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Diastereoselective Control Through Hydrogen Bonding in the Aziridination of the Chiral Allylic Alcohols by Acetoxyaminoquinazolinone

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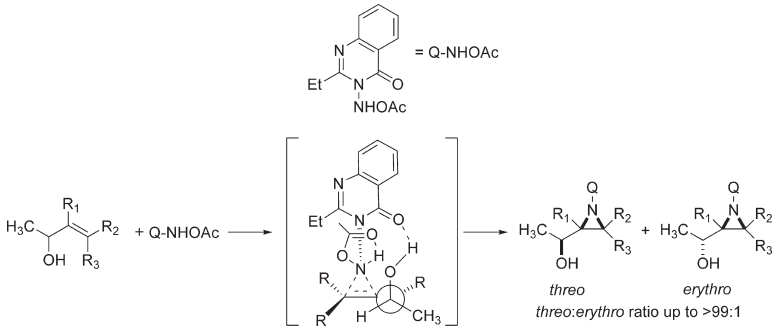

A high diastereoselectivity (up to >99:1) is found for the aziridinations of chiral allylic alcohols with acetoxyaminoquinazolinone (Q-NHOAc). The selectivity is explained in terms of hydrogen bonding between the hydroxy functionality of the allylic alcohol and the remote carbonyl group of the quinazolinone.

Introduction

The oxidation of *N*-amino heterocycles[1] such as 3-amino-2-ethylquinazolin-4(3*H*)-one (Q-NH_2) (**1**) with lead tetraacetate in the presence of olefinic substrates provides a general method for the synthesis of the *N*-aminoaziridines (oxidative aminoaziridination of olefins). Atkinson showed that the active aziridinating species is the corresponding *N*-acetoxylated hydrazine derivatives, rather than nitrenes.[2] The reaction of Q-NH_2 **1** with lead tetraacetate at low temperature generates the corresponding 3-(acetoxyamino)-2-ethylquinazolin-4(3*H*)-one (Q-NHOAc) (**2**) as a relatively stable intermediate.[3] This compound, and its analogues, convert alkenes into aziridines in a reaction which resembles the conversion of alkenes into epoxides by peracids. Atkinson has documented that olefin aziridination by **2** is hydroxy-directed as are peracid epoxidations.[4] For example, treatment of cyclohex-3-en-1-ol with this reagent furnishes the *syn* isomer **3** in high stereoselectivity. (Scheme 1); peroxyacid epoxidation of this homoallylic alcohol is hardly diastereoselective at all.

Reaction of geraniol occurs preferentially at the double bond proximal to the hydroxy group (92:8), whereas that of geranyl chloride proceeds predominantly at the site distant from the heteroatom (85:15).[5] Definitely, Q-NHOAc **2** is subject to stronger directivity effects than *m*-CPBA **4**, although the structural similarities between Q-NHOAc **2** and the *m*-CPBA **4** are clearly evident (Figure 1). Thus, it should be of mechanistic importance to understand what structural and geometrical factors control the hydroxy-group directivity in the aziridination of the allylic alcohol (e.g., geraniol) by Q-NHOAc **2**. For this purpose, the chiral allylic alcohols **5** were chosen as a stereochemical probe. By comparison of the observed diastereoselectivity with those of the established oxidant *m*-CPBA, these stereolabeled allylic alcohols should serve as a mechanistic tool to define the

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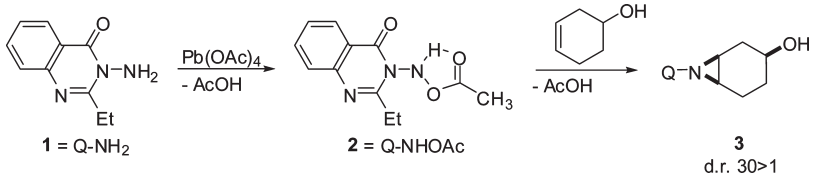
SCHEME 1. Atkinson's Aziridination



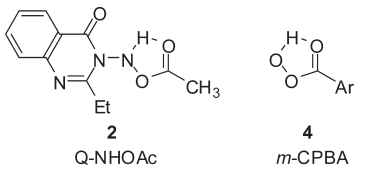


FIGURE 1. Comparison of the Q-NHOAc **2** and *m*-CPBA **4** structures.

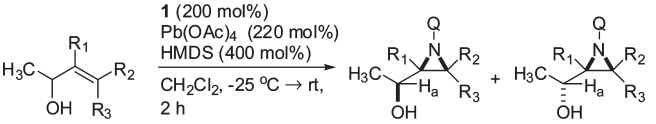
transition-state structure of the aziridination process.[6] Herein we report that the chiral allylic alcohols **5** undergo highly diastereoselective (up to >99:1) aziridination with Q-NHOAc **2**. The diastereoselectivity is controlled by hydrogen bonding with the remote quinazolinone carbonyl group rather than the acetoxy functionality.

Results

The aziridinations (Table 1) were conducted at ca. −25 °C in CH_2Cl_2, at the **1**/allylic alcohol/$Pb(OAc)_4$/hexamethyldisilazane (HDMS)[7] ratio of 2:1:2.2:4. The diastereoselectivities for the chiral allylic alcohols **5a**−**h** are listed in Table 1, together with the literature data for the *m*-CPBA[6] epoxidation for comparison. The results in Table 1 reveal that the in situ generated Q-NHOAc **2** aziridinates the allylic alcohols **5** in excellent conversions (100%) to the aziridine alcohols **6**. As demonstrated by the eight preparative runs, the aziridine alcohols **6a**−**h** were isolated in 42−95% yields. For the azirinidation of the *cis*- and *trans*-allylic alcohols **5b**,**d**,**e**,**g**, the configuration around the C=C bond was retained in the corresponding aziridine alcohols (Table 1, entries 2, 4, 5, and 7), suggesting that radical intermediates are not involved in the present aziridination. The aziridinations of substrates **5a**,**b** (entries 1 and 2) without allylic strain, as well as the substrates **5c**,**d** (entries 3 and 4) with 1,2-allylic strain, displays already excellent (ca. 95%) *threo* selectivity, which is difficult to improve. Nevertheless, the 1,3-allylic strain present in the derivatives **5e**,**f** (entries 5 and 6) induces expectedly perfect (>99:1) *threo* preference.

From a green chemistry point of view, the aziridination of alkenes with Q-NH_2 **2** generated in situ from QNH_2 **1** and nontoxic hypervalent iodine reagent diacetoxy(phenyl)-λ^3-iodane (PIDA)[1c,e] in place of $Pb(OAc)_4$ (LTA) is very attractive. For comparison, the aziridinations of the allylic alcohols **5a**−**d**,**f**,**g** were repeated by using PIDA in place of

TABLE 1. Aziridination of the Allylic Alcohols 5 by Q-NHOAc 2 Generated in situ from Q-NH_2 1 and $Pb(OAc)_4$ and Comparison with *m*-CPBA[a]



							diastereoselectivity[b]	
							threo/*erythro*	
entry	substrate	R_1	R_2	R_3	convn[b] [%]	yield [%]	Q-NHOAc **2**	*m*-CPBA[c] **4**
1	**5a**	H	H	H	100	78	97:3	60:40
2	**5b**	H	CH_3	H	100	78	95:5	64:36
3	**5c**	CH_3	H	H	100	42	95:5[d]	45:55
4	**5d**	CH_3	CH_3	H	100	95	97:3[e]	48:52
5	**5e**	H	H	CH_3	100	82	>99:1	95:5
6	**5f**	H	CH_3	CH_3	100	90	>99:1	95:5
7	**5g**	CH_3	H	CH_3	100	84	95:5	90:10
8	**5h**	CH_3	CH_3	CH_3	100	87	97:3	90:10

[a]Stoichiometric amounts: allylic alcohol **5** (1 mmol); Q-NH_2 **1** (2 mmol); $Pb(OAc)_4$ (2.2 mmol); HMDS (4 mmol); CH_2Cl_2 (5 mL). [b]Conversion of the allylic alcohol **5** after complete consumption of **1** (determined by TLC); an aliquot of the crude reaction mixture was taken, and the conversions and *threo*-**6**/*erythro*-**6** ratios were assessed by ^{1}H NMR analysis. [c]Reference 6. [d]Ratio of *threo* invertomers 5:1 determined by ^{1}H NMR. [e]Ratio of *erythro* invertomers 3:1 determined by ^{1}H NMR.

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(7) (a) Atkinson found that decomposition of in situ generated QNHOAc 2 was retarded by the removal of acetic acid, a byproduct both in acetoxylation of the 3-aminoquinazolinone 1 with lead tetraacetate (LTA) and in the aziridination of alkenes by QNHOAc 2, and thus, in the presence of HMDS scavenging AcOH, the yields of aziridines from reaction of Q-NHOAc 2 and alkenes were improved, especially for otherwise less reactive alkenes. (b) Karabuga, S.; Kazaz, C.; Kilic, H.; Ulukanli, S.; Celik, A. *Tetrahedron Lett*. **2005**, *46*, 5225–5227.

SCHEME 2. Synthesis of Aziridine Alcohols

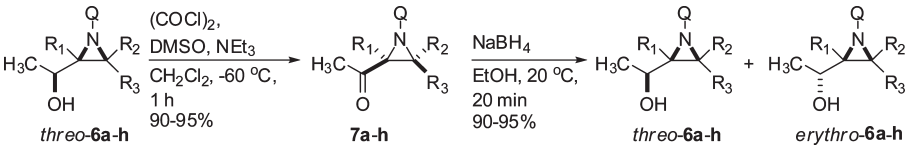
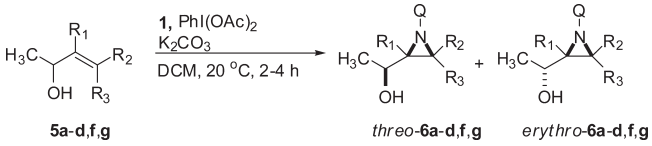


TABLE 2. Aziridination of the Allylic Alcohols 5 by Q-NHOAc 2 Generated in Situ from Q-NH_2 1 and $PhI(OAc)_2$ (PIDA)[a]



							diastereoselectivity[b]
entry	substrate	R_1	R_2	R_3	convn[b] [%]	mb[c] [%]	*threo*/*erythro*
1	**5a**	H	H	H	90	77	96:4
2	**5b**	H	CH_3	H	100	88	95:5
3	**5c**	CH_3	H	H	90	65	82:18
4	**5d**	CH_3	CH_3	H	100	91	95:5
5	**5f**	H	CH_3	CH_3	100	95	>99:1
6	**5g**	CH_3	H	CH_3	100	95	96:4

[a]Stoichiometric amounts: allylic alcohol **5** (1 mmol); Q-NH_2 **1** (2 mmol); K_2CO_3 (4 mmol); $PhI(OAc)_2$ (2.2 mmol) and 4 mL of CH_2Cl_2. [b]Conversion of the allylic alcohol **5** after complete consumption of the Q-NH_2 **1** (determined by TLC). An aliquot was taken of the crude reaction mixture, and the conversions and diastereomeric ratios were assessed by ^1H NMR analysis with diphenylmethane as internal standard; error ca. ±5% of the stated values. [c]Mass balance refers to the characterized products *threo*-**6** and *erythro*-**6** and recovered allylic alcohol **5**.

LTA and gave almost identical results as shown in Table 2. The *threo*-aziridine alcohols **6** were formed preferentially in the aziridination of chiral allylic alcohols **5a**−**d**,**f**,**g** with Q-NH_2 **1** and PIDA as the oxidant. Conversions and mass balances were high to excellent in every case. For the aziridination of *cis*- and *trans*-allylic alcohols, the configurations around the C=C moieties were retained in the corresponding aziridine alcohols (Table 2, entries 2, 4 and 6). The allylic alcohols **5a** and **5b** without allylic strain were aziridinated in high *threo* diastereoselectivities (entries 1 (96%) and 2 (95%)). For the substrates **5c**,**d** (Table 2, entries 3 and 4) with 1,2-allylic strain, also a high, significant *threo* diastereoselectivity was found, suggesting no influence of 1,2-allylic strain. Aziridination of the allylic alcohol **5f** possessing 1,3-allylic strain proceeded with high *threo* diastereoselectivity (entry 5). The *threo*-aziridine alcohol was dominantly produced (96:4) for the aziridination of the stereochemical probe (*Z*)-3-methyl-3-penten-2-ol (**5g**) with both 1,2- and 1,3-allylic strains (Table 2, entry 6).

To confirm the diastereoisomeric authenticity of the aziridine alcohols **6a**−**h**, we synthesized all diastereoisomers by the Swern oxidation[8] of the aziridine alcohol to the corresponding aziridinyl ketones **7a**−**h**. Subsequent reduction of each of the resulting aziridinyl ketones **7a**−**h** with sodium borohydride regenerated the diastereomeric mixtures of the aziridine alcohols **6a**−**h** for comparison with the product mixtures obtained in the aziridination (Scheme 2). The structures of the compounds **6a**−**h** were assigned by ^1H NMR, ^{13}C NMR, mass, and IR spectra. The assignment of the relative configuration of the products was made by comparison of the chemical shift for the methine proton (H_a) on the hydroxy-bearing carbon atom and X-ray analysis. Thus, the H_a proton of the *erythro*-configurated isomer **6** absorbs at lower field than that of the corresponding *threo* isomer. For example, the resonances of the H_a proton of the *erythro*-configurated aziridine alcohols **6** are shifted as much as 1.24 ppm downfield relative to those of the corresponding *threo* diastereomer. This upfield chemical shift is most pronounced for the signals of the carbon atom which bears the H_a proton ($\Delta\delta_C$ up to 5.9 ppm). This trend is general, as observed for the *threo* epoxy alcohols **5**[9] and aziridine alcohols **6**.[10] The configurations of diastereomerically pure *threo* aziridine alcohols **6d** and **6e** (as *p*-nitrobenzoate derivative **8a**) were also established by X-ray analysis (see Supporting Information).

Discussion

These stereochemical results in Tables 1 and 2 disclose that allylic strain is not decisive in the stereocontrol of the nitrogen transfer to the chiral acyclic allylic alcohols **5**. Consequently, the conformationally mobile acyclic substrates **5a**,**b** (Table 1, entries 1 and 2) without allylic strain are comparable (≥95%) to the conformationally restrained acyclic chiral substrates **5g**,**h** (Table 1, entries 7 and 8) with both 1,2- and 1,3-allylic strain in *threo*-stereoselective aziridination. This strong *threo* preference (≥95%) in the aziridination of the substrates **5a**,**b** without allylic strain is to be contrasted with the modest *threo* selectivity (ca. 60%) of the *m*-CPBA epoxidation (Table 1, entries 1 and 2). Mechanistically equally significant are the substrates **5c** and **5d** with 1,2-allylic strain, for which also excellent *threo* diastereoselectivity (≥95%) is expressed in the aziridination, but essentially none (ca. 45:55) in the *m*-CPBA[6] epoxidation (Table 1, entries 3 and 4). The composite set of selectivity data unequivocally proclaims that the observed hydroxy-group directivity derives from hydrogen bonding between the carbonyl group in Q-NHOAc **2** and the hydroxy functionality in the allylic alcohols **5**. The hydroxy-protected derivative of mesitylol (**5f**), namely, the benzoate ester **5i**, displayed a reversed diastereoselectivity (*erythro*) in this aziridination by **2** (Scheme 3). This favorable hydroxy-directing effect accelerates the reaction rate because the hydroxyl-protected derivative **5i** is less efficiently aziridinated (convn 50%) than the parent allylic alcohol **5f** (Table 1, entry 6). Moreover, the substrates **5i** possess no

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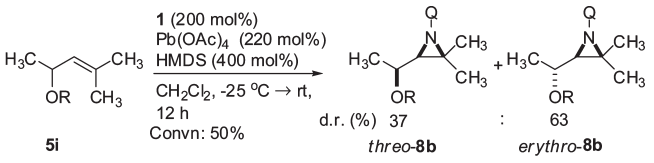
SCHEME 3. Aziridination of Hydroxy-Protected Allylic Alcohol Derivative 5i



R= *p*-nitrobenzoate

hydrogen-bonding donors, and hence, since there is no hydroxy-group directivity, steric effects promote *erythro* (63%) diastereoselectivity.

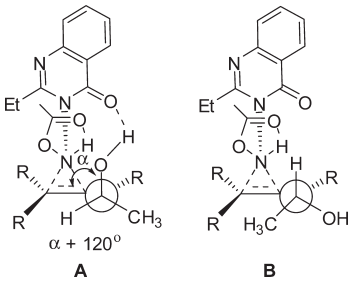


FIGURE 2. Transition-state structures for the aziridination by **2**.

This mechanistic rationale of hydrogen bonding constitutes an unprecedented fact for the aziridination with Q-NHOAc **2**, which reflects valuable geometrical information about the transition-state structure. The dihedral angle (α) between the π plane of the double bond and the hydroxy group in the C═C—C—O structural fragment of the allylic system is definitive (Figure 2). This dihedral angle (α) assumes characteristic values, ideally about 120°, in the stoichiometric epoxidations of chiral allylic alcohols with allylic strain.[6,11] Hence, we propose the transition-state structure **A** in Figure 2 to account for the stereochemical course in the aziridination of the chiral allylic alcohols **5**, irrespective of whether these acyclic substrates possess allylic strain or not. In view of the high *threo* selectivity (≥95%) observed in the present aziridination, we presume that the dihedral angle (α) in the C═C—C—O fragment is ca. 120°. This value is inferred from the *m*-CPBA epoxidation of chiral allylic alcohols **5**, which are diastereocontrolled by 1,3-allylic strain.[6,11f] In the *threo* **TS** (structure **A** in Figure 2), the π system is oriented favorably for hydrogen bonding[12] with the quinazoline carbonyl functionality.

For comparison, in the *erthro* **TS** (structure **B** in Figure 2), the hydroxy group is located away from the carbonyl group and hydrogen bonding is not possible. Thus, the *threo* conformer is preferentially populated through efficient hydrogen bonding to affect very high *threo* diastereoselectivity in the aziridination even without the assistance of allylic strain. To assess this, DFT calculations (B3LYP/6-31G*) of the model substrate **5c** with 1,2-allylic strain were carried out. The hydrogen-bonding conformer (structure **A** in Figure 2) is favored by 5.0 kcal/mol over **B**. The novelty of the present contribution is the realization that favorable bonding conditions combined with optimal geometrical provisions may obviate conformational impositions.

Experimental Section

Representative Procedure for Aziridination of Allylic Alcohols 5 by Using LTA. 3-Amino-2-ethyl-3*H*-quinazolin-4-one (Q-NH_2) (**1**) (0.75 g, 4 mmol) was added in small portions within 10 min to a vigorously stirred solution of acetic acid free lead tetraacetate (LTA) (1.95 g, 4.4 mmol) in 10 mL of CH_2Cl_2 at −25 °C, and stirring was continued for a further 10 min to give a solution of the 3-acetoxy-aminoquinazolinone (Q-NHOAc) (**2**). Then, a solution of allylic alcohol **5** (2 mmol) and hexamethyldisilazane (HMDS) (1.29 g, 8 mmol) in CH_2Cl_2 (2 mL) was added, and the final mixture was stirred for 30 min. The temperature of the solution was then allowed to rise to ambient over 20−25 min with stirring throughout. The mixture was extracted with CH_2Cl_2 (2 × 15 mL), washed with water (2 mL), and saturated $NaHCO_3$ (2 × 10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure (20 °C, 450 Torr), and the conversion and diastereoselectivity were determined by ^{1}H NMR analysis directly on the crude mixture (Table 1).

Representative Procedure for Aziridination of Allylic Alcohols 5 by Using PIDA. Into a 10-mL, one-necked, round-bottomed flask, equipped with a magnetic stirrer were placed 4 mL of CH_2Cl_2, allylic alcohol (1 mmol), Q-NH_2 **1** (378 mg, 2 mmol), anhydrous K_2CO_3 (552 mg, 4 mmol), and diphenylmethane (1 mmol) (as internal standard) at room temperature. The reaction was initiated by addition of PIDA (708 mg, 2.2 mmol), while the reaction progress was monitored by TLC. After completion of the reaction (2−4 h), the reaction mixture was passed through a short silica gel column (150 mg) and the solvent was removed under reduced pressure (25 °C, 450 Torr). The conversion, mass balance, and diastereoselectivities were determined by ^{1}H NMR analysis directly on the crude mixture (Table 2).

2-Ethyl-3-(2-(1-hydroxyethyl)aziridin-1-yl)quinazolin-4(3*H*)-one (6a). A mixture of the diastereoisomeric aziridines (*threo*-**6a** and ***erythro*-6a** in a 97:3 ratio by integration of the signals at 3.56 and 4.54 ppm respectively) was chromatographed on a silica gel column to give the major diastereoisomer ***threo*-6a** (395 mg, 1.53 mmol) in a yield of 76%.

***threo*-6a.** Recrystallization from EtOAc−hexane gave a white powder. R_f 0.11 (hexane−EtOAc = 2:1); mp 95−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (dd, J = 8.1, 1.4 Hz, 1H), 7.70 (ddd, J = 8.3, 7.0, 1.4 Hz, 1H), 7.63 (d, J = 8.3 Hz, 1H), 7.43 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 5.09 (bs, −O*H*, 1H), 3.56 (dqd, J = 8.2, 6.4, 1.2 Hz, 1H), 3.15 (dq, J = 16.5, 7.3 Hz, 1H, A part of AB system), 2.97 (dq, J = 16.5, 7.3 Hz, 1H, B part of AB system), 2.84 (td, J = 8.2, 5.8 Hz, 1H), 2.52 (dd, J = 5.8, 1.7 Hz, 1H), 2.31 (dd, J = 8.2, 1.7 Hz, 1H), 1.43 (t, J = 7.3 Hz, 3H), 1.32 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 156.5, 146.3, 134.2, 127.1, 126.7, 126.4, 120.9, 69.9, 52.1, 40.5, 27.3, 20.0, 10.9; IR (KBr, cm^{-1}) 3385, 2975, 2936, 1667, 1592, 1471, 1365, 1278, 1253, 1155, 1044; MS (FAB) m/z 260 (MH^+); HRMS (FAB) calcd for $C_{14}H_{18}N_3O_2$ (MH^+) 260.1399, found 260,1395. Anal. Calcd for $C_{14}H_{17}N_3O_2$: C, 64.85; H, 6.61; N, 16.20. Found: C, 64.63; H, 6.64; N, 16.23. ***erythro*-6a:** Colorless oil. R_f 0.09 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (ddd, J = 8.1, 1.5, 0.6 Hz, 1H), 7.69 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.62 (ddd, J = 8.3, 1.2, 0.6 Hz, 1H), 7.41 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 4.58−4.49 (m, 1H), 3.27

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(d, J = 3.2 Hz, −O*H*, 1H), 3.20−3.07 (m, 2H), 2.98 (dq, J = 16.5, 7.3 Hz, 1H, B part of AB system), 2.70 (dd, J = 5.9, 1.5 Hz, 1H), 2.28 (dd, J = 8.1, 1.5 Hz, 1H), 1.43 (t, J = 7.3, Hz, 3H), 1.22 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4, 157.1, 146.3, 134.0, 127.1, 126.6, 126.3, 121.2, 64.0, 49.7, 38.6, 27.4, 18.6, 10.9; IR (KBr, cm^{-1}) 3424, 2976, 2935, 1672, 1595, 1473, 1369, 1337, 1288, 1224, 1065; MS (FAB) m/z 260 (MH^+); HRMS (FAB) calcd for $C_{14}H_{18}N_3O_2$ (MH^+) 260.1399, found 260.1394. Anal. Calcd for $C_{14}H_{17}N_3O_2$: C, 64.85; H, 6.61; N, 16.20. Found: C, 64.73; H, 6.60; N, 15.33.

(***E***)**-2-Ethyl-3-(2-(1-hydroxyethyl)-3-methylaziridin-1-yl)quinazolin-4(3*H*)-one (6b).** A mixture of the diastereoisomeric aziridines (*threo*-**6b** and ***erythro*-6b** in a 95:5 ratio by integration of the signals at 3.61 and 4.48 ppm respectively) was chromatographed on a silica gel column to give the major diastereoisomer *threo*-**6b** (404 mg, 1.48 mmol) in a yield of 74%.

***threo*-6b:** Colorless oil. R_f 0.19 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (ddd, J = 8.1, 1.5, 0.5 Hz, 1H), 7.69 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.62 (ddd, J = 8.3, 1.3, 0.5 Hz, 1H), 7.40 (ddd, J = 8.1, 7.0, 1.3 Hz, 1H), 4.72 (d, J = 2.1 Hz, O*H*, 1H), 3.61 (dqd, J = 8.2, 6.4, 2.1, 1H), 3.13 (dq, J = 16.1, 7.3 Hz, 1H, A part of AB system), 2.86 (dq, J = 16.1, 7.3 Hz, 1H, B part of AB system), 2.81 (dd, J = 8.2, 5.4 Hz, 1H), 2.69−2.61 (m, 1H), 1.39 (t, J = 7.3 Hz, 3H), 1.33 (d, J = 6.4 Hz, 3H), 1.15 (d, J = 5.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 158.0, 146.3, 133.9, 127.1, 126.5, 126.3, 121.2, 69.4, 57.2, 45.1, 27.6, 20.2, 13.0, 11.0; IR (KBr, cm^{-1}) 3450, 2973, 2935, 1661, 1594, 1472, 1368, 1218, 1143, 1078; MS (FAB) m/z 274 (MH^+); HRMS (FAB) calcd for $C_{15}H_{20}N_3O_2$ (MH^+) 274.1556, found 274.1551. Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.91; H, 7.01; N, 15.37. Found: C, 65.97; H, 6.98; N, 15.34. ***erythro*-6b:** Colorless oil. R_f 0.13 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (ddd, J = 8.1, 1.5, 0.5 Hz, 1H), 7.69 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.63 (ddd, J = 8.3, 1.2, 0.5 Hz, 1H), 7.41 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 4.48 (q, J = 6.4 Hz, 1H), 3.21 (bs, O*H*, 1H), 3.19−3.08 (m, 2H), 2.86 (dq, J = 16.2, 7.4 Hz, 1H, B part of AB system), 2.79 (p, J = 5.8 Hz, 1H), 1.40 (t, J = 7.4 Hz, 1H), 1.24 (d, J = 6.4 Hz, 1H), 1.15 (d, J = 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.3, 158.4, 146.4, 133.9, 127.1, 126.4, 126.3, 121.4, 64.4, 55.2, 43.2, 27.7, 18.7, 13.0, 10.9; IR (KBr, cm^{-1}) 3372, 2980, 2924, 1671, 1592, 1466, 1401, 1357, 1158, 1057; MS (FAB) m/z 274 (MH^+); HRMS (FAB) calcd for $C_{15}H_{20}N_3O_2$ (MH^+) 274.1556, found 274,1551. Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.91; H, 7.01; N, 15.37. Found: C, 65.04; H, 6.95; N, 15.15.

2-Ethyl-3-(2-(1-hydroxyethyl)-2-methylaziridin-1-yl)quinazolin-4(3*H*)-one (6c). A mixture of the diastereoisomeric aziridines (*threo*-**6c** and ***erythro*-6c** in a 95:5 ratio by integration of the signals at 3.57 and 4.24 ppm respectively) was chromatographed on a silica gel column to give the major diastereoisomer ***threo*-6c** (218 mg, 0.8 mmol) in a yield of 40%.

***threo*-6c:** Colorless oil. R_f 0.21 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): (Two invertomers = 5:1) major invertomer δ 8.17 (ddd, J = 8.1, 1.5, 0.6 Hz, 1H), 7.69 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 7.62 (ddd, J = 8.4, 1.2, 0.6 Hz, 1H), 7.41 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 4.91 (bs, O*H*, 1H), 3.57 (q, J = 6.6 Hz, 1H), 3.14−2.91 (m, 2H), 2.64 (d, J = 1.9 Hz, 1H), 2.20 (bs, 1H), 1.39 (t, J = 7.3 Hz, 3H), 1.25 (d, J = 6.6 Hz, 3H), 1.19 (s, 3H); minor invertomer (observable signals) δ 8.21 (ddd, J = 8.1, 1.5, 0.6 Hz, 1H), 2.71 (d, J = 1.9 Hz, 1H), 2.02 (bs, 1H), 1.55 (s, 3H), 1.40 (t, J = 7.3 Hz, 3H), 1.20 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): (Two invertomers) major invertomer δ 161.9, 156.9, 146.3, 134.0, 126.9, 126.5, 126.4, 120.5, 73.3, 54.6, 44.4, 27.6, 18.3, 11.2, 11.0; minor invertomer (observable signals) δ 162.2, 157.3, 146.3, 134.2, 126.7, 126.5, 66.7, 55.0, 45.7, 20.2, 15.8, 10.9; IR (KBr, cm^{-1}) 3430, 2976, 2937, 1662, 1593, 1569, 1472, 1371, 1286, 1223, 1114; MS (FAB) m/z 274 (MH^+); HRMS (FAB) calcd for $C_{15}H_{20}N_3O_2$ (MH^+) 274.1556, found 274.1551. Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.91; H, 7.01; N, 15.37. Found: C, 65.68; H, 7.12; N, 15.42. ***erythro*-6c:** Colorless oil. R_f 0.13 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (dd, J = 8.1, 1.5 Hz, 1H), 7.70 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.63 (dd, J = 8.3, 1.2 Hz, 1H), 7.42 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 4.24 (q, J = 6.2 Hz, 1H), 3.22 (bs, O*H*, 1H), 3.07−2.79 (m, 3H), 2.49 (bs, 1H), 1.40 (t, J = 7.3 Hz, 3H), 1.24 (d, J = 6.2 Hz, 3H), 1.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 157.5, 146.2, 133.9, 127.0, 126.5, 126.4, 121.2, 67.5, 53.2, 41.1, 27.6, 18.5, 15.4, 10.9; IR (KBr, cm^{-1}) 3430, 2976, 2936, 1674, 1593, 1568, 1472, 1369, 1276, 1222, 1116; MS (FAB) m/z 274 (MH^+); HRMS (FAB) calcd for $C_{15}H_{20}N_3O_2$ (MH^+) 274.1556, found 274.1550. Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.91; H, 7.01; N, 15.37. Found: C, 65.54; H, 7.07; N, 15.23.

(***E***)**-2-Ethyl-3-(2-(1-hydroxyethyl)-2,3-dimethylaziridin-1-yl)-quinazolin-4(3*H*)-one (6d).** A mixture of the diastereoisomeric aziridines (*threo*-**6d** and ***erythro*-6d** in a 97:3 ratio by integration of the signals at 8.21 and 8.12 ppm respectively) was chromatographed on a silica gel column to give the major diastereoisomer ***threo*-6d** (528 mg, 1.84 mmol) in a yield of 92%.

***threo*-6d:** Recrystallization from EtOAc−hexane gave colorless needles. R_f 0.22 (hexane−EtOAc = 2:1); mp 125−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (ddd, J = 8.1, 1.5, 0.5 Hz, 1H), 7.71 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.64 (ddd, J = 8.3, 1.2, 0.5 Hz, 1H), 7.43 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 3.70 (bs, O*H*, 1H), 3.16−2.83 (m, 3H), 2.23 (s, 1H), 1.49 (s, 3H), 1.49 (d, J = 5.6 Hz, 3H), 1.41 (t, J = 7.3 Hz, 3H), 1.17 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 157.3, 146.2, 134.2, 126.9, 126.6, 126.5, 120.6, 67.6, 57.6, 49.2, 28.2, 20.3, 12.3, 10.9, 10.8; IR (KBr, cm^{-1}) 3436, 2975, 2935, 1655, 1594, 1472, 1369, 1338, 1221, 1137, 1083; MS (FAB) m/z 288 (MH^+); HRMS (FAB) calcd for $C_{16}H_{22}N_3O_2$ (MH^+) 288.1712, found 288.1707. Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.88; H, 7.37; N, 14.62. Found: C, 66.54; H, 7.29; N, 14.69. ***erythro*-6d:** Recrystallization from EtOAc−hexane gave a white powder. R_f 0.11 (hexane−EtOAc = 2:1); mp 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): (Two invertomers = 3:1) major invertomer δ 8.12 (dd, J = 8.1, 1.5 Hz, 1H), 7.62 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 7.56 (ddd, J = 8.4, 1.2, 0.6 Hz, 1H), 7.34 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 3.99−3.87 (m, 1H), 3.59 (bs, 1H), 3.14−2.94 (m, 1H), 2.94−2.75 (m, 1H), 1.48 (d, J = 5.9 Hz, 3H), 1.39 (t, J = 7.4 Hz, 3H), 1.38 (s, 3H), 1.21 (d, J = 6.3 Hz, 3H); minor invertomer (observable signals) δ 7.69 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 7.40 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 4.26 (dq, J = 6.3, 1.5 Hz, 1H), 3.38 (bs, 1H), 1.36 (t, J = 7.4 Hz, 3H), 1.18 (d, J = 6.8 Hz, 3H), 1.13 (d, J = 6.3 Hz, 3H), 1.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): (Two invertomers) major invertomer δ 160.7, 157.8, 146.2, 133.4, 126.8, 126.3, 126.0, 121.4, 68.6, 56.1, 44.1, 28.2, 22.5, 15.4, 13.1, 11.0; minor invertomer (observable signals) δ 161.8, 133.8, 126.2, 126.2, 68.7, 53.9, 42.5, 28.0, 17.8, 13.3, 11.3, 10.0; IR (KBr, cm^{-1}) 3415, 2974, 2930, 1672, 1593, 1473, 1370, 1289, 1226, 1140, 1059; MS (FAB) m/z 288 (MH^+); HRMS (FAB) calcd for $C_{16}H_{22}N_3O_2$ (MH^+) 288.1712, found 288.1707. Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.88; H, 7.37; N, 14.62. Found: C, 66.56; H, 7.20; N, 14.67.

(***Z***)**-2-Ethyl-3-(2-(1-hydroxyethyl)-3-methylaziridin-1-yl)quinazolin-4(3*H*)-one (6e).** A mixture of the diastereoisomeric aziridines (*threo*-**6e** and ***erythro*-6e** in a 97:3 ratio by integration of the signals at 3.81 and 4.49 ppm respectively) was chromatographed on a silica gel column to give the major diastereoisomer ***threo*-6e** (448 mg, 1.64 mmol) in a yield of 82%.

***threo*-6e:** Recrystallization from EtOAc−hexane gave colorless needles. R_f 0.26 (hexane−EtOAc = 2:1); mp 138−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (dd, J = 8.1, 1.4 Hz, 1H), 7.70 (ddd, J = 8.3, 7.1, 1.4 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.42 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H), 5.58 (bs, O*H*, 1H), 3.81 (dqd, J = 9.1, 6.5, 1.1 Hz, 1H), 3.10 (dq, J = 16.5, 7.3 Hz, 1H,

A part of AB system), 2.90 (dq, J = 16.5, 7.3 Hz, 1H, B part of AB system), 2.71 (t, J = 8.9 Hz, 1H), 2.51 (dq, J = 8.6, 6.1 Hz, 1H), 1.47 (d, J = 6.1 Hz, 3H), 1.44 (t, J = 7.3 Hz, 3H), 1.29 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 156.4, 146.1, 134.1, 127.0, 126.6, 126.4, 120.9, 66.3, 55.4, 47.7, 27.8, 20.4, 12.1, 10.7; IR (KBr, cm^{-1}) 3436, 2972, 2936, 1659, 1594, 1569, 1472, 1365, 1286, 1223, 1115, 1079; MS (FAB) m/z 274 (MH^+); HRMS (FAB) calcd for $C_{15}H_{20}N_3O_2$ (MH^+) 274.1556, found 274.1552. Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.91; H, 7.01; N, 15.37. Found: C, 65.71; H, 7.06; N, 15,27. ***erythro*-6e:** Colorless oil. R_f 0.14 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (ddd, J = 8.1, 1.5, 0.5 Hz, 1H), 7.68 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.61 (ddd, J = 8.3, 1.2, 0.5 Hz, 1H), 7.40 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 4.55−4.42 (m, 1H), 3.07 (dq, J = 16.3, 7.4 Hz, 1H, A part of AB system), 2.99−2.86 (m, 2H), 2.62 (dq, J = 8.3, 6.1 Hz, 1H), 2.56 (bs, O*H*, 1H), 1.61 (d, J = 6.1 Hz, 3H), 1.44 (d, J = 6.5 Hz, 3H), 1.43 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.3, 157.3, 146.2, 133.9, 127.0, 126.4, 126.3, 121.4, 64.9, 52.6, 47.2, 27.9, 20.5, 12.5, 10.9; IR (KBr, cm^{-1}) 3436, 2973, 2936, 1659, 1594, 1569, 1472, 1365, 1287, 1223, 1119, 1079; MS (FAB) m/z 274 (MH^+); HRMS (FAB) calcd for $C_{15}H_{20}N_3O_2$ (MH^+) 274.1556, found 274.1550. Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.91; H, 7.01; N, 15.37. Found: C, 65.71; H, 7.08; N, 15.30.

2-Ethyl-3-(3-(1-hydroxyethyl)-2,2-dimethylaziridin-1-yl)quinazolin-4(3*H*)-one (6f). A mixture of the diastereoisomeric aziridines (*threo*-**6f** and ***erythro*-6f** in a 99:1 ratio by integration of the signals at 3.76 and 4.31 ppm respectively) was chromatographed on a silica gel column to give the major diastereoisomer ***threo*-6f** (522 mg, 1.82 mmol) in a yield of 91%.

***threo*-6f:** Recrystallization from EtOAc−hexane gave a white powder. R_f 0.19 (hexane−EtOAc = 2:1); mp 144−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (dd, J = 8.0, 0.9 Hz, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 5.42 (bs, O*H*, 1H), 3.76 (m, 1H), 3.07 (dq, J = 14.8, 7.4 Hz, 1H, A part of AB system), 2.76 (dq, J = 14.8, 7.4 Hz, 1H, B part of AB system), 2.70 (d, J = 9.0 Hz, 1H), 1.45 (s, 3H), 1.39 (t, J = 7.4 Hz, 3H), 1.29 (d, J = 6.4 Hz, 3H), 1.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 158.0, 146.0, 134.1, 127.0, 126.6, 126.4, 121.1, 67.2, 59.3, 51.4, 27.9, 20.8, 20.8, 19.2, 10.8; IR (KBr, cm^{-1}) 3449, 2972, 2934, 1659, 1594, 1472, 1364, 1337, 1220, 1158, 1109, 1074; MS (FAB) m/z 288 (MH^+); HRMS (FAB) calcd for $C_{16}H_{22}N_3O_2$ (MH^+) 288.1712, found 288.1707. Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.88; H, 7.37; N, 14.62. Found: C, 66.50; H, 7.38; N, 14.63. ***erythro*-6f:** Colorless oil. R_f 0.10 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 8.0 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.39 (t, J = 7.4 Hz, 1H), 4.31 (m, 1H), 3.04−3.13 (m, 2H), 2.74 (dq, J = 14.9, 7.4, Hz, 1H, B part of AB system), 2.48 (bs, O*H*, 1H), 1.58 (s, 3H), 1.48 (d, J = 6.5 Hz, 3H), 1.39 (t, J = 7.4, Hz, 3H), 1.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 158.5, 146.1, 133.7, 127.0, 126.3, 121.5, 65.9, 57.1, 51.2, 27.9, 21.3, 20.6, 19.3, 10.8; IR (KBr, cm^{-1}) 3421, 2976, 2933, 1677, 1595, 1472, 1366, 1336, 1221, 1156, 1107, 1077; MS (FAB) m/z 288 (MH^+); HRMS (FAB) calcd for $C_{16}H_{22}N_3O_2$ (MH^+) 288.1712, found 288.1706. Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.88; H, 7.37; N, 14.62. Found: C, 67.06; H, 7.44; N, 14.57.

(*Z*)-2-Ethyl-3-(2-(1-hydroxyethyl)-2,3-dimethylaziridin-1-yl)-quinazolin-4(3*H*)-one (6g). A mixture of the diastereoisomeric aziridines (*threo*-**6g** and ***erythro*-6g** in a 95:5 ratio by integration of the signals at 3.86 and 4.31 ppm respectively) was chromatographed on a silica gel column to give the major diastereoisomer ***threo*-6g** (460 mg, 1.60 mmol) in a yield of 80%.

***threo*-6g:** Recrystallization from EtOAc−hexane gave a white powder. R_f 0.19 (hexane−EtOAc = 2:1); mp 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 8.1 Hz, 1H), 7.70 (ddd, J = 8.3, 7.0, 1.3 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.42 (t, J = 7.5 Hz, 1H), 5.40 (bs, O*H*, 1H), 3.86 (q, J = 6.5, Hz, 1H), 3.12−2.72 (m, 2H), 2.36 (bs, 1H), 1.49 (d, J = 6.0 Hz, 3H), 1.41 (t, J = 7.3 Hz, 3H), 1.25 (d, J = 6.5 Hz, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 156.7, 146.2, 134.1, 126.9, 126.5, 126.5, 120.5, 69.8, 57.1, 51.4, 28.1, 18.7, 12.4, 12.3, 10.9; IR (KBr, cm^{-1}) 3450, 2973, 2934, 1661, 1594, 1472, 1367, 1337, 1219, 1144, 1078; MS (FAB) m/z 288 (MH^+); HRMS (FAB) calcd for $C_{16}H_{22}N_3O_2$ (MH^+) 288.1712, found 288.1706. Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.88; H, 7.37; N, 14.62. Found: C, 66.62; H, 7.61; N, 14.63. ***erythro*-6g:** Colorless oil. R_f 0.17 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (dd, J = 8.1, 1.5 Hz, 1H), 7.70 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.63 (dd, J = 8.3, 1.2 Hz, 1H), 7.42 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 4.31 (q, J = 6.4 Hz, 1H), 3.03 (bs, O*H*, 1H), 2.98−2.88 (m, 1H), 2.87−2.77 (m, 2H), 1.72 (d, J = 6.1 Hz, 3H), 1.41 (t, J = 7.3 Hz, 3H), 1.37 (d, J = 6.4 Hz, 3H), 1.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 157.5, 146.2, 133.9, 127.0, 126.4, 126.4, 121.4, 68.5, 56.6, 51.0, 27.6, 18.8, 16.9, 12.8, 10.9; IR (KBr, cm^{-1}) 3444, 2975, 2930, 1656, 1594, 1472, 1368, 1334, 1214, 1137; MS (FAB) m/z 288 (MH^+); HRMS (FAB) calcd for $C_{16}H_{22}N_3O_2$ (MH^+) 288.1712, found 288.1707. Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.88; H, 7.37; N, 14.62. Found: C, 66.08; H, 7.32; N, 14.56.

2-Ethyl-3-(2-(1-hydroxyethyl)-2,3,3-trimethylaziridin-1-yl)-quinazolin-4(3*H*)-one (6h). A mixture of the diastereoisomeric aziridines (*threo*-**6h** and ***erythro*-6h** in a 97:3 ratio by integration of the signals at 3.92 and 4.37 ppm respectively) was chromatographed on a silica gel column to give the major diastereoisomer ***threo*-6h** (524 mg, 1.74 mmol) in a yield of 87%.

***threo*-6h:** Colorless oil. R_f 0.19 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (dd, J = 8.1, 1.4 Hz, 1H), 7.70 (ddd, J = 8.3, 7.1, 1.4 Hz, 1H), 7.62 (dd, J = 8.3, 1.2 Hz, 1H), 7.41 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H), 5.32 (bs, O*H*, 1H), 3.92 (q, J = 6.6 Hz, 1H), 2.97 (dq, J = 14.8, 7.4 Hz, 1H, A part of AB system), 2.78 (dq, J = 14.8, 7.4 Hz, 1H, B part of AB system), 1.50 (s, 3H), 1.37 (t, J = 7.4 Hz, 3H), 1.19 (d, J = 6.6 Hz, 3H), 1.12 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 158.4, 146.1, 134.0, 126.8, 126.3, 126.3, 120.8, 71.0, 57.5, 50.5, 28.1, 20.9, 18.4, 18.1, 11.2, 9.5; IR (KBr, cm^{-1}) 3438, 2977, 2935, 1666, 1593, 1568, 1472, 1378, 1285, 1210, 1109, 1055; MS (FAB) m/z 302 (MH^+); HRMS (FAB) calcd for $C_{17}H_{24}N_3O_2$ (MH^+) 302.1869, found 302.1862. Anal. Calcd for $C_{17}H_{23}N_3O_2$: C, 67.75; H, 7.69; N, 13.94. Found: C, 67.12; H, 7.50; N, 14.03. ***erythro*-6h:** Colorless oil. R_f 0.16 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (ddd, J = 8.1, 1.5, 0.5 Hz, 1H), 7.68 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.61 (ddd, J = 8.3, 1.2, 0.5 Hz, 1H), 7.39 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 4.37 (q, J = 6.4 Hz, 1H), 3.05 (bs, O*H*, 1H), 2.91 (dq, J = 14.8, 7.4 Hz, 1H, A part of AB system), 2.77 (dq, J = 14.8, 7.4 Hz, 1H, B part of AB system), 1.69 (s, 3H), 1.36 (t, J = 7.4 Hz, 3H), 1.35 (d, J = 6.4 Hz, 3H), 1.12 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 158.7, 146.2, 133.8, 126.8, 126.2, 121.4, 70.3, 55.6, 50.8, 28.0, 20.9, 19.2, 18.1, 14.9, 11.2; IR (KBr, cm^{-1}) 3445, 2977, 2937, 1688, 1593, 1568, 1472, 1374, 1287, 1211, 1108, 1054; MS (FAB) m/z 302 (MH^+); HRMS (FAB) calcd for $C_{17}H_{24}N_3O_2$ (MH^+) 302.1869, found 302.1861. Anal. Calcd for $C_{17}H_{23}N_3O_2$: C, 67.75; H, 7.69; N, 13.94. Found: C, 67.29; H, 7.47; N, 14.03.

4-Methylpent-3-en-2-yl 4-Nitrobenzoate (5i). To a stirred solution of 4-methylpent-3-en-2-ol (**5f**) (300 mg, 3 mmol) in 20 mL of ethyl acetate were added *p*-nitrobenzoyl chloride (2.78 g, 15 mmol), anhydrous K_2CO_3 (2.07 g, 15 mmol), and *N*,*N*-dimethyl-amino pyridine (DMAP) (18 mg, 0.15 mmol). The reaction mixture was stirred at room temperature for 12 h. The mixture was filtered by suction using a sintered glass funnel, and the solid residue was washed with 2 × 15 mL portions of EtOAc. The organic layer was concentrated under reduced pressure, and the residue was chromatographed on a silica gel column by elution with hexane−EtOAc (95:5) to give 4-methylpent-3-en-2-yl

4-nitrobenzoate (**5i**) (0.68 g, 2.71 mmol, 90%). Recrystallization from hexane−EtOAc afforded colorless needles. R_f 0.58 (hexane−EtOAc = 19:1); mp 67−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, J = 9.0 Hz, 2H, A part of AB system), 8.20 (d, J = 9.0 Hz, 2H, B part of AB system), 5.86 (dq, J = 9.0, 6.4 Hz, 1H), 5.35−5.16 (m, 1H), 1.78 (s, 3H), 1.75 (s, 3H), 1.42 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 150.6, 137.5, 136.6, 130.9, 124.5, 123.6, 70.4, 25.9, 21.2, 18.6; IR (KBr, cm^{-1}) 3112, 2973, 2918, 1714, 1608, 1525, 1445, 1352, 1331, 1276, 1104, 1064.

1-(1-(2-Ethyl-4-oxoquinazolin-3(4*H*)-yl)-3,3-dimethylaziridin-2-yl)ethyl 4-Nitrobenzoate (8b). A mixture of the diastereoisomeric aziridines (*threo*-**8b** and ***erythro*-8b** in a 37:63 ratio by integration of the signals at 3.70 and 3.66 ppm respectively) was chromatographed on a silica gel column to give the diastereoisomers **8b** (170 mg, 0.39 mmol) in a yield of 78%.

***threo*-8b:** Recrystallization from EtOH afforded pale yellow needles. R_f 0.44 (hexane−EtOAc = 2:1); mp 157−159 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.46 (d, J = 9.0 Hz, 2H, A part of AB system), 8.30 (d, J = 9.0 Hz, 2H, B part of AB system), 8.14 (d, J = 8.0 Hz, 1H), 7.72−7.57 (m, 2H), 7.44−7.36 (m, 1H), 5.15 (dq, J = 9.1, 6.5 Hz, 1H), 3.70 (d, J = 9.1 Hz, 1H), 3.12 (dq, J = 16.5, 7.3 Hz, 1H, A part of AB system), 2.71 (dq, J = 16.5, 7.3 Hz, 1H, B part of AB system), 1.55 (s, 3H), 1.53 (d, J = 6.5 Hz, 3H), 1.37 (t, J = 7.3 Hz, 3H), 1.18 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.5, 162.3, 160.2, 152.5, 147.9, 138.3, 135.5, 133.2, 128.8, 128.3, 128.1, 125.4, 123.6, 73.6, 56.8, 51.2, 29.8, 22.5, 21.5, 20.1, 12.5; IR (KBr, cm^{-1}) 2982, 2930, 1724, 1674, 1596, 1528, 1472, 1339, 1270, 1165, 1102; HRMS (FAB+) calcd for $C_{23}H_{25}N_4O_5$ $[M+H]^+$ 437.1825, found 437.1820. ***erythro* 8b:** Recrystallization from EtOH afforded pale yellow needles. R_f 0.80 (hexane−EtOAc = 2:1); mp 122−124 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.34−8.16 (m, 5H), 7.75−7.61 (m, 2H), 7.42 (ddd, J = 8.2, 6.6, 1.7 Hz, 1H), 5.17 (dq, J = 8.2, 6.5 Hz, 1H), 3.66 (d, J = 8.2 Hz, 1H), 3.10 (dq, J = 16.4, 7.3 Hz, 1H, A part of AB system), 2.73 (dq, J = 16.4, 7.3 Hz, 1H, B part of AB system), 1.86 (d, J = 6.5 Hz, 3H), 1.50 (s, 3H), 1.41 (t, J = 7.3 Hz, 3H), 1.15 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 165.7, 162.5, 160.2, 152.6, 147.9, 137.7, 135.7, 132.8, 128.9, 128.2, 125.6, 123.5, 74.0, 56.3, 52.7, 29.9, 22.3, 21.3, 20.6, 12.6; IR (KBr, cm^{-1}) 2986, 2924, 1724, 1675, 1596, 1528, 1468, 1334, 1270, 1163, 1102. Anal. Calcd for $C_{23}H_{24}N_4O_5$: C, 63.29; H, 5.54; N, 12.84. Found: C, 62.53; H, 5.53; N, 12.79.

Representative Procedure for Swern Oxidation of Aziridine Alcohols to Aziridinyl Ketones 7. To a solution of oxalyl chloride (115 mg, 1.1 mmol) in 1 mL of CH_2Cl_2 under a nitrogen atmosphere at −60 °C was added DMSO (390 mg, 5 mmol) in 1 mL of CH_2Cl_2. The solution was stirred for 10 min at −60 °C, and *threo*-**6** (1 mmol) in 1 mL of CH_2Cl_2 was added to the above solution. Then the resulting mixture was stirred for 5 min. To the above reaction mixture was added Et_3N (232 mg, 2.3 mmol) at −60 °C. The mixture was stirred for another 15 min and warmed to room temperature. The mixture was treated with 3.0 mL of water, and the aqueous layer was separated and extracted with CH_2Cl_2 (3 × 5.0 mL). The combined organic extracts were washed with saturated $NaHCO_3$ and 10 mL of brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. Purification by column chromatography (hexane−EtOAc = 2:1) provided the corresponding aziridinyl ketone **7**.

3-(2-Acetylaziridin-1-yl)-2-ethylquinazolin-4(3*H*)-one (7a). Colorless oil. R_f 0.25 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (ddd, J = 8.1, 1.5, 0.5 Hz, 1H), 7.72−7.66 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.61 (ddd, J = 8.3, 1.2, 0.5 Hz, 1H), 7.40 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 3.57 (dd, J = 8.1, 5.2 Hz, 1H), 3.01 (m, 3H), 2.91 (dd, J = 5.2, 1.4 Hz, 1H), 2.34 (s, 3H), 1.40 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.3, 160.1, 157.2, 146.3, 134.2, 127.2, 126.6, 126.3, 121.4, 48.4, 39.3, 27.6, 27.1, 10.9; IR (KBr, cm^{-1}) 2975, 2936, 1706, 1675, 1596, 1471, 1362, 1287, 1222, 1186, 1130; MS (FAB) m/z 258 (MH^+); HRMS (FAB) calcd for $C_{14}H_{16}N_3O_2$ (MH^+) 258.1243, found 258.1239. Anal. Calcd for $C_{14}H_{15}N_3O_2$: C, 65.35; H, 5.88; N, 16.33. Found: C, 65.01; H, 5.64; N, 15.67.

(*E*)-3-(2-Acetyl-3-methylaziridin-1-yl)-2-ethylquinazolin-4(3*H*)-one (7b). Colorless oil, R_f 0.23 (hexane−EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): (Two invertomers = 3.5:1) major invertomer δ 8.09 (ddd, J = 8.1, 1.5, 0.6 Hz, 1H), 7.73−7.60 (m, 2H), 7.38 (ddd, J = 8.1, 7.0, 1.5 Hz, 1H), 3.53 (d, J = 4.7 Hz, 1H), 3.20−3.00 (m, 1H), 2.89 (m, 2H), 2.48 (s, 3H), 1.55 (d, J = 5.7 Hz, 3H), 1.44 (t, J = 7.3 Hz, 3H); minor invertomer (observable signals) δ 8.17 (ddd, J = 8.1, 1.5, 0.6 Hz, 1H), 7.43 (ddd, J = 8.1, 7.0, 1.5 Hz, 1H), 3.64 (d, J = 5.0 Hz, 1H), 2.45 (s, 3H), 1.41 (t, J = 7.3 Hz, 3H), 1.23 (d, J = 5.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): (Two invertomers) major invertomer δ 198.1, 160.0, 155.7, 146.1, 133.7, 127.1, 126.3, 126.3, 121.1, 52.3, 49.7, 31.0, 27.7, 16.3, 10.7; minor invertomer (observable signals) δ 160.7, 157.6, 146.3, 134.0, 127.2, 126.6, 126.4, 121.4, 54.7, 46.0, 27.6, 24.0, 12.7, 10.9; IR (KBr, cm^{-1}) 2969, 2924, 1701, 1671, 1593, 1472, 1351, 1292, 1161, 1055; MS (FAB) m/z 272 (MH^+); HRMS (FAB) calcd for $C_{15}H_{18}N_3O_2$ (MH^+) 272.1399, found 272.1394. Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.94; H, 6.35; N, 15.09.

3-(2-Acetyl-2-methylaziridin-1-yl)-2-ethylquinazolin-4(3*H*)-one (7c). Colorless oil. R_f 0.23 and 0.36 (hexane−EtOAc = 2:1); (Two invertomers = 1:1) ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (ddd, J = 8.1, 1.5, 0.5 Hz, 1H), 8.07 (ddd, J = 8.1, 1.5, 0.5 Hz, 1H), 7.71 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 7.66 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 7.65−7.61 (m, 1H), 7.43 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 7.37 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 3.36 (bs, 1H), 3.33 (bs, 1H), 3.07 (s, 1H), 3.05 (dq, J = 16.3, 7.3 Hz, 1H), 2.97 (dq, J = 16.3, 7.3 Hz, 1H), 2.82 (dq, J = 16.3, 7.3 Hz, 1H), 2.66 (s, 1H), 2.62 (dq, J = 16.3, 7.3 Hz, 1H), 2.44 (s, 3H), 2.21 (s, 3H), 1.90 (s, 3H), 1.43 (t, J = 7.3 Hz, 3H), 1.36 (t, J = 7.3 Hz, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): (Two invertomers) δ 205.5, 199.4, 160.4, 160.2, 157.5, 155.6, 146.3, 146.2, 134.1, 133.6, 127.2, 127.1, 126.6, 126.5, 126.3, 126.1, 121.5, 121.1, 54.2, 51.2, 49.1, 45.2, 27.7, 27.6, 27.2, 23.9, 19.9, 12.8, 10.8, 10.7; IR (KBr, cm^{-1}) 2981, 2938, 1701, 1672, 1594, 1472, 1360, 1297, 1225, 1149; MS (FAB) m/z 272 (MH^+); HRMS (FAB) calcd for $C_{15}H_{18}N_3O_2$ (MH^+) 272.1399, found 272.1394. Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.82; H, 6.49; N, 15.03.

(*E*)-3-(2-Acetyl-2,3-dimethylaziridin-1-yl)-2-ethylquinazolin-4(3*H*)-one (7d). Recrystallization from EtOAc−hexane gave a white powder. R_f 0.23 (hexane−EtOAc = 2:1); mp 140−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 8.0 Hz, 1H), 7.69−7.60 (m, 2H), 7.37 (ddd, J = 8.0, 6.3, 1.9 Hz, 1H), 3.28 (q, J = 5.9 Hz, 1H), 2.91 (q, J = 7.3 Hz, 2H), 2.40 (s, 3H), 1.82 (s, 3H), 1.49 (d, J = 5.9 Hz, 3H), 1.43 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.1, 160.1, 155.6, 146.1, 133.6, 127.1, 126.3, 126.1, 121.0, 54.3, 53.5, 27.8, 15.4, 12.6, 10.6; IR (KBr, cm^{-1}) 2980, 2935, 1695, 1668, 1592, 1471, 1348, 1262, 1166, 1090; MS (FAB) m/z 286 (MH^+); HRMS (FAB) calcd for $C_{16}H_{20}N_3O_2$ (MH^+) 286.1556, found 286.1550. Anal. Calcd for $C_{16}H_{19}N_3O_2$: C, 67.35; H, 6.71; N, 14.73. Found: C, 67.68; H, 6.88; N, 14.61.

(*Z*)-3-(2-Acetyl-3-methylaziridin-1-yl)-2-ethylquinazolin-4(3*H*)-one (7e). Recrystallization from EtOAc−hexane gave a white powder. R_f 0.29 (hexane−EtOAc = 2:1); mp 96−98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 7.5 Hz, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 3.54 (d, J = 8.6 Hz, 1H), 3.16−3.09 (m, 1H), 3.06−2.88 (m, 2H), 2.42 (s, 3H), 1.47 (d, J = 5.9 Hz, 3H), 1.42 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.9, 160.0, 157.0, 146.2, 134.1, 127.2, 126.6, 126.3, 121.4, 53.8, 48.3, 29.8, 27.6, 12.5, 10.8; IR (KBr, cm^{-1}) 2977, 2936, 1704, 1671, 1594, 1472, 1357, 1290, 1228, 1182, 1158, 1059; MS (FAB) m/z 272 (MH^+); HRMS (FAB) calcd for $C_{15}H_{18}N_3O_2$ (MH^+) 272.1399, found 272.1394.

Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.35; H, 6.38; N, 15.50.

3-(3-Acetyl-2,2-dimethylaziridin-1-yl)-2-ethylquinazolin-4(3*H*)-one (7f). Recrystallization from EtOAc−hexane gave a white powder. R_f 0.24 (hexane−EtOAc = 2:1); mp 126−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 3.59 (s, 1H), 3.08 (dq, J = 14.7, 7.3 Hz, 1H), 2.74 (dq, J = 14.7, 7.3 Hz, 1H), 2.45 (s, 3H), 1.44 (s, 3H), 1.41 (t, J = 7.3 Hz, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.9, 160.5, 157.6, 146.1, 134.0, 127.1, 126.5, 126.3, 121.4, 58.4, 53.7, 29.5, 27.7, 20.2, 19.6, 10.7; IR (KBr, cm^{-1}) 2981, 2937, 1709, 1675, 1595, 1472, 1379, 1354, 1218, 1182, 1107; MS (FAB) m/z 286 (MH^+); HRMS (FAB) calcd for $C_{16}H_{20}N_3O_2$ (MH^+) 286.1556, found 286.1550. Anal. Calcd for $C_{16}H_{19}N_3O_2$: C, 67.35; H, 6.71; N, 14.73. Found: C, 67.07; H, 6.65; N, 14.74.

(*Z*)-3-(2-Acetyl-2,3-dimethylaziridin-1-yl)-2-ethylquinazolin-4(3*H*)-one (7g). Recrystallization from EtOAc−hexane gave a white powder. R_f 0.33 (hexane−EtOAc = 2:1); mp 98−100 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.6, Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.42 (t, J = 7.5 Hz, 1H), 3.05 (bs, 1H), 2.93 (dq, J = 14.7, 7.3 Hz, 1H), 2.71 (dq, J = 14.7, 7.3 Hz, 1H), 2.40 (s, 3H), 1.55 (d, J = 5.9 Hz, 3H), 1.40 (t, J = 7.3 Hz, 3H), 1.34 (bs, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.1, 160.6, 157.2, 146.2, 134.0, 127.1, 126.5, 126.4, 121.3, 60.0, 53.4, 28.2, 27.8, 15.3, 13.6, 10.9; IR (KBr, cm^{-1}) 2981, 2938, 1682, 1595, 1569, 1472, 1357, 1284, 1223, 1132, 1060; MS (FAB) m/z 286 (MH^+); HRMS (FAB) calcd for $C_{16}H_{20}N_3O_2$ (MH^+) 286.1556, found 286.1550. Anal. Calcd for $C_{16}H_{19}N_3O_2$: C, 67.35; H, 6.71; N, 14.73. Found: C, 67.69; H, 6.70; N, 14.66.

3-(2-Acetyl-2,3,3-trimethylaziridin-1-yl)-2-ethylquinazolin-4(3*H*)-one (7h). Recrystallization from EtOAc−hexane gave a white powder. R_f 0.34 (hexane−EtOAc = 2:1); mp 144−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (dd, J = 8.1, 1.5 Hz, 1H), 7.69 (ddd, J = 8.3, 7.1, 1.5 Hz, 1H), 7.62 (dd, J = 8.3, 1.2 Hz, 1H), 7.40 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H), 2.92 (dq, J = 14.8, 7.3 Hz, 1H), 2.79 (dq, J = 14.8, 7.3 Hz, 1H), 2.54 (s, 3H), 1.41 (s, 3H), 1.39 (t, J = 7.3 Hz, 3H), 1.26 (s, 3H), 1.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.8, 161.4, 158.1, 146.2, 133.9, 126.8, 126.3, 126.2, 121.3, 59.8, 51.7, 28.3, 28.0, 22.5, 17.2, 14.1, 11.1; IR (KBr, cm^{-1}) 2986, 2939, 1683, 1594, 1568, 1471, 1354, 1295, 1211, 1167, 1106, 1071; MS (FAB) m/z 300 (MH^+); HRMS (FAB) calcd for $C_{17}H_{22}N_3O_2$ (MH^+) 300.1712, found 300.1707. Anal. Calcd for $C_{17}H_{21}N_3O_2$: C, 68.20; H, 7.07; N, 14.04. Found: C, 67.94; H, 6.97; N, 14.03.

Representative Procedure for Reduction of Aziridinyl Ketone 7 with Sodium Borohydride to *threo*- and *erythro*-Aziridine Alcohols 6. To a stirred solution of aziridinyl ketone **7** (1 mol equiv) in dry CH_3OH (3 mL) was added $NaBH_4$ (1 mol equiv) in small portions over 10 min, and the reaction mixture stirred until the starting material aziridinyl ketone disappeared as monitored by TLC (10 min). The reaction mixture was poured into water (3 mL), and the bulk of the methanol was removed by evaporation under reduced pressure. The residual solution was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried over Na_2SO_4. After removal of the solvent, *threo* and *erythro* diastereoisomers were separated on a silica gel column by elution with hexane−EtOAc.

***threo*-1-(2-Ethyl-4-oxoquinazolin-3(4*H*)-yl)-3-methylaziridin-2-yl)ethyl 4-Nitrobenzoate (8a).** To a stirred solution of ***threo*-6e** (45 mg, 0.16 mmol) in dichloromethane (2 mL) were added pyridine (19 mg, 0.24 mmol) and *p*-nitrobenzoyl chloride (92 mg, 0.49 mmol) at 0 °C. The final mixture was stirred at room temperature for 6 h and quenched by the addition of saturated aqueous sodium bicarbonate. The aqueous layer was extracted with dichloromethane (3 × 3 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. Further purification by chromatography on silica gel (hexane−EtOAc = 2:1) gave ***threo*-8a** (55 mg, 0.13 mmol) in a yield of 81%. Recrystallization from EtOH afforded pale yellow needles. R_f 0.40 (hexane−EtOAc = 2:1); mp 129−131 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.39−8.27 (m, 4H), 8.13 (dd, J = 8.1, 1.4 Hz, 1H), 7.72−7.57 (m, 2H), 7.43−7.35 (m, 1H), 5.22 (dq, J = 9.1, 6.5 Hz, 1H), 3.57 (t, J = 8.6 Hz, 1H), 3.22−2.95 (m, 3H), 1.54 (d, J = 6.0, 3H), 1.51 (d, J = 6.5 Hz, 3H), 1.29 (t, J = 7.3 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.1, 162.5, 160.4, 152.7, 148.1, 137.9, 135.7, 132.9, 128.8, 128.1, 125.4, 123.7, 73.4, 50.7, 44.4, 29.8, 20.1, 14.7, 12.8; IR (KBr, cm^{-1}) 2980, 2936, 1724, 1676, 1597, 1528, 1473, 1340, 1268, 1102; MS (FAB) m/z 423 (MH^+); HRMS (FAB) calcd for $C_{22}H_{23}N_4O_5$ (MH^+) 423.1668, found 423.1662. Anal. Calcd for $C_{22}H_{22}N_4O_5$: C, 62.55; H, 5.25; N, 13.26. Found: C, 62.32; H, 5.36; N, 13.25.

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Supporting Information Available: X-ray structures and crystallographic data for compounds *threo*-**6d** and *threo*-**8a**, DFT calculations, and copies of the ^{1}H−^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.