NaN_3 (9.75 g, 0.15 mol) in MeCN (60 mL) was treated dropwise at -20°C with ICl (10.88 g, 67.0 mmol). After 10 min at the same temperature a solution of olefin **24** (5.0 g, 59.5 mmol) dissolved in MeCN (5.0 mL) was added and the reaction mixture was left to warm at rt and stirred at this temperature overnight. Dilution with water, extraction with ether and evaporation of the washed (10% aqueous $Na_2S_2O_3$, and water) organic solvent afforded iodo azide **25** (14.15 g, 94% yield), as a liquid, which was directly utilized in the next step: ^{1}H NMR δ 4.03–4.22 (m, 2H), 3.92 (ddd, 1H, *J*=10.3 and 4.4 Hz), 3.45-3.71 (m, 3H), 2.16 (dddd, 1H, *J*=13.5, 4.6 and 2.3 Hz), 1.83 (dddd, 1H, *J*=13.5, 11.2 and 4.5 Hz). ^{13}C NMR δ 74.03, 67.04, 65.40, 34.30, 29.71. An analytical sample was purified by semipreparative TLC (an 8:2 mixture of hexane an AcOEt was used as the eluant). Extraction of the most intense band afforded pure **25**, as a liquid. Anal.Calcd for $C_5H_8IN_3O$: C, 23.73; H, 3.19; N 16.61. Found: C, 23.56; H, 3.24; N 16.70.

3-Oxa-7-azabicyclo[4.1.0]heptane (5). A suspension of $LiAlH_4$ (4.11 g, 108.1 mmol) in anhydrous Et_2O (160 mL) was treated dropwise at 0°C with a solution of iodo azide **25** (14.15 g, 0.056 mol) in anhydrous Et_2O (10 mL).[11b] The reaction mixture was left to warm at rt and after 1 h stirring at this temperature it was treated with 10% aqueous NaOH in order to destroy the excess of hydride. The organic solution, filtered on celite, was evaporated to give practically pure aziridine **5** (4.66 g, 84% yield): ^{1}H NMR δ 3.93 (d, 2H, *J*=2.0 Hz), 3.60 (ddd, 1H, *J*=11.3 and 5.6 Hz), 3.32 (ddd, 1H, *J*=11.6 and 6.8 Hz), 2.33 (quintet, 1H, *J*=3.2 Hz), 2.17 (ddd, 1H, *J*=6.0 and 1.9 Hz), 1.85-2.00 (m, 2H). ^{13}C NMR δ 66.15, 63.17, 28.84, 27.54, 24.54. An analytical sample was purified by semipreparative TLC (a 7:3:1 mixture of hexane, AcOEt and NEt_3 was used as the eluant). Extraction of the most intense band afforded pure **5**. Anal.Calcd for C_5H_9NO: C, 60.58; H, 9.15; N, 14.13. O 16.14. Found: C, 60.79; H, 9.00; N, 14.40.

7-(Ethoxycarbonyl)-3-oxa-7-azabicyclo[4.1.0]heptane (6). A solution of aziridine **5** (0.20 g, 2.0 mmol) in anhydrous Et_2O (10 mL) in the presence of NEt_3 (2.4 mmol, 0.34 mL) was treated at 0°C with ClCOOEt (2.4 mmol, 0.26 g) under stirring. After 1 h stirring at the same temperature, evaporation of the filtered organic solution afforded a crude reaction product which was filtered through a short silica gel column. Elution with Et_2O afforded pure aziridine **6** (0.328 g, 95% yield), as a liquid: ^{1}H NMR δ 4.16 (q, 2H, *J*=7.2 Hz), 3.99 (d, 2H, *J*=2.5 Hz), 3.53 (ddd, 1H, *J*=11.6, 6.8 and 4.8 Hz), 3.40 (dd, 1H, *J*=11.6 and 5.8 Hz), 2.85 (ddd, 1H, *J*=6.4, 4.7 and 1.6 Hz), 2.71 (ddd, 1H, *J*=6.4 and 2.5 Hz), 1.84-2.15 (m, 2H), 1.28 (t, 3H, *J*=7.2 Hz). ^{13}C NMR δ 163.63, 65.65, 63.11, 62.45, 35.69, 34.98, 23.89, 14.96. Anal.Calcd for $C_8H_{13}NO_3$: C, 56.13; H, 7.65; N, 8.18. Found: C, 56.24; H, 7.70; N, 8.08.

7-(Benzyloxycarbonyl)-3-oxa-7-azabicyclo[4.1.0]heptane (7). Treatment of aziridine **5** (0.50 g, 5.0 mmol) with ClCOOBn (1.024 g, 6.0 mmol) following the procedure previously described for the synthesis of **6**, afforded a crude reaction product (1.29 g) which was subjected to flash chromatography. Elution with a 6:4 mixture of hexane and AcOEt afforded pure aziridine **7** (1.11 g, 94% yield), as a liquid: ^{1}H NMR δ 7.23-7.40 (m, 5H), 5.12 (s, 2H), 3.98-3.94 (m, 2H), 3.30-3.59 (m, 2H), 2.86 (ddd, 1H, *J*= 6.4, 4.8 and 1.4 Hz), 2.72 (ddd, 1H, *J*=6.4, 3.0 and 1.9 Hz), 1.79-2.19 (m, 2H). ^{13}C NMR δ 163.32, 136.29, 129.13, 128.93, 128.84, 68.69, 65.48, 62.42, 35.71, 35.02, 23.67. Anal.Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.74; H, 6.56; N, 6.10.

Synthesis of Aziridines cis 11 and trans 12. A solution of the 27:73 mixture (7.2 g, 0.035 mol) of epoxides cis **30** and trans **29** (from the reaction of olefin **26** with *m*-CPBA)[4] in an 8:1 MeOH/H_2O mixture (75 mL) was treated with NaN_3 (0.175 mol, 11.37 g) and NH_4Cl (0.07 mol, 3.74 g) and the reaction mixture was stirred at 80°C for 18 h. Dilution with ether and evaporation of the washed (saturated aqueous $NaHCO_3$

and water) organic solvent afforded a crude product (8.41 g, 0.034 mmol) consisting of a 61:12:27 mixture of azido alcohols **35**, **36**, and **37** (Scheme 2). This mixture was treated with triphenylphosphine (PPh_3) (8.92 g, 0.034 mmol) and the resulting solution was stirred at rt until evolution of N_2 was observed (about 30 min), and then refluxed overnight.[12] After cooling, the solvent was removed (rotating evaporator) and the residue was repeatedly extracted with petroleum ether. Evaporation of the organic extracts afforded an oily residue (8.39 g) consisting of a 73:27 mixture of aziridines **9** and **10** with PPh_3 and triphenylphosphine oxide ($POPh_3$). Proceeding as previously described for the preparation of **6**, the crude reaction mixture was dissolved in anhydrous Et_2O (100 mL) and treated with ClCOOEt (4.48 g, 0.041 mol) in the presence of NEt_3 (7 mL, 0.041 mol) to give a reaction product consisting of a 73:27 mixture of aziridines cis **11** and trans **12**, which was subjected to flash chromatography. Elution with an 8:2 mixture of hexane and AcOEt afforded pure aziridines cis **11** (5.52 g) and trans **12** (1.93 g) (79% yield).

(1β, 2β, 6β)-2-(Benzyloxy)-7-(ethoxycarbonyl)-7-azabicyclo[4.1.0]heptane (11), a liquid: ^{1}H NMR δ 7.20-7.47 (m, 5H), 4.71 and 4.86 (AB, 2H, J=11.8), 4.17 (q, 2H, J=7.2), 2.92 (dd, 1H, J=6.4 and 3.6 Hz), 2.80 (ddd, 1H, J=6.4, 4.4 and 2.1 Hz), 1.74-1.90 (m, 2H), 1.46-1.72 (m, 4H), 1.29 (t, 3H, J=7.1 Hz), and see Table 4, ^{13}C NMR δ 164.39, 139.26, 128.87, 128.38, 128.03, 72.59, 70.24, 63.06, 39.50, 39.29, 26.79, 23.50, 20.04, 14.90. Anal.Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.68; H, 7.80; N, 4.85.

(1α, 2β, 6α)-2-(Benzyloxy-7-(ethoxycarbonyl)-7-azabicyclo[4.1.0]heptane (12), a liquid: ^{1}H NMR δ 7.23-7.44 (m, 5H), 4.63 and 4.67 (AB, 2H, J=11.8 Hz), 4.15 (q, 2H, J=7.2 Hz), 2.70-2.80 (m, 2H), 1.92-2.09 (m, 1H), 1.64-1.92 (m, 2H), 1.40-1.58 (m, 1H), 1.15-1.47 (m, 2H), 1.28 (t, 3H, J=7.2 Hz), and see Table 4. ^{13}C NMR δ 164.21, 138.81, 129.01, 128.32, 128.23, 73.60, 71.46, 63.03, 40.52, 38.63, 27.45, 24.10, 15.76, 14.92. Anal.Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.89; H, 7.74; N, 4.88.

Synthesis of Aziridines cis 9 and trans 10. The following procedure is typical. A solution of aziridine **11** (1.0 g, 3.64 mmol) in a 1.5M MeONa solution in anhydrous MeOH (20 mL) was stirred at rt for 18 h. After concentration of the solution, the residue was taken up in ether. Evaporation of the washed (saturated aqueous NaCl solution) organic solvent afforded pure **(1β, 2β, 6β)-2-(benzyloxy)-7-azabicyclo[4.1.0]heptane (9)** (0.723 g, 98 % yield), as a liquid: ^{1}H NMR δ 7.20-7.43 (m, 5H), 4.64 and 4.71 (AB, 2H, J=12.0 Hz), 2.39 (dd, 1H, J=5.8 and 4.1 Hz), 2.30 (ddd, 1H, J=6.0, 4.4 and 1.7), 1.68-1.89 (m, 2H), 1.40-1.63 (m, 3H), 1.08-1.34 (m, 1H), and see Table 4. ^{13}C NMR δ 139,49, 128.94, 128.33, 128.07, 73.94, 70.56, 32.90, 32.34, 26.69, 24.19, 19.95. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.95; H, 8.68; N, 6.70.

The same procedure starting from **12** (0.2 g) afforded pure **(1α, 2β, 6α)-2-(benzyloxy)-7-azabicyclo[4.1.0]heptane (10)** (0.145 g, 98 % yield), as a liquid: ^{1}H NMR δ 7.20-7.47 (m, 5H), 4.62 (s, 2H), 2.23-2.40 (m, 2H), 1.63-1.98 (m, 3H), 1.06-1.57 (m, 3H), and see Table 4. ^{13}C NMR δ 139.24, 129.01, 128.30, 128.18, 75.10, 71.46, 34.10, 30.75, 27.54, 24.77, 15.79. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 77.00; H, 8.55; N, 6.69.

Synthesis of Aziridines 13-16. Following the procedure previously described for the synthesis of aziridines **9-12**, the treatment of the 28:72 mixture (3.4 g) of epoxides cis **32** and trans **31** (from the reaction of olefin **27** with *m*-CPBA)[8] with NaN_3/NH_4Cl in 8:1 $MeOH/H_2O$ afforded a 14:58:26:2 mixture (3.31 g, 97.3% yield) of azido alcohols **38**, **39**, **40** and **41** (Scheme 2), which was directly treated with PPh_3 to give a 72:28 mixture (3.82 g) of aziridines cis **13** and trans **14** with substantial amounts of PPh_3 and $POPh_3$. The treatment of this crude mixture with ClCOOEt afforded a corresponding mixture (72:28) of aziridines cis **15** and trans **16** (3.95 g) which was subjected to flash chromatography. Elution with an 8:2 mixture of hexane:AcOEt afforded pure aziridine **15** (1.80 g) and **16** (0.70 g) (68% yield).

(1β, 4β, 6β)-4-(Benzyloxy)-7-(ethoxycarbonyl)-3-oxa-7-azabicyclo[4.1.0]-heptane (15), a solid, mp 47.5-48.5°C (from hexane): ^{1}H NMR δ 7.20-7.37 (m, 5H), 4.48 and 4.70 (AB, 2H, J=12.1 Hz), 4.29 (d, 1H, J=12.7 Hz), 4.14 (q, 2H, J=7.1 Hz), 3.83 (dd, 1H, J=12.7 and 2.0 Hz), 2.72 (ddd, 1H, J=5.7 and 2.3 Hz), 2.55 (ddd, 1H, J=6.7 and 2.0 Hz), 2.04-2.16 (m, 2H), 1.25 (t, 3H, J=7.1 Hz), and see Table 4. ^{13}C NMR δ 162.75,

137.88, 128.78, 128.38, 128.15, 97.30, 69.93, 62.77, 62.56, 34.41, 33.58, 28.35, 14.78. Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 65.10; H, 7.15; N, 4.80.

(1α, 4β, 6α)-4-(Benzyloxy)-7-(ethoxycarbonyl)-3-oxa-7-azabyciclo[4.1.0]-heptane (16), a solid, mp 55-56.5°C (from hexane): ^{1}H NMR δ 7.21-7.43 (m, 5H), 4.43 and 4.68 (AB, 2H, J=11.9 Hz), 4.14 (q, 2H, J=7.1 Hz), 4.10 (dd, 1H, J=12.2 and 2.8 Hz), 3.97 (d, 1H, J=12.5 Hz), 2.80 (unresolved dd, 1H, J=6.0 Hz), 2.70 (dd, 1H, J=6.5 and 1.9 Hz), 2.30 (dd, 1H, J=15.1 and 4.8 Hz), 1.93 (ddd, 1H, J=15.1, 6.0 and 2.7 Hz), 1.26 (t, 3H, J=7.1 Hz), and see Table 4. ^{13}C NMR δ 162.94, 137.85, 128.90, 128.32, 128.23, 93.81, 69.73, 62.83, 57.83, 34.79, 33.20, 27.77, 14.78. Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.87; H, 6.88; N, 5.20.

Separate treatment of aziridines **15** (0.465 g) and **16** (0.40 g) with a 1.5 M MeONa solution in anhydrous MeOH afforded pure aziridines cis **13** (0.336 g, 98% yield) and trans **14** (0.29 g, 98% yield).

(1β, 4β, 6β)-4-(Benzyloxy)-3-oxa-7-azabicyclo[4.1.0]heptane (13), a solid, mp 56-58°C (from hexane) : ^{1}H NMR δ 7.20-7.44 (m, 5H), 4.19 and 4.50 (AB, 2H, J = 11.9 Hz), 4.13 (d, 1H, J = 12.5 Hz), 3.97 (dd, 1H, J = 12.6 and 2.4 Hz), 2.01-2.34 (m, 3H), 1.82-2.01 (m, 1H), and see Table 4. ^{13}C NMR δ 137.99, 129.05, 128.53, 128.42, 97.97, 70.37, 63.13, 30.00, 29.10, 27.65. Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.42; H, 7.18; N, 6.90.

(1α, 4β, 6α)-4-(Benzyloxy)-3-oxa-7-azabicyclo[4.1.0]heptane (14), a solid, mp 60-62°C (from hexane): ^{1}H NMR δ 7.18-7.46 (m, 5H), 4.46 and 4.71 (AB, 2H, J = 11.9 Hz), 4.61-4.80 (m, 1H), 4.15 (dd, 1H, J = 12.1 and 2.0 Hz), 3.84 (d, 1H, J = 12.1 Hz), 2.11-2.40 (m, 2H), 1.86-2.11, (m, 2H), and see Table 4. ^{13}C NMR δ 138.27, 129.10, 128.55, 128. 41, 94.21, 69.88, 58.67, 29.46, 28.61, 26.35. Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.35; H, 7.56; N, 6.68.

Synthesis of Aziridines 19-22. Following the procedure previously described for the synthesis of aziridines **9-12**, the treatment of the 52:48 mixture (2.10 g, 9.5 mmol) of epoxides cis **34** and trans **33** (from the reaction of olefin **28** with *m*-CPBA)[9] with NaN_3/NH_4Cl in 8:1 MeOH/H_2O afforded a 15:33:52 mixture (2.44 g) of azido alcohols **42**, **43** and **44** (Scheme 2), which was directly treated with PPh_3 (2.49 g, 9.5 mmol) to give a 48:52 mixture (2.59 g) of aziridines cis **19** and trans **20** with PPh_3 and $POPh_3$. The treatment of this mixture with ClCOOEt in the presence of NEt_3 afforded a 48:52 mixture of aziridines cis **21** and trans **22**, which was subjected to flash chromatography. Elution with an 85:15 mixture of hexane and AcOEt afforded pure aziridine cis **21** (0.65 g) and trans **22** (1.04 g).

(1β, 2β, 4β, 6β)-4-(Benzyloxy)-7-(ethoxycarbonyl)-2-methyl-3-oxa-7-aza bicyclo[4.1.0]heptane (21), a liquid: ^{1}H NMR δ 7.22-7.45 (m, 5H), 4.52 and 4.84 (AB, 2H, J=11.9 Hz), 4.14 (q, 2H, J=7.1 Hz), 3.91 (dq, 1H, J=6.3 and 1.4 Hz), 2.52 (ddd, 1H, J=6.3 and 1.4 Hz), 2.45 (dd, 1H, J=6.3 and 1.4 Hz), 1.88-2.18 (m, 2H), 1.46 (d, 3H, J=6.3 Hz), 1.26 (t, 3H, J=7.1 Hz), and see Table 4. ^{13}C NMR δ 163.88, 138.05, 128.94, 128.62, 128.29, 98.32, 70.08, 69.09, 63.06, 39.55, 35.12, 29.33, 19.19, 14.90. Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 70.10; H, 7.38; N, 4.72.

(1α, 2β, 4β, 6α)-4-(Benzyloxy)-7-(ethoxycarbonyl)-2-methyl-3-oxa-7-aza bicyclo[4.1.0]heptane (22), a liquid: ^{1}H NMR δ 7.20-7.40 (m, 5H), 4.51 and 4.83 (AB, 2H, J=12.0 Hz), 4.13 (q, 2H, J=7.1 Hz), 4.00 (dq, 1H, J=6.8 and 1.3 Hz), 2.92 (ddd, 1H, J=6.6, 3.3 and 1.2 Hz), 2.52 (dd, J=6.6 and 1.3 Hz), 2.26 (ddd, 1H, J=13.9, 3.0 e 1.3 Hz), 1.78 (ddd, 1H, J=13.9, 8.8 and 3.4 Hz), 1.50 (d, 3H, J=6.8 Hz), 1.26 (t, 3H, J=7.1 Hz), and see Table 4. ^{13}C NMR δ 163.70, 138.20, 129.04, 128.59, 128.38, 97.29, 72.04, 71.09, 63.35, 40.94, 39.09, 30.61, 21.16, 14.94. Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.86; H, 7.19; N, 4.99.

Separate treatment of aziridine **21** (0.2 g) and **22** (0.59 g) with a 1.5M MeONa in anhydrous MeOH afforded pure aziridines cis **19** (0.147 g) and trans **20** (0.44 g) (98% yield).

(1β, 2β, 4β, 6β)-4-(Benzyloxy)-2-methyl-3-oxa-7-azabicyclo[4.1.0]heptane (19), a liquid: ^{1}H NMR δ 7.21-7.41 (m, 5H), 4.53 and 4.84 (AB 2H, J=12.0), 4.05 (q, 2H, J=6.3), 2.00-2.22 (m, 2H), 1.80 (dd, 1H,

J=13.9 and 8.8), 1.37 (d, 3H, J=6.3), and see Table 4. ^{13}C NMR δ 138.14, 129.05, 128.62, 128.41, 99.15, 70.32, 69.34, 34.17, 29.85, 28.67. 19.25. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.34; H, 7.93; N, 6.20.

(1α, 2β, 4β, 6α)-4-(Benzyloxy)-2-methyl-3-oxa-7-azabicyclo[4.1.0]heptane (20), a liquid: ^1H NMR δ 7.39-7.20 (m, 7H), 4.50 and 4.84 (AB, 2H, J=12.0 Hz), 3.90 (q, 1H, J=6.6 and 1.7 Hz), 2.06-2.21 (m, 2H), 1.77 (ddd, 1H, J=13.4, 9.0 and 3.7 Hz), 1.46 (d, 3H, J=6.8 Hz), and see Table 4. ^{13}C NMR δ 138.48, 128.99, 128.55, 128.24, 97.54, 73.32, 71.07, 34.27, 31.25, 21.65. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.40; H, 7.99; N, 6.50.

Synthesis of Aziridines 8, 17, 18 and 23. The following procedure is typical. A solution of aziridine **5** (0.20 g, 2.0 mmol) in anhydrous pyridine (2 mL) was treated at 0°C with TsCl (0.42 g, 2.2 mmol) and the reaction mixture was maintained at the same temperature for 1h and then for 2h at -20°C. The usual procedure afforded pure **7-(tosyl)-3-oxa-7-azabiciclo[4.1.0]heptane (8)** (0.497 g, 97% yield), as a solid, mp 66-68.5°C (from hexane):^1H NMR δ 7.75 (d, 2H, J=8.1 Hz), 7.27 (d, 2H, J=8.1 Hz), 3.90 (dd, 1H, J=13.0 and 4.0 Hz), 3.72 (dd, 1H, J=13.1 and 0.7 Hz), 3.25-3.49 (m, 2H), 3.10 (ddd, 1H, J=7.4, 4.3 and 1.6 Hz), 2.96 (ddd, 1H, J=7.4, 4.0 and 1.0 Hz), 2.37 (s, 3H), 1.67-1.97 (m, 2H). ^{13}C NMR δ 145.09, 135.83, 130.33, 128.86, 64.70, 61.99, 38.59, 37.65, 23.49, 22.25. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53. Found: C, 57.04; H, 6.10; N, 5.43.

The same procedure starting from aziridine **13** (0.336 g) gave pure **(1β, 4β, 6β)-4-(benzyloxy)-7-(tosyl)-3-oxa-7-azabicyclo[4.1.0]heptane (17)** (0.477 g, 81% yield), as a solid mp 129-130.5°C (from hexane/acetone): ^1H NMR δ 7.85 (d, 2H, J=8.2 Hz), 7.21-7.40 (m, 7H), 4.46 and 4.78 (AB, 2H, J=11.9 Hz), 4.15 (d, 1H, J = 13.1 Hz), 3.86 (dd, 1H, J=13.1 and 2.0 Hz), 3.08 (ddd, 1H, J=6.9 and 0.8 Hz), 2.95 (dd, 1H, J=6.9 and 2.0 Hz), 2.44 (s, 3H), 2.09 (ddd, 1H, J=15.1, 6.9 and 4.2 Hz), 1.88 (ddd, 1H, J=15.1, 8.2 and 0.8 Hz), and see Table 4. ^{13}C NMR δ 145.16, 137.85, 136.02, 130.32, 129.07, 128.55, 128.45, 97.15, 70.39, 62.60, 37.24, 37.01, 28.76, 22.29. Anal. Calcd for $C_{19}H_{21}NO_4S$: C, 63.49; H, 5.89; N, 3.90. Found: C, 63.66; H, 6.05; N, 3.74.

The same procedure starting from aziridine **14** (0.291 g) afforded pure **(1α, 4β, 6α)-4-(benzyloxy)-7-(tosyl)-3-oxa-7-azabicyclo[4.1.0]heptane (18)** (0.426 g, 83% yield), as a solid, mp 97-99°C (from hexane): ^1H NMR δ 7.83 (d, 2H, J=8.3 Hz), 7.22-7.41 (m, 7H), 4.44 and 4.67 (AB, 2H, J=11.8 Hz), 4.07 (dd, 1H, J = 12.9 and 2.8 Hz), 3.82 (d, 1H, J=12.9 Hz), 3.16 (ddd, 1H, J=7.3, 5.6 and 1.6 Hz), 3.04 (dd, 1H, J=7.3 and 2.8 Hz), 2.44 (s, 3H), 2.05 (ddd, 1H, J=15.2, 4.5 and 1.6 Hz), 1.94 (ddd, 1H, J=15.2, 5.6 and 3.1 Hz), and see Table 4. ^{13}C NMR δ 145.24, 137.86, 135.72, 130.40, 129.16, 128.53, 128.47, 93.82, 70.16, 58.00, 38.89, 36.65, 28.21, 22.31. Anal. Calcd $C_{19}H_{21}NO_4S$: C, 63.49; H, 5.89; N, 3.90. Found: C, 63.52; H, 5.96; N, 3.70.

The same treatment using aziridine **20** afforded pure **(1α, 2β, 4β, 6α)-4-(benzyloxy)-2-methyl-7-(tosyl)-3-oxa-7-azabicyclo[4.1.0]heptane (23)** (0.70 g, 92% yield), as a solid, mp 101-102°C (from hexane/acetone): ^1H NMR δ 7.78 (d, 2H, J=8.2 Hz), 7.20-7.40 (m, 7H), 4.45 and 4.80 (AB, 2H, J=11.8 Hz), 3.91 (dq, 1H, J=6.7 and 0.8 Hz), 3.20 (ddd, 1H, J=7.3, 3.4 and 0.8 Hz), 2.85 (dd, 1H, J=7.3 and 1.0 Hz), 2.45 (s, 3H), 2.06 (ddd, 1H, J=14.0, 2.9 and 0.7 Hz), 1.77 (ddd, 1H, J=14.2, 8.8 and 3.6 Hz), and see Table 4. ^{13}C NMR δ 145.33, 138.06, 135.52, 130.46, 129.04, 128.49, 128.41, 97.28, 71.20, 43.22, 41.36, 29.60, 22.32, 21.23. Anal. Calcd for $C_{20}H_{23}NO_4S$: C, 64.32; H, 6.21; N, 3.75. Found: C, 64.22; H, 6.38; N, 3.92.

Reaction of Aziridines 5 and 9 with HCl-Et_2O. The following procedure is typical. A solution of aziridine **5** (0.060 g, 0.5 mmol) in an HCl-saturated solution in anhydrous Et_2O (2.0 ml) was stirred at 0°C for 1 h then left overnight at -20°C. Filtration of the reaction mixture afforded a crude reaction product (0.070 g) which was washed with anhydrous ether to give pure **45·HCl**, as a solid, mp 183-185°C (dec.).

The crude reaction product (0.117 g) from aziridine **9** was washed with ether to give pure **63·HCl**, as a solid, mp 191-194°C.

Reaction of Aziridines 6, 7, 11, 12, 15, 16, 21 and 22 with HCl in $CHCl_3$. General procedure. A solution of the aziridine (0.50 mmol) in $CHCl_3$ (3.0 ml) was treated with 36% aqueous HCl (2.0 ml) and the reaction mixture was stirred vigorously for 10 min at rt. Evaporation of the washed (saturated aqueous $NaHCO_3$) organic solution afforded an oily residue consisting of the corresponding chloroderivatives (^1H NMR, see Tables 1-3).

Reaction of Aziridines 6, 7, 11, 12, 15, 16, 21, and 22 with NaCl-DMF. General procedure. A solution of the aziridine (0.50 mmol) in DMF (4 ml) containing NaCl (0.87 g, 15.0 mmol) was stirred at 120°C for 3 days. Dilution with ether, and evaporation of the washed (saturated aqueous NaCl) organic solution afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1-3).

Methanolysis of Aziridines 7, 8, 15-18, and 23 with 0.2 N H_2SO_4-MeOH. General procedure. A solution of the aziridine (0.50 mmol) in 0.2 N H_2SO_4-MeOH (5 ml) (10 ml of a 1:1 mixture of MeOH and $CHCl_3$ in the case of **17** and **18**) was stirred at r.t. for the time shown in Tables 1-3. Dilution with saturated aqueous $NaHCO_3$, extraction with ether ($CHCl_3$ in the case of **17** and **18**) and evaporation of the washed (water) ether extracts afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1-3).

Methanolysis of Aziridines 7, 8, 15-18, and 23 in the Presence of $LiClO_4$. General procedure. A solution of the aziridine (0.50 mmol) in anhydrous MeOH (2 ml) containing $LiClO_4$ (17 M solution) was stirred at 70°C for 2 h. Dilution with ether and evaporation of the washed (water) organic solution, afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1-3).

Methanolysis of Aziridines 8, 17, 18 and 23 with MeONa in MeOH. General procedure. A solution of the aziridine (0.5 mmol) in 2.0 M MeONa in anhydrous MeOH (4 ml) [$CHCl_3$ (1 ml) was added in the case of aziridines **17** and **18**] was stirred at the temperature and for the time shown in Tables 1-3. Dilution with ether ($CHCl_3$ in the case of **17** and **18**) and evaporation of the washed (water) organic solution afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1-3).

Azidolysis of Aziridines 5, 7, 9-11, 15, and 16 with NaN_3-NH_4Cl. General procedure. A solution of the aziridine (0.50 mmol) in a 4:1 MeOH-H_2O mixture (4.5 ml) was treated with NaN_3 (0.13 g, 2.0 mmol) and NH_4Cl (0.109 g, 2.0 mmol) and the reaction mixture was stirred for the time and at the temperature shown in Tables 1-3. Dilution with ether and evaporation of the washed (water) ether solution afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1-3).

Azidolysis of Aziridines 5, 7, 9-12, 15, 16 and 21-23 with NaN_3-$LiClO_4$ in MeCN. General procedure. A solution of the aziridine (0.50 mmol) in anhydrous MeCN (THF in the case of **5** , **9** and **10**) (2.0 ml) was treated with NaN_3 (0.13 g, 2.0 mmol) and $LiClO_4$ [$Mg(ClO_4)_2$ in the case of aziridines **5**, **9** and **10**] at the molar concentration as shown in Tables 1-3. The reaction mixture was stirred at the temperature and for the time indicated in Tables 1-3. Dilution with ether, and evaporation of the washed (water) ether solution afforded a crude reaction mixture which was analyzed by ^1H NMR (Tables 1-3).

Azidolysis of Aziridines 7, 11, 12, 15, 16, 21-23 with NaN_3 in DMF or DMSO. General procedure. A solution of the aziridine (0.50 mmol) in anhydrous DMF (or DMSO) (2.0 ml) containing NaN_3 (0.13 g, 2.0 mmol) was stirred at the temperature and for the time indicated in Tables 1-3. Dilution with water, extraction with ether, and evaporation of the washed (water) ether extracts afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1-3).

Aminolysis of Aziridines 7, 11, 15, 16 and 23 with Et_2NH-EtOH. General procedure. A solution of the aziridine (0.50 mmol) in EtOH (2.0 mL) containing Et_2NH (0.15 ml, 1.5 mmol) was stirred at 80°C for the time shown in the Tables 1-3; after cooling, the solution was diluted with ether, and evaporation of the washed (water) ether solution afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1-3).

Aminolysis of Aziridines 7, 11, 15, 16 and 23 with Et_2NH-$LiClO_4$ in MeCN. General procedure. A solution of the aziridine (0.50 mmol) in anhydrous MeCN (2.0 ml) was treated with $NHEt_2$ (0.15 ml, 1.5 mmol) and $LiClO_4$ (0.42 g, 4.0 mmol) and the reaction mixture was stirred at the temperature and for the time

shown in Tables 1-3. Dilution with ether and evaporation of the washed (water) ether solution afforded a crude product which was analyzed by ^{1}H NMR (Tables 1-3).

Reaction of Aziridines 7, 11 and 12 with PhSH-Et$_3$N (Corey's Protocol). General procedure. A solution of the aziridine (0.50 mmol) in MeOH (0.5 ml) was treated with Et$_3$N (0.28 ml, 2.8 mmol) and PhSH (0.14 ml, 1.50 mmol) and the reaction mixture was stirred for the time and at the temperature shown in Tables 1-3. Dilution with ether and evaporation of the washed (saturated aqueous NaHCO$_3$ and water) ether extracts afforded a crude reaction product which was analyzed by ^{1}H NMR (Tables 1-3).

Reaction of Aziridines 7, 11 and 12 with PhSH-LiClO$_4$ in MeCN. General procedure. A solution of the aziridine (0.50 mmol) in anhydrous MeCN (2.0 ml) was treated with PhSH (0.14 ml, 1.5 mmol) and LiClO$_4$ (0.42 g, 4.0 mmol) and the reaction mixture was stirred at 80°C for the time shown in Tables 1-3. The usual work-up afforded a crude reaction product which was analyzed by ^{1}H NMR (Tables 1-3).

Reaction of Aziridine 7 with PhSH or PhSNa in DMF. A solution of aziridine 7 (0.116 g, 0.5 mmol) in DMF (2 ml) was treated with PhSH (0.06 ml, 0.6 mmol) or PhSNa (0.164 g, 2.0 mmol) and the reaction mixture was stirred for 2 h at 80°C (1 h at rt in the case of PhSNa). Dilution with ether and evaporation of the washed (saturated aqueous NaHCO$_3$ and water) organic solution afforded a crude reaction product consisting of practically pure **59** (Tables 1 and 4).

General Procedure for the Deprotection of Urethanes. A solution of the urethane (0.25 mmol) in a 1:1 mixture of ethylene glycol and 2N aqueous KOH solution was stirred at 100°C for 18 h. Dilution with ether and evaporation of the washed (water) organic solution afforded a crude reaction product containing the corresponding *N*-deprotected compound.

The crude reaction product (0.072 g) from azido urethane **85** afforded pure ***t*-2-(benzyloxy)-*t*-5-(amino)-*r*-4-methoxytetrahydropyran**, as a liquid (0.047 g) (85% yield): ^{1}H NMR δ 7.13-7.31 (m, 5H), 4.37 and 4.62 (AB, 2H, *J*=11.9 Hz), 3.60 (dd, 1H, *J*=11.3 and 5.1 Hz), 3.43 (t, 1H, *J*=11.3 Hz), 3.20-3.36 (m, 1H), 3.30 (s, 3H), 2.22 (ddd, 1H, *J*=12.9, 4.9 and 2.0 Hz), 1.43 (ddd, 1H, *J*=12.9, 9.9 and 3.2 Hz). ^{13}C NMR δ 138.31, 129.04, 128.53, 128.33, 97.92, 77.06, 69.36, 64.60, 56.99, 53.19, 34.47. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.8; H, 8.07; N, 5.9. Found: C, 65.97; H, 8.23; N, 5.69.

References and Notes

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13. Standard reaction conditions: opening reactions carried out in the presence of the nucleophile in an appropriate solvent (NaCl and NaN_3 in DMF or DMSO; $NHEt_2$ in EtOH; PhSH in MeOH-NEt_3; MeONa in MeOH). Proton acid-catalyzed reaction conditions: opening reactions carried out with a nucleophile under proton acid catalysis (HCl in $CHCl_3$; NaN_3-NH_4Cl in MeOH-H_2O; MeOH-H_2SO_4). Metal salt-promoted reaction conditions: opening reactions carried out with a nucleophile in the presence of a metal salt: NaN_3-$LiClO_4$ in MeCN; MeOH-$LiClO_4$; $NHEt_2$-$LiClO_4$ in MeCN; PhSH-$LiClO_4$ in MeCN.
14. The *C-1* and *C-2 products* nomenclature refers to the attacking site of the nucleophile, *i.e.* at the C-(1) or C-(2) aziridine carbon of aziridines **5-12**, **15-18**, and **21-23**, in accordance with the arbitrary numbering given in Schemes 3-7.
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