

Introduction of hydroxyl- or keto- functionalities into the side chain of azetidin-2-ones via allylic bromide rearrangement, followed by supported reagent substitution

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Dedicated to our friend Prof. Eusebio Juaristi on the occasion of his 55th birthday
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Abstract

This paper reports the allylic bromide rearrangement of 3-bromo-3-alkenyl-azetidin-2-ones, induced by *m*-chloroperbenzoic acid, *N*-bromosuccinimide or benzoylperoxide as radical initiators. The substitution of bromide by resin supported acids, followed by hydrolysis of the ester moiety, allowed an hydroxyl- or keto- function to be introduced in the C3 side chain of the azetidinone, thus giving access to a new class of potential cholesterol absorption inhibitors.

Keywords: Azetidinones, allylic bromide, rearrangement, supported reagents

Introduction

The nucleophilic substitution of allylic halides continues to draw great attention as it leads to a variety of derivatives, which can be converted into a wide spectrum of synthetically important molecules.¹ Among the most interesting aspects of allylic compounds, the stereo- and regio-chemistry of their reactions have received considerable attention.

In recent reports from our laboratory, the use of 3-bromo-3-alkenyl-azetidin-2-one as a particular allylic system has been studied.² In fact, the bimolecular nucleophilic displacement with allylic rearrangement (S_N2' reaction) easily occurred on this kind of substrates either with azide anion³ or under palladium catalyzed benzylamine attack.⁴ Both reactions afforded complete regio- and stereoselective substitution at C2' side chain with C-N bond formation. The stereoselective anti S_N2' attack of NaN_3 to 3-alkenyl-3-bromo-azetidin-2-ones, followed by the stereoselective [3,3]-sigmatropic rearrangement of allylic azides, gave diastereomeric azides, useful precursors of 3(2'-amino)- β -lactams (Figure 1, pathway A).

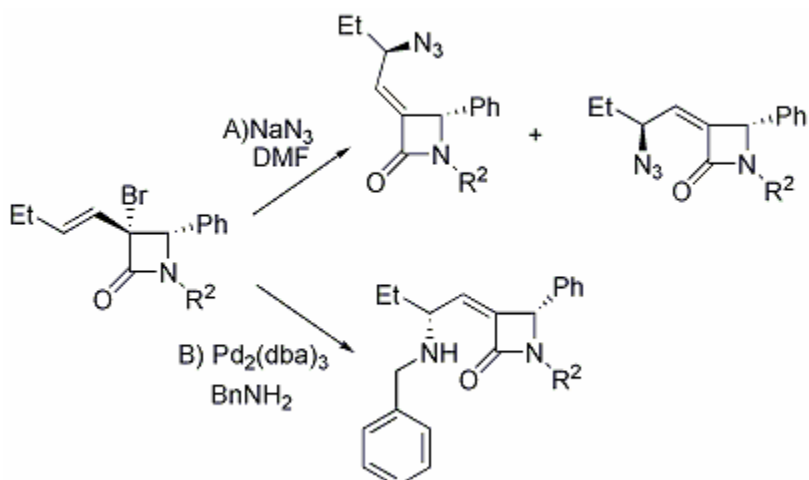


Figure 1. Reactions performed on 3-bromo-azetidin-2-ones.

On the other hand, palladium-catalyzed allylic substitution, provides one of the most efficient methods for the stereoselective construction of carbon-carbon or carbon-heteroatom bond. Therefore the palladium-catalyzed benzylamine attack to 3-alkenyl-3-bromo-azetidin-2-ones allowed the amino function in the C3 side chain of the non conventional β -lactams to be introduced in a highly regio- and stereoselective fashion (Figure 1, pathway B).

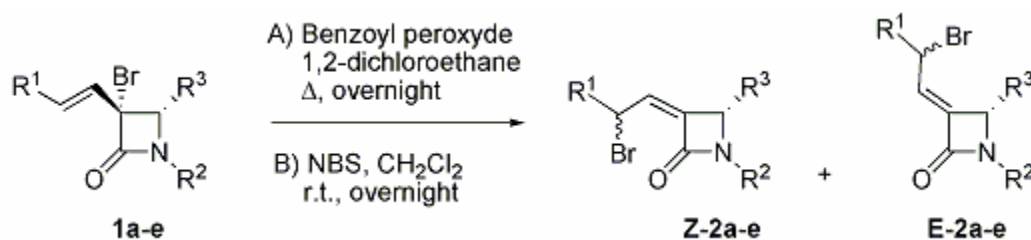
The search for lead structures for the discovery of new protease inhibitors is a field of growing interest. Beside the high antibacterial activity showed by various natural β -lactams, new applications of azetidin-2-ones in the field of enzyme inhibition of proteases have been recently reported.⁵ The β -lactam ring represents the most important pharmacophore group for the inhibition activity, nevertheless the activity can be enhanced by proper functionalization at the side chain in C3 and C4 position of the ring.

Results and Discussion

During our investigation on the reactivity of α -alkenyl- α -bromo- β -lactams **1a-e**, we observed an unusual behavior of these substrates. When they were treated with *m*-chloroperoxybenzoic acid (MCPBA) in 2M solution in CH₂Cl₂, the exclusive formation of the epoxides was observed. On the other hand a 40:60 mixture of epoxide and bromine rearrangement products, in *E* and *Z* configuration of the double bond, was observed when the reaction was stirred for three hours at r.t. under diluted conditions (1 mmol of **1a** with 1.5 equivalents of MCPBA in 5 mL of CH₂Cl₂).

The dependence of the reaction upon the dilution, suggested a radical mechanism. In agreement with recent reports⁶ that propose unsymmetrical biradical transition state in the epoxidation of the double bond performed with peracids, the possibility that MCPBA could act as radical initiator could explain the outcome of the reaction.

Starting from the hypothesis of a radical mechanism,⁷ we treated compound **1a** in refluxing 1,2-dichloroethane with benzoylperoxide (method A) or in CH₂Cl₂ with *N*-bromosuccinimide at r.t. (method B), reagents that are well known radical initiators (Scheme 1). Under these conditions the same mixture of *E*- and *Z*-bromo derivatives was obtained in quantitative yield.



Scheme 1. Radical rearrangement of **1a-e** with benzoylperoxide or *N*-bromosuccinimide.

The extraction of the organic phase afforded 80% of a 1:1 easily separable mixture of *Z* and *E* diastereomers of 2'-bromolactam **2a**. Each *Z* or *E* compound was obtained with a low control of the selectivity in the formation of the newly introduced stereogenic C2' centre (70:30). The stereochemistry on the newly introduced stereocentre was not investigated. The *Z* and *E* configuration was attributed on the basis of vinyl H₁ chemical shift of the ¹H NMR spectrum, as reported in the literature.⁸ Then, we applied the same reaction to substrates **1b-e** and the results are reported in Table 1. Racemic mixtures of *Z*-**2a-e** and *E*-**2a-e** were separated by flash chromatography on silica gel.

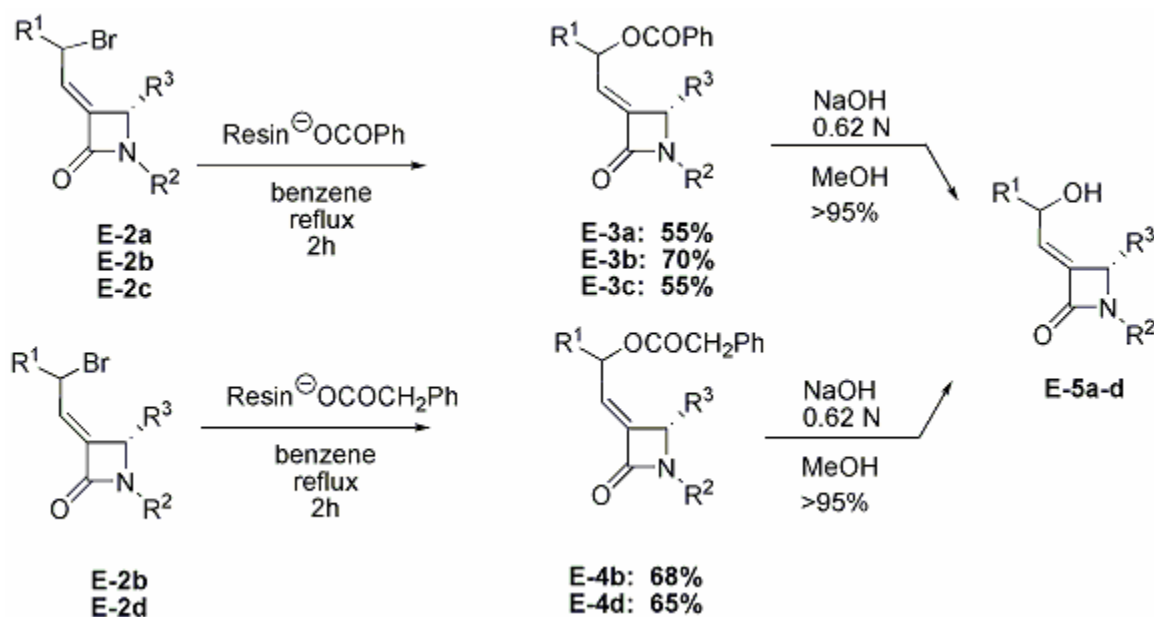
Table 1. Rearrangement of **1** to *Z/E*-**2**

Entry ^(a)		R ¹	R ²	R ³	Yield <i>Z</i> + <i>E</i> ^a (%)
1	1a	H	CH ₂ Ph	Ph	95
2	1b	Et	CH ₂ Ph	Ph	97
3	1c	Et	(CH ₂) ₂ CO ₂ Et	Ph	92
4	1d	Et	CH ₂ Ph	<i>p</i> -NO ₂ Ph	78
5	1e	Et	(<i>S</i>)-phenylethyl	Ph	80

^a Equimolar amount of *Z* and *E* diastereomers were obtained with 70/30 d.r. The diastereomeric mixtures were separated by flash chromatography on silica gel.

Aiming to introduce functionalities into the C3 side chain, we carried out a series of simple substitution reactions on *Z*-**2** and *E*-**2** derivatives. Many examples of β -lactam based cholesterol

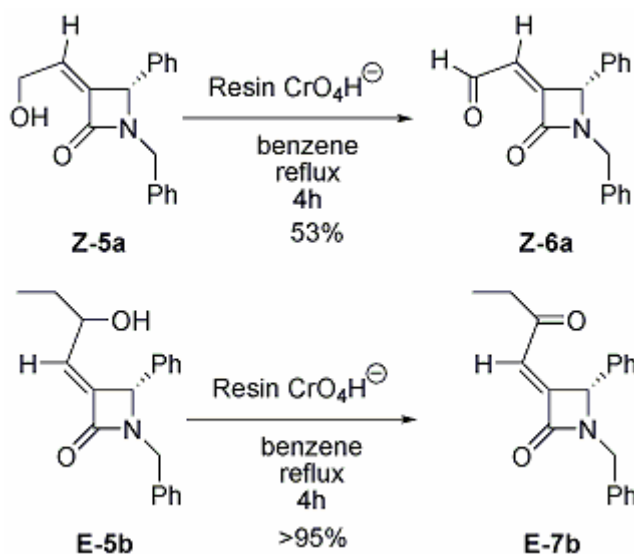
absorption inhibitors containing hydroxyl- and keto- functions in the C3 side chain have been recently reported in the literature.⁹ Therefore, in connection with our scientific interests, we developed an efficient and very mild process to convert allyl bromides to the corresponding alcohols. Each *E*-bromo derivatives **E-2a-c** was treated with benzoic acid supported on macroreticular styrene-divinylbenzene resin with quaternary ammonium functionality, for 2 h in benzene at reflux.¹⁰ Under the same reaction conditions **E-2b** and **E-2d** were treated with supported phenylacetic acid, with the aim to perform the enzymatic resolution of the racemic phenylacetates by treatment with penicillin G acylase. The bromides were easily substituted and the corresponding benzoates **E-3a-c** or phenylacetates **E-4b-d** were obtained in good yield with complete stereo- and regiocontrol (Scheme 2). It is well known that the supported reagents are very useful since they show high nucleophilicity, the reaction occurs under very mild conditions and in a variety of organic solvents, the usual work-up is avoided and it is reduced to the simple filtration of the resin and evaporation of organic solvents.¹¹



Scheme 2. Reaction of **E-2** with resin supported benzoic acid and phenyl acetic acid followed by hydrolysis to **E-5**.

In a similar way, **Z-2a-b** afforded after treatment with benzoic acid supported on resin, the corresponding benzoates **Z-3a** and **Z-3b** in 87% and 70% yields respectively. By treating **Z-2b** and **Z-2d** with phenylacetate resin **Z-4b** and **Z-4d** were isolated in 72% and 55% yield respectively. In order to avoid the opening of the β -lactam ring the hydrolysis of the esters was carried out under mild conditions with NaOH 0.6N in methanol. The hydrolysis smoothly occurred in 48 h, affording the *E* or *Z* allylic alcohols **5a-d** in quantitative yield.

On pursuing the investigation on the reactivity of our substrates with supported reagents, we performed the oxidation of the alcohols **5** with chromic acid supported on anion exchange resin.¹² Among the variety of procedures for the oxidation of alcohols, this method is remarkably efficient in the clean conversion of primary and secondary alcohols into aldehydes and ketones respectively. The reaction was tested on the primary alcohol **Z-5a** and **E-5a** and on the secondary **E-5b**. By refluxing **Z-5a** and **E-5a** in benzene, in the presence of 3 equiv. of chromic acid supported on anion exchange resin (loading 2.1 mmol/g), the formation of the aldehyde **Z-6a** and **E-6a** in 53% yield and 55% yield respectively, was observed in 4h. Under the same reaction conditions, **E-5b** was quantitatively converted into ketone **E-7b** (Scheme 3).



Scheme 3. Oxidation of hydroxy-derivatives **Z-5a** and **E-6a** to carbonyl derivatives.

In conclusion, this paper reports the allylic bromide rearrangement of 3-bromo-3-alkenyl-azetidin-2-ones, induced by MCPBA, NBS or benzoylperoxide as radical initiators. The substitution of bromide by resin supported acids followed by hydrolysis of the ester moiety, allows to introduce an hydroxyl- or keto- function in the C3 side chain of the azetidinone, thus giving access to a new class of potential cholesterol absorption inhibitors.

Experimental Section

General Procedures. Unless stated otherwise, solvents and chemicals were obtained from commercial sources and used without further purification. Flash chromatography was performed on silica gel (230-400 mesh). NMR Spectra were recorded with 300 MHz spectrometers. Chemical shifts were reported as δ values (ppm) relative to the solvent peak of CDCl₃ set at $\delta = 7.27$ (¹H NMR) or $\delta = 77.0$ (¹³C NMR). Infrared spectra were recorded with an FT-IR

spectrometer. Melting points are uncorrected. MS analyses were performed on a liquid chromatograph coupled with an electrospray ionization-mass spectrometer (LC-ESI-MS), using H₂O/CH₃CN as solvent at 25 °C (positive scan 100-500 m/z, fragmentor 70V). Chiral HPLC analysis were performed on Chiralcel-OD Daicel column, Cellulose tris(3,5-dimethylphenyl)carbamate phase coated on 10µm silica gel, *n*-hexane/2-propanol 90:10 solvent mixture, flow 0.5 mL/min.

General procedure for the rearrangement of 1a-e to Z/E-2a-e

Method A: To a stirred solution of **1** (1 mmol) in 1,2-dichloroethane (5 mL), benzoylperoxide (1.1 mmol, 1.1 equiv., 266 mg) was added in one portion. The reaction was refluxed overnight and then quenched with water (5 mL). After dilution with 1,2-dichloroethane (10 mL), the organic layer was washed twice with water and dried over Na₂SO₄. The products were isolated by flash chromatography on silica gel (cyclohexane/diethyl ether 9/1 as eluant).

Method B: To a stirred solution of **1** (1 mmol) in CH₂Cl₂ (5 mL), *N*-bromosuccinimide (0.5 mmol, 0.5 equiv., 89 mg.) was added in one portion. The reaction was stirred at r.t. overnight and then quenched with water (5 mL). After dilution with CH₂Cl₂ (10 mL), the organic layer was washed twice with water and dried over Na₂SO₄. The products were isolated by flash chromatography on silica gel (cyclohexane/diethyl ether 9/1 as eluant).

(Z)-1-Benzyl-3-(2-bromoethylidene)-4-phenylazetid-2-one (2a). ¹H NMR (300MHz, CDCl₃) δ_H 3.92 (1H, d, *J*=15.0 Hz, CH₂Ph), 4.38 (1H, dd, *J*=8.7, 10.5 Hz, CH₂Br), 4.47 (1H, dd, *J*=8.7, 10.5 Hz, CH₂Br), 4.84 (1H, s, CHPh), 4.94 (1H, d, *J*=15.0 Hz, CH₂Ph), 5.71 (1H, t, *J*=8.7 Hz, CH=C), 7.17-7.50 (10H, m, Ar); ¹³C NMR (75MHz, CDCl₃) δ_C 26.1, 44.3, 61.6, 124.1, 127.4, 127.8, 128.5, 128.8, 128.9, 129.0, 135.0, 135.8, 145.2, 162.8; LC-ESI-MS rt 12.3 min., m/z 342-344 (M+1), 364-366 (M+Na); IR (film) 3065, 2913, 1739, 1706, 1428, 1315, 1262, 1070 cm⁻¹; Calcd for C₁₈H₁₆BrNO: C, 63.17; H, 4.71; N, 4.09. Found: C, 63.15; H, 4.70; N, 4.11.

(E)-1-benzyl-3-(2-bromoethylidene)-4-phenylazetid-2-one (2a). ¹H NMR (300MHz, CDCl₃) δ_H 3.62 (1H, dd, *J*=8.4, 10.5 Hz, CH₂Br), 3.65 (1H, dd, *J*=8.4, 10.5 Hz, CH₂Br), 3.87 (1H, d, *J*=15.0 Hz, CH₂Ph), 4.91 (1H, d, *J*=15.0 Hz, CH₂Ph), 4.96 (1H, s, CHPh), 6.39 (1H, t, *J*=8.4 Hz, CH=C), 7.05-7.10 (2H, m, Ar), 7.10-7.50 (8H, m, Ar); ¹³C NMR (75MHz, CDCl₃) δ_C 25.0, 44.3, 61.3, 121.1, 127.5, 127.9, 128.1, 128.5, 128.8, 129.2, 134.9, 138.8, 145.6, 163.0; LC-ESI-MS rt 11.8 min., m/z 342-344 (M+1), 364-366 (M+Na); IR (film) 3066, 2910, 1733, 1429, 1315, 1261, 1077cm⁻¹; Calcd for C₁₈H₁₆BrNO: C, 63.17; H, 4.71; N, 4.09. Found: C, 63.18; H, 4.74; N, 4.06.

(Z)-1-benzyl-3-(2-bromobutylidene)-4-phenylazetid-2-one (2b). First diastereomer: ¹H NMR (300MHz, CDCl₃) δ_H 1.00 (3H, t, *J*=7.8 Hz, CH₂CH₃), 1.77-2.05 (2H, m, CH₂CH₃), 3.87 (1H, d, *J*=15.0 Hz, CH₂Ph), 4.81 (1H, s, CHPh), 4.88 (1H, d, *J*=15.0 Hz, CH₂Ph), 5.42 (1H, dt, *J*=7.4, 10.8 Hz, CHBr), 5.61 (1H, d, *J*=10.8 Hz, CH=C), 7.05-7.55 (10H, m, Ar); ¹³C NMR (75MHz, CDCl₃) δ_C 11.9, 32.3, 44.1, 49.5, 61.2, 125.3, 127.1, 127.2, 127.5, 127.6, 128.3, 128.4, 128.6, 128.7, 128.8, 128.9, 134.8, 141.2, 143.1, 162.6; LC-ESI-MS rt 17.5 min., m/z 370-372 (M+1), 392-394 (M+Na); IR (film) 3031, 2968, 2931, 1748, 1655, 1496, 1456, 1381, 1353, 1288 cm⁻¹; Calcd for C₂₀H₂₀BrNO: C, 64.87; H, 5.44; N, 3.78. Found: C, 64.86; H, 5.46; N, 3.80.

Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 1.06 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.81-2.02 (2H, m, CH_2CH_3), 3.86 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.82 (1H, s, CHPh), 4.87 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.44 (1H, dt, $J=7.4$, 10.8 Hz, CHBr), 5.64 (1H, d, $J=10.8$ Hz, $\text{CH}=\text{C}$), 7.05-7.60 (10H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.8, 32.0, 44.1, 50.0, 61.4, 125.9, 127.1, 127.2, 127.5, 127.6, 128.3, 128.4, 128.6, 128.7, 128.8, 128.9, 135.0, 142.5, 144.0, 162.8; LC-ESI-MS rt 17.1 min., m/z 370-372 ($\text{M}+1$), 392-394 ($\text{M}+\text{Na}$); IR (film) 3032, 2967, 2931, 1748, 1654, 1496, 1455, 1380, 1070 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{20}\text{BrNO}$: C, 64.87; H, 5.44; N, 3.78. Found: C, 64.85; H, 5.43; N, 3.78.

(E)-1-Benzyl-3-(2-bromobutylidene)-4-phenylazetid-2-one (2b). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.53 (3H, t, $J=7.2$ Hz, CH_2CH_3), 1.50-1.75 (2H, m, CH_2CH_3), 3.87 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.10 (1H, dt, $J=7.0$, 10.8 Hz, CHBr), 4.88 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.95 (1H, s, CHPh), 6.25 (1H, d, $J=10.8$ Hz, $\text{CH}=\text{C}$), 7.00-7.50 (10H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.4, 31.7, 44.2, 48.8, 61.3, 125.4, 127.3, 127.8, 128.4, 128.7, 128.9, 129.1, 134.5, 134.9, 144.0, 163.0; LC-ESI-MS rt 16.4 min., m/z 370-372 ($\text{M}+1$), 392-394 ($\text{M}+\text{Na}$); IR (film) 3031, 2969, 2929, 1753, 1560, 1496, 1456, 1382, 1353, 1354 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{20}\text{BrNO}$: C, 64.87; H, 5.44; N, 3.78. Found: C, 64.88; H, 5.42; N, 3.79. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.93 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.77-1.90 (2H, m, CH_2CH_3), 3.84 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.01 (1H, dt, $J=7.0$, 10.6 Hz, CHBr), 4.86 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.87 (1H, s, CHPh), 6.30 (1H, d, $J=10.8$ Hz, $\text{CH}=\text{C}$), 7.00-7.50 (10H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.9, 31.7, 44.2, 49.3, 61.5, 125.5, 127.3, 127.8, 128.4, 128.7, 128.9, 129.0, 135.0, 135.7, 142.2, 163.0; LC-ESI-MS rt 15.3 min., m/z 370-372 ($\text{M}+1$), 392-394 ($\text{M}+\text{Na}$); IR (film) 3031, 2967, 2927, 1751, 1685, 1676, 1495, 1456, 1354 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{20}\text{BrNO}$: C, 64.87; H, 5.44; N, 3.78. Found: C, 64.86; H, 5.44; N, 3.79.

Ethyl 3-((Z)-3-(2-bromobutylidene)-2-oxo-4-phenylazetid-1-yl)propanoate (2c). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 1.04 (3H, t, $J=7.2$ Hz, CH_2CH_3), 1.22 (3H, t, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$), 1.80-2.05 (2H, m, CH_2CH_3), 2.50-2.80 (2H, m, CH_2COOEt), 3.32 (1H, dt, $J=6.8$, 14.4 Hz, NCH_2CH_2), 3.75 (1H, dt, $J=6.8$, 14.4 Hz, NCH_2CH_2), 4.10 (2H, q, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$), 5.00 (1H, s, CHPh), 5.33 (1H, dt, $J=7.0$, 11.0 Hz, CHBr), 5.60 (1H, d, $J=11.0$ Hz, $\text{CH}=\text{C}$), 7.20-7.50 (5H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.9, 14.1, 32.5, 33.0, 36.4, 49.6, 60.9, 63.0, 125.4, 127.2, 128.9, 129.2, 135.6, 142.0, 163.2, 172.1; LC-ESI-MS rt 14.8 min., m/z 380-382 ($\text{M}+1$), 402-404 ($\text{M}+\text{Na}$); IR (film) 2940, 2923, 2853, 1700, 1456, 1419, 1402, 1377, 1305, 1200, 1173 cm^{-1} ; Calcd for $\text{C}_{18}\text{H}_{22}\text{BrNO}_3$: C, 56.85; H, 5.83; N, 3.68. Found: C, 56.87; H, 5.85; N, 3.71. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 1.02 (3H, t, $J=7.2$ Hz, CH_2CH_3), 1.23 (3H, t, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$), 1.60-1.80 (2H, m, CH_2CH_3), 2.50-2.70 (2H, m, CH_2COOEt), 3.35 (1H, dt, $J=7.5$, 14.4 Hz, NCH_2CH_2), 3.76 (1H, dt, $J=6.9$, 14.4 Hz, NCH_2CH_2), 4.12 (2H, q, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$), 5.03 (1H, s, CHPh), 5.37 (1H, dt, $J=6.6$, 10.5 Hz, CHBr), 5.64 (1H, d, $J=10.5$ Hz, $\text{CH}=\text{C}$), 7.20-7.45 (5H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 12.0, 14.1, 32.4, 33.0, 37.2, 50.0, 61.0, 62.7, 125.6, 127.6, 128.7, 129.0, 137.1, 141.8, 163.1, 172.0; LC-ESI-MS rt 13.9 min., m/z 380-382 ($\text{M}+1$), 402-404 ($\text{M}+\text{Na}$); IR (film) 2924, 2854,

1706, 1454, 1416, 1403, 1376, 1305, 1199 cm^{-1} ; Calcd for $\text{C}_{18}\text{H}_{22}\text{BrNO}_3$: C, 56.85; H, 5.83; N, 3.68. Found: C, 56.84; H, 5.82; N, 3.64.

Ethyl 3-((E)-3-(2-bromobutylidene)-2-oxo-4-phenylazetid-1-yl)propanoate (2c). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.52 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.22 (3H, t, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$), 1.45-1.80 (2H, m, CH_2CH_3), 2.40-2.70 (2H, m, CH_2COOEt), 3.33 (1H, dt, $J=7.0, 14.6$ Hz, NCH_2CH_2), 3.75 (1H, dt, $J=6.6, 14.6$ Hz, NCH_2CH_2), 4.00-4.10 (1H, m, CHBr), 4.09 (2H, q, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$), 5.14 (1H, d, $J_{1,3}=1.5$ Hz, CHPh), 6.21 (1H, dd, $J=11.0$ Hz, $J_{1,3}=1.5$ Hz, $\text{CH}=\text{C}$), 7.25-7.45 (5H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.5, 14.0, 31.8, 33.1, 36.4, 48.8, 60.8, 62.7, 125.5, 127.3, 129.1, 129.7, 133.5, 144.1, 163.5, 171.0; LC-ESI-MS rt 14.2 min., m/z 380-382 (M+1), 402-404 (M+Na); IR (film) 2972, 2932, 1734, 1457, 1376, 1189, 1112, 1071, 1020 cm^{-1} ; Calcd for $\text{C}_{18}\text{H}_{22}\text{BrNO}_3$: C, 56.85; H, 5.83; N, 3.68. Found: C, 56.83; H, 5.81; N, 3.70. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.96 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.23 (3H, t, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$), 1.81-1.96 (2H, m, CH_2CH_3), 2.40-2.80 (2H, m, CH_2COOEt), 3.34 (1H, dt, $J=6.6, 14.8$ Hz, NCH_2CH_2), 3.71 (1H, dt, $J=6.2, 14.8$ Hz, NCH_2CH_2), 3.96-4.10 (1H, m, CHBr), 4.09 (2H, q, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$), 5.08 (1H, s, CHPh), 6.28 (1H, dd, $J=11.0$ Hz, $\text{CH}=\text{C}$), 7.25-7.45 (5H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 12.0, 14.1, 31.8, 33.1, 36.4, 49.2, 60.9, 63.1, 125.6, 127.8, 129.1, 130.2, 135.0, 142.2, 163.6, 171.2; LC-ESI-MS rt 13.7 min., m/z 380-382 (M+1), 402-404 (M+Na); IR (film) 2985, 2928, 1734, 1457, 1376, 1243 cm^{-1} ; Calcd for $\text{C}_{18}\text{H}_{22}\text{BrNO}_3$: C, 56.85; H, 5.83; N, 3.68. Found: C, 56.82; H, 5.87; N, 3.72.

(Z)-1-Benzyl-3-(2-bromobutylidene)-4-(4-nitrophenyl)azetid-2-one (2d). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.98 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.76-2.05 (2H, m, CH_2CH_3), 4.02 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.86 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.90 (1H, s, CHPh), 5.32 (1H, dt, $J=7.4, 10.6$ Hz, CHBr), 5.63 (1H, d, $J=10.6$ Hz, $\text{CH}=\text{C}$), 7.00-7.20 (2H, m, Ar), 7.20-7.40 (5H, m, Ar), 8.20 (2H, d, $J=7.8$ Hz, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 12.0, 32.2, 44.9, 49.1, 60.7, 124.1, 127.9, 128.1, 128.5, 128.9, 129.7, 134.3, 142.3, 143.8, 148.1, 162.4; LC-ESI-MS rt 15.8 min., m/z 415-417 (M+1), 437-439 (M+Na); IR (film) 3066, 2969, 2932, 1751, 1603, 1522, 1496, 1349, 1291, 1106, 1072 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{19}\text{BrN}_2\text{O}_3$: C, 57.84; H, 4.61; N, 6.75. Found: C, 57.80; H, 4.58; N, 6.78. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 1.05 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.86-2.05 (2H, m, CH_2CH_3), 3.98 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.84 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.88 (1H, s, CHPh), 5.37 (1H, dt, $J=6.6, 10.6$ Hz, CHBr), 5.64 (1H, d, $J=10.6$ Hz, $\text{CH}=\text{C}$), 7.11-7.14 (2H, m, Ar), 7.28-7.47 (5H, m, Ar), 8.18-8.24 (2H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.8, 32.0, 44.8, 49.6, 60.4, 124.1, 126.4, 128.5, 128.9, 129.8, 134.3, 141.6, 143.6, 148.1, 162.6; LC-ESI-MS rt 15.5 min., m/z 415-417 (M+1), 437-439 (M+Na); IR (film) 3061, 3029, 2968, 2931, 1752, 1654, 1522, 1349 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{19}\text{BrN}_2\text{O}_3$: C, 57.84; H, 4.61; N, 6.75. Found: C, 57.85; H, 4.59; N, 6.74.

(E)-1-Benzyl-3-(2-bromobutylidene)-4-(4-nitrophenyl)azetid-2-one (2d). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.57 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.57-1.77 (2H, m, CH_2CH_3), 3.98 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.05 (1H, m, CHBr), 4.84 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.03 (1H, s, CHPh), 6.32 (1H, d, $J=10.8$ Hz, $\text{CH}=\text{C}$), 7.12-7.14 (2H, m, Ar), 7.28-7.46

(5H, m, Ar), 8.20 (2H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.6, 31.6, 44.9, 48.0, 60.5, 124.2, 126.4, 128.3, 128.8, 129.8, 134.5, 141.6, 143.3, 148.1, 162.4; LC-ESI-MS rt 14.6 min., m/z 415-417 (M+1), 437-439 (M+Na); IR (film) 3065, 2970, 2927, 1752, 1656, 1607, 1522, 1349 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{19}\text{BrN}_2\text{O}_3$: C, 57.84; H, 4.61; N, 6.75. Found: C, 57.81; H, 4.63; N, 6.74. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.94 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.78-2.05 (2H, m, CH_2CH_3), 3.89-3.97 (1H, m, CHBr), 3.98 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.84 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.96 (1H, s, CHPh), 6.35 (1H, d, $J=11.0$ Hz, $\text{CH}=\text{C}$), 7.10-7.15 (2H, m, Ar), 7.28-7.47 (5H, m, Ar), 8.21-8.32 (2H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.9, 31.6, 44.8, 48.9, 60.6, 124.2, 126.5, 128.1, 128.5, 128.8, 128.9, 134.4, 141.5, 142.4, 148.3, 162.6; LC-ESI-MS rt 14.2 min., m/z 415-417 (M+1), 437-439 (M+Na); IR (film) 3061, 2970, 2933, 1751, 1606, 1521, 1345 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{19}\text{BrN}_2\text{O}_3$: C, 57.84; H, 4.61; N, 6.75. Found: C, 57.83; H, 4.61; N, 6.77.

(Z)-1-(1'S-Phenylethyl)-3-(2-bromobutylydene)-4-(4-nitrophenyl)azetid-2-one (2e). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 1.00 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.32 (1H, d, $J=7.4$ Hz, CHCH_3), 1.80-1.95 (2H, m, CH_2CH_3), 4.68 (1H, bs, CHPh), 5.11 (1H, q, $J=7.4$ Hz, CHCH_3), 5.35 (1H, m, CHBr) 5.53 (1H, d, $J=11.8$ Hz, $\text{CH}=\text{C}$), 7.21-7.39 (10H, m, Ar), ^{13}C NMR (75MHz, CDCl_3) δ_{C} 12.0, 32.2, 44.9, 49.1, 60.7, 124.1, 127.9, 128.1, 128.5, 128.9, 129.7, 134.3, 142.3, 143.8, 148.1, 162.4; LC-ESI-MS rt 15.2 min., m/z 384-386 (M+1), 406-408 (M+Na); IR (film) 3066, 2969, 2932, 1751, 1603, 1522, 1496, 1349, 1291, 1106, 1072 cm^{-1} ; Calcd for $\text{C}_{21}\text{H}_{22}\text{BrNO}$: C, 65.63; H, 5.77; N, 3.64. Found: C, 65.61; H, 5.75; N, 3.62. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 1.03 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.22 (1H, d, $J=7.4$ Hz, CHCH_3), 1.88-2.00 (2H, m, CH_2CH_3), 4.61 (1H, bs, CHPh), 5.05 (1H, q, $J=7.4$ Hz, CHCH_3), 5.39 (1H, m, CHBr) 5.52 (1H, d, $J=11.5$ Hz, $\text{CH}=\text{C}$), 7.19-7.45 (10H, m, Ar), ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.8, 32.0, 44.8, 49.6, 60.4, 124.1, 126.4, 128.5, 128.9, 129.8, 134.3, 141.6, 143.6, 148.1, 162.6; LC-ESI-MS rt 14.4 min., m/z 384-386 (M+1), 406-408 (M+Na); IR (film) 3061, 3029, 2968, 2931, 1752, 1654, 1522, 1349 cm^{-1} ; Calcd for $\text{C}_{21}\text{H}_{22}\text{BrNO}$: C, 65.63; H, 5.77; N, 3.64. Found: C, 65.60; H, 5.78; N, 3.64.

(E)-1-(1'S-Phenylethyl)-3-(2-bromobutylydene)-4-(4-nitrophenyl)azetid-2-one (2e).

First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.53 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.34 (1H, d, $J=7.4$ Hz, CHCH_3), 1.42-1.70 (2H, m, CH_2CH_3), 3.99 (1H, dt, $J=10.5, 16.3$ Hz, CHBr), 4.82 (1H, bs, CHPh), 5.15 (1H, q, $J=7.4$ Hz, CHCH_3), 6.20 (1H, d, $J=10.5$ Hz, $\text{CH}=\text{C}$), 7.22-7.40 (10H, m, Ar), ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.6, 31.6, 44.9, 48.0, 60.5, 124.2, 126.4, 128.3, 128.8, 129.8, 134.5, 141.6, 143.3, 148.1, 162.4; LC-ESI-MS rt 15.3 min., m/z 384-386 (M+1), 406-408 (M+Na); IR (film) 3065, 2970, 2927, 1752, 1656, 1607, 1522, 1349 cm^{-1} ; Calcd for $\text{C}_{21}\text{H}_{22}\text{BrNO}$: C, 65.63; H, 5.77; N, 3.64. Found: C, 65.63; H, 5.79; N, 3.66. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.98 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.30 (1H, d, $J=7.4$ Hz, CHCH_3), 1.40-1.60 (2H, m, CH_2CH_3), 3.90 (1H, dt, $J=11.1, 6.9$ Hz, CHBr), 4.74 (1H, bs, CHPh), 5.17 (1H, q, $J=7.4$ Hz, CHCH_3), 6.28 (1H, d, $J=11.1$ Hz, $\text{CH}=\text{C}$), 7.20-7.45 (10H, m, Ar), ^{13}C NMR (75MHz, CDCl_3) δ_{C} 11.9, 31.6, 44.8, 48.9, 60.6, 124.2, 126.5, 128.1, 128.5, 128.8, 128.9, 134.4, 141.5, 142.4, 148.3, 162.6; LC-ESI-MS rt 15.8 min., m/z 384-386 (M+1),

406-408 (M+Na); IR (film) 3061, 2970, 2933, 1751, 1606, 1521, 1345 cm^{-1} ; Calcd for $\text{C}_{21}\text{H}_{22}\text{BrNO}$: C, 65.63; H, 5.77; N, 3.64. Found: C, 65.61; H, 5.74; N, 3.67.

General procedure for the formation of esters **Z/E-3** and **Z/E-4**

Bromoderivative **2** (1 mmol) and resin supported benzoic acid or phenylacetic acid (3 mmol, 3 equiv., 1.43 g of resin with 2.1mmol/g loading) were stirred in refluxing hexane for three hours. The resin was then separated by filtration and solvent removed under reduced pressure. The products of the reaction were purified by flash chromatography on silica gel (cyclohexane/ethyl acetate 8/2 as eluant).

(Z)-2-(1-Benzyl-2-oxo-4-phenylazetid-3-ylidene)ethyl benzoate (3a). ^1H NMR (300MHz, CDCl_3) δ_{H} 3.92 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.83 (1H, s, CHPh), 4.95 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.25 (1H, dd, $J=6.6, 14.0$ Hz, CH_2OCOPh), 5.32 (1H, dd, $J=6.6, 14.0$ Hz, CH_2OCOPh), 5.71 (1H, t, $J=6.6$ Hz, $\text{CH}=\text{C}$), 7.05-7.50 (15H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 44.3, 60.6, 61.6, 122.7, 127.3, 127.8, 128.3, 128.4, 128.5, 128.7, 128.8, 128.9, 129.6, 133.0, 135.1, 135.9, 146.0, 163.0, 166.2; LC-ESI-MS rt 12.8 min., m/z 384 (M+1), 406 (M+Na); IR (film) 2966, 2918, 2846, 1766, 1455, 1375, 1260, 1102, 1001 cm^{-1} ; Calcd for $\text{C}_{25}\text{H}_{21}\text{NO}_3$: C, 78.31; H, 5.52; N, 3.65. Found: C, 78.32; H, 5.55; N, 3.64.

(E)-2-(1-Benzyl-2-oxo-4-phenylazetid-3-ylidene)ethyl benzoate (3a). ^1H NMR (300MHz, CDCl_3) δ_{H} 3.85 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.57 (1H, dd, $J=6.0, 14.0$ Hz, CH_2OCOPh), 4.91 (1H, dd, $J=6.0, 14.0$ Hz, CH_2OCOPh), 4.91 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.02 (1H, s, CHPh), 6.40 (1H, t, $J=6.0$ Hz, $\text{CH}=\text{C}$), 7.05-7.50 (15H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 44.2, 60.3, 62.0, 119.6, 127.6, 127.7, 128.2, 128.3, 128.4, 128.7, 129.0, 129.5, 130.1, 133.4, 135.0, 135.3, 145.5, 163.3, 165.8; LC-ESI-MS rt 12.4 min., m/z 384 (M+1), 406 (M+Na); IR (film) 2966, 2919, 2840, 1759, 1713, 1454, 1375, 1250, 1103, 1010 cm^{-1} ; Calcd for $\text{C}_{25}\text{H}_{21}\text{NO}_3$: C, 78.31; H, 5.52; N, 3.65. Found: C, 78.33; H, 5.54; N, 3.64.

(Z)-1-(1-Benzyl-2-oxo-4-phenylazetid-3-ylidene)butan-2-yl benzoate (3b). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 1.08 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.85-2.00 (2H, m, CH_2CH_3), 3.90 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.82 (1H, bs, CHPh), 4.93 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.54 (1H, d, $J=8.1$ Hz, $\text{CH}=\text{C}$), 6.15 (1H, dt, $J=8.1, 6.6$ Hz, CHOCOPh), 7.20-7.49 (13H, m, Ar), 8.07-8.11 (2H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.3, 27.8, 44.2, 61.5, 72.6, 127.1, 127.3, 127.4, 127.7, 128.2, 128.5, 128.7, 128.8, 129.0, 129.6, 132.8, 135.1, 144.8, 162.6, 168.4; LC-ESI-MS rt 19.2 min., m/z 412 (M+1), 434 (M+Na), 845 (2M+Na); IR (film): 3063, 2930, 2876, 1751, 1674, 1455, 1269 cm^{-1} ; Calcd for $\text{C}_{27}\text{H}_{25}\text{NO}_3$: C, 78.81; H, 6.12; N, 3.40. Found: C, 78.83; H, 6.11; N, 3.44. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.75 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.80-1.95 (2H, m, CH_2CH_3), 3.91 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.84 (1H, bs, CHPh), 4.92 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.44 (1H, m, CHOCOPh), 5.70 (1H, d, $J=10.4$ Hz, $\text{CH}=\text{C}$), 7.16-7.46 (15H, m, Ar), ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.6, 26.5, 44.2, 61.3, 72.5, 126.1, 127.3, 127.6, 127.7, 127.9, 128.2, 128.5, 128.7, 128.8, 128.9, 133.9, 134.9, 143.2, 162.8, 168.6; LC-ESI-MS rt 17.6 min., m/z 412 (M+1), 434 (M+Na), 845 (2M+Na); IR (film): 2956,

2925, 28726, 1751, 1654, 1457, 1380 cm^{-1} ; Calcd for $\text{C}_{27}\text{H}_{25}\text{NO}_3$: C, 78.81; H, 6.12; N, 3.40. Found: C, 78.79; H, 6.10; N, 3.41.

(E)-1-(1-Benzyl-2-oxo-4-phenylazetid-3-ylidene)butan-2-yl benzoate (3b). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.91 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.58-1.80 (2H, m, CH_2CH_3), 3.78 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.83 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.84 (1H, bs, CHPh), 5.34 (1H, q, $J=6.3$ Hz, CHOCOPh), 6.37 (1H, dd, $J=6.3$ Hz, $J_{1,3}=1.5$ Hz, $\text{CH}=\text{C}$), 7.13-7.19 (4H, m, Ar), 7.27-7.40 (8H, m, Ar), 7.55 (1H, t, $J=7.5$ Hz, Ar), 7.76 (2H, t, $J=8.4$ Hz, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.4, 27.4, 44.1, 62.5, 72.3, 124.3, 127.7, 128.0, 128.2, 128.4, 128.7, 128.8, 128.9, 129.6, 129.7, 132.9, 135.3, 143.2, 163.7, 165.3; LC-ESI-MS rt 13.0 min., m/z 412 (M+1), 434 (M+Na); IR (film): 3061, 2929, 1712, 1656, 1455, 1270 cm^{-1} ; Calcd for $\text{C}_{27}\text{H}_{25}\text{NO}_3$: C, 78.81; H, 6.12; N, 3.40. Found: C, 78.80; H, 6.14; N, 3.38. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.58 (3H, t, $J=7.2$ Hz, CH_2CH_3), 1.46 (1H, ddq, $J=6.6$, 13.8, 7.2 Hz, CH_2CH_3), 1.59 (1H, ddq, $J=6.9$, 13.8, 7.2 Hz, CH_2CH_3), 3.92 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.89 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.18 (1H, bs, CHPh), 5.26 (1H, ddd, $J=6.6$, 6.9, 9.0 Hz, CHOCOPh), 6.11 (1H, d, $J=9.0$ Hz, $\text{CH}=\text{C}$), 7.32-7.48 (13H, m, Ar), 7.98 (2H, d, $J=8.1$ Hz, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 8.8, 26.9, 44.2, 62.4, 71.7, 122.6, 127.5, 127.7, 128.3, 128.5, 128.7, 128.8, 128.9, 129.5, 129.6, 132.9, 133.0, 136.3, 146.0, 165.5, 168.8; LC-ESI-MS rt 18.6 min., m/z 412 (M+1), 434 (M+Na), 823 (2M+1), 845 (2M + Na); IR (film): 2970, 2928, 1710, 1654, 1456, 1268 cm^{-1} ; Calcd for $\text{C}_{27}\text{H}_{25}\text{NO}_3$: C, 78.81; H, 6.12; N, 3.40. Found: C, 78.81; H, 6.13; N, 3.42.

Ethyl 3-((E)-3-(2-benzoyloxybutylidene)-2-oxo-4-phenylazetid-1-yl)propanoate (3c). ^1H NMR (300MHz, CDCl_3) δ_{H} 0.90 (3H, t, $J=7.6$ Hz, CH_2CH_3), 1.20 (3H, t, $J=7.2$ Hz, COCH_2CH_3), 1.65 (2H, m, CH_2CH_3), 2.48 (2H, m), 3.27 (1H, dt, $J=14.2$, 7.0 Hz, CH_2COO), 3.68 (1H, dt, $J=14.2$, 6.6 Hz, CH_2COO), 4.05 (2H, q, $J=7.2$ Hz, COCH_2CH_3), 4.97 (1H, bs, CHPh), 5.30 (1H, pseudo quartet, $J=6.6$ Hz, CHOCOPh), 6.32 (1H, d, $J=6.6$ Hz, $\text{CH}=\text{C}$), 7.20-7.60 (8H, m, Ar), 7.70-7.90 (2H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.4, 14.0, 27.2, 33.0, 36.3, 60.7, 63.7, 72.3, 124.2, 127.9, 128.1, 128.4, 128.7, 129.6, 130.0, 133.5, 135.6, 143.1, 165.2, 171.0; LC-ESI-MS rt 16.7 min., m/z 422 (M+1), 865 (2M+Na); IR (film): 3062, 3033, 2980, 2933, 2367, 1754, 1725, 1377 cm^{-1} ; Calcd for $\text{C}_{25}\text{H}_{27}\text{NO}_5$: C, 71.24; H, 6.46; N, 3.32. Found: C, 71.22; H, 6.48; N, 3.30.

(Z)-1-(1-Benzyl-2-oxo-4-phenylazetid-3-ylidene)butan-2-yl 2-phenylacetate (4b). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.95 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.70-1.85 (2H, m, CH_2CH_3), 3.71 (2H, s, COCH_2Ph), 3.87 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.78 (1H, bs, CHPh) 4.90 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.38 (1H, ddd, $J=7.5$, 4.2, $J_{1,3}=1.0$ Hz, CHOCOPh), 5.90 (1H, d, $J=7.5$ Hz, $\text{CH}=\text{C}$), 7.15-7.45 (15H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.1, 26.7, 41.4, 44.1, 61.2, 72.3, 125.9, 126.7, 126.9, 127.2, 127.5, 128.2, 128.5, 128.7, 129.0, 129.1, 134.1, 135.2, 144.6, 162.4, 170.6; LC-ESI-MS rt 18.3 min., m/z 427 (M+1), 449 (M+Na); IR (film): 3063, 3031, 2967, 2850, 1748, 1661, 1381 cm^{-1} ; Calcd for $\text{C}_{28}\text{H}_{27}\text{NO}_3$: C, 79.03; H, 6.40; N, 3.29. Found: C, 79.00; H, 6.38; N, 3.29. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.75 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.65-1.82 (2H, m, CH_2CH_3), 3.42 (2H, s, COCH_2Ph), 3.91 (1H, d,

$J=15.0$ Hz, NCH_2Ph), 4.43 (1H, s, $CHPh$), 4.91 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.00 (1H, m, $CHOCOPh$), 5.87 (1H, d, $J=8.7$ Hz, $CH=C$), 7.18-7.40 (15H, m, Ar); ^{13}C NMR (75MHz, $CDCl_3$) δ_C 10.8, 27.3, 41.3, 44.0, 60.5, 72.4, 125.9, 126.7, 126.9, 127.5, 128.2, 128.4, 128.5, 128.7, 129.0, 129.1, 134.0, 136.1, 144.3, 162.4, 170.5; LC-ESI-MS rt 18.5 min., m/z 427 (M+1), 449 (M+Na), 853 (2M+1); IR (film): 3087, 3032, 2925, 1746, 1661, 1495; Calcd for $C_{28}H_{27}NO_3$: C, 79.03; H, 6.40; N, 3.29. Found: C, 79.01; H, 6.43; N, 3.28.

(E)-1-(1-Benzyl-2-oxo-4-phenylazetid-3-ylidene)butan-2-yl 2-phenylacetate (4b). First diastereomer: 1H NMR (300MHz, $CDCl_3$) δ_H 0.76 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.26-1.56 (2H, m, CH_2CH_3), 3.38 (2H, s, $COCH_2Ph$), 3.80 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.84 (1H, d, $J_{1,3}=1.5$ Hz, $CHPh$) 4.87 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.00 (1H, m, $CHOCOPh$), 6.22 (1H, dd, $J=6.3$ Hz, $J_{1,3}=1.5$ Hz, $CH=C$), 7.15-7.45 (15H, m, Ar); ^{13}C NMR (75MHz, $CDCl_3$) δ_C 9.0, 27.0, 41.0, 44.1, 62.2, 71.9, 123.8, 127.0, 127.4, 127.6, 127.8, 128.4, 128.7, 128.8, 128.9, 129.0, 135.2, 136.3, 145.7, 163.5, 170.0; LC-ESI-MS rt 16.0 min., m/z 427 (M+1), 449 (M+Na) 853 (2M+1); IR (film): 3064, 3031, 2926, 1751, 1456, 1383; Calcd for $C_{28}H_{27}NO_3$: C, 79.03; H, 6.40; N, 3.29. Found: C, 79.04; H, 6.42; N, 3.26. Second diastereomer: 1H NMR (300MHz, $CDCl_3$) δ_H 0.45 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.28-1.52 (2H, m, CH_2CH_3), 3.42 (1H, d, $J=15.0$ Hz, $COCH_2Ph$), 3.50 (1H, d, $J=15.0$ Hz, $COCH_2Ph$), 3.90 (1H, d, $J=15.0$ Hz, NCH_2Ph), 4.87 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.01 (1H, m, $CHOCOPh$), 5.09 (1H, d, $J_{1,3}=1.5$ Hz, $CHPh$), 6.00 (1H, dd, $J=8.7$ Hz, $J_{1,3}=1.5$ Hz, $CH=C$), 7.15-7.45 (15H, m, Ar); ^{13}C NMR (75MHz, $CDCl_3$) δ_C 8.5, 26.6, 41.0, 44.2, 62.3, 71.6, 122.4, 127.0, 127.5, 127.7, 127.8, 128.4, 128.6, 128.8, 128.9, 129.1, 135.0, 135.4, 145.7, 163.4, 170.7; LC-ESI-MS rt 17.3 min., m/z 427 (M+1), 449 (M+Na); IR (film): 3063, 2924, 2854, 1712, 1655, 1457, 1377; Calcd for $C_{28}H_{27}NO_3$: C, 79.03; H, 6.40; N, 3.29. Found: C, 79.02; H, 6.40; N, 3.27.

(Z)-1-(1-Benzyl-2-(4-nitrophenyl)-4-oxoazetid-3-ylidene)butan-2-yl 2-phenylacetate (4d). First diastereomer: 1H NMR (300MHz, $CDCl_3$) δ_H 0.94 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.60-1.80 (2H, m, CH_2CH_3), 3.65 (2H, s, $COOCH_2Ph$), 3.98 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.82 (1H, bs, $CHPh$), 4.85 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.32 (1H, d, $J=7.8$ Hz, $CH=C$), 5.81 (1H, broad dt=q, $J=7.2$ Hz, $CHOCOPh$), 7.10-7.20 (2H, m, Ar), 7.22-7.40 (8H, m, Ar), 7.40 (2H, d, $J=8.7$ Hz, Ar), 8.15 (2H, t, $J=8.7$ Hz, Ar); ^{13}C NMR (75MHz, $CDCl_3$) δ_C 9.1, 27.3, 41.4, 44.8, 60.5, 72.4, 124.0, 127.0, 127.9, 128.0, 128.4, 128.5, 128.6, 128.8, 129.1, 133.9, 134.6, 137.4, 144.0, 148.0, 162.1, 170.8; LC-ESI-MS rt 16.5 min., m/z 471 (M+1), 493 (M+Na); IR (film): 3010, 2925, 1751, 1653, 1521, 1457, 1349, 1073 cm^{-1} ; Calcd for $C_{28}H_{26}N_2O_5$: C, 71.47; H, 5.57; N, 5.95. Found: C, 71.49; H, 5.55; N, 5.92. Second diastereomer: 1H NMR (300MHz, $CDCl_3$) δ_H 0.89 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.60-1.80 (2H, m, CH_2CH_3), 3.70 (2H, s, $COOCH_2Ph$), 4.02 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.84 (1H, s, $CHPh$), 4.87 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.37 (1H, d, $J=7.2$ Hz, $CH=C$), 5.77 (1H, q, $J=7.2$ Hz, $CHOCOPh$), 7.10-7.20 (2H, m, Ar), 7.22-7.45 (10H, m, Ar), 8.21 (2H, d, $J=8.4$ Hz, Ar); ^{13}C NMR (75MHz, $CDCl_3$) δ_C 9.2, 27.5, 41.4, 45.0, 60.6, 72.4, 124.1, 127.0, 128.0, 128.4, 128.5, 128.6, 128.8, 129.1, 129.3, 134.0, 134.5, 137.3, 143.5, 148.1, 162.1, 170.8; LC-ESI-MS rt 16.6 min., m/z 471 (M+1), 493 (M+Na); IR (film): 2995, 2925, 1751,

1637, 1522, 1455, 1349, 1259, 1073, 1073 cm^{-1} ; Calcd for $\text{C}_{28}\text{H}_{26}\text{N}_2\text{O}_5$: C, 71.47; H, 5.57; N, 5.95. Found: C, 71.45; H, 5.56; N, 5.95.

(E)-1-(1-Benzyl-2-(4-nitrophenyl)-4-oxoazetidino-3-ylidene)butan-2-yl 2-phenylacetate (4d). ^1H NMR (300MHz, CDCl_3) δ_{H} 0.44 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.33-1.51 (2H, m, CH_2CH_3), 3.52 (1H, d, $J=15.6$ Hz, COOCH_2Ph), 3.58 (1H, d, $J=15.6$ Hz, COOCH_2Ph), 4.05 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.80 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.84 (1H, dt, $J=6.9, 9.3$ Hz, CHOCOPh), 5.16 (1H, s, CHPh), 5.01 (1H, d, $J=9.3$ Hz, $\text{CH}=\text{C}$), 7.10-7.15 (2H, m, Ar), 7.20-7.40 (8H, m, Ar), 7.46 (2H, d, $J=8.4$ Hz, Ar), 8.19 (2H, d, $J=8.4$ Hz, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 8.7, 26.9, 41.2, 45.0, 61.5, 71.3, 123.3, 124.0, 127.2, 128.1, 128.4, 128.5, 128.6, 128.8, 129.1, 133.4, 134.3, 144.2, 145.7, 148.0, 163.1, 170.9; LC-ESI-MS rt 15.7 min., m/z 471 (M+1), 493 (M+Na); IR (film): 2995, 2926, 1756, 1637, 1522, 1456, 1349, 1258, 1157, 1074 cm^{-1} ; Calcd for $\text{C}_{28}\text{H}_{26}\text{N}_2\text{O}_5$: C, 71.47; H, 5.57; N, 5.95. Found: C, 71.48; H, 5.60; N, 5.96.

General procedure for the hydrolysis of ester 3 or 4 to hydroxy-derivatives 5

Compound **3** or **4** (1 mmol) was dissolved in a 0.62 M solution of NaOH in methanol (3 ml) and stirred at room temperature for 72 h. The reaction was then diluted with water (10 ml) and methanol removed under reduced pressure. The residue was then extracted twice with CH_2Cl_2 (10 mL). The organic layers were dried over Na_2SO_4 and solvent was removed under reduced pressure. Hydroxyderivative **5** was isolated by flash chromatography on silica gel (cyclohexane/ethyl acetate 8/2).

(Z)-1-Benzyl-3-(2-hydroxyethylidene)-4-phenylazetidino-2-one (5a). ^1H NMR (300MHz, CDCl_3) δ_{H} 3.92 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.42 (2H, d, $J=4.0$ Hz, CH_2OH), 4.81 (1H, s, CHPh), 4.89 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.75 (1H, t, $J=4.0$ Hz, $\text{CH}=\text{C}$), 7.00-7.40 (10H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 44.7, 61.3, 61.4, 127.4, 127.9, 128.5, 128.8, 128.9, 129.0, 130.5, 134.9, 135.8, 140.8, 164.4; LC-ESI-MS rt 10.2 min., m/z 280 (M+1), 302 (M+Na); IR (film) 3417, 3039, 2952, 2906, 1606, 1454, 1375, 1250, 1103, 1010 cm^{-1} ; Calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.42; H, 6.12; N, 5.00.

(E)-1-Benzyl-3-(2-hydroxyethylidene)-4-phenylazetidino-2-one (5a). ^1H NMR (300MHz, CDCl_3) δ_{H} 2.40 (1H, bs, OH), 3.80 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.04 (2H, d, $J=5.1$ Hz, CH_2OH), 4.87 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.97 (1H, s, CHPh), 6.27 (1H, t, $J=5.1$ Hz, $\text{CH}=\text{C}$), 7.15 (2H, d, $J=6.6$ Hz, Ar), 7.25-7.40 (8H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 44.1, 59.5, 62.1, 124.7, 127.5, 127.7, 128.3, 128.7, 128.8, 128.9, 135.2, 136.6, 142.6, 164.0; LC-ESI-MS rt 9.6 min., m/z 280 (M+1), 302 (M+Na); IR (film) 2966, 2846, 1646, 1394, 1262, 1096, 1010 cm^{-1} ; Calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.37; H, 6.16; N, 5.04.

(Z)-1-Benzyl-3-(2-hydroxybutylidene)-4-phenylazetidino-2-one (5b). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.99 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.60-1.68 (2H, m, CH_2CH_3), 3.92 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.51 (1H, m, CHOH), 4.81 (1H, bs, CHPh), 4.90 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.72 (1H, d, $J=4.8$ Hz, $J_{1,3}=1.0$ Hz, $\text{CH}=\text{C}$), 7.17-7.41 (10H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.5, 30.3, 44.6, 61.4, 71.3, 127.4, 127.8, 128.3, 128.4, 128.5, 128.8, 128.9, 134.0, 135.9, 140.9, 162.1; LC-ESI-MS rt 12.3 min., m/z 308 (M+1), 330 (M+Na), 637 (2M+Na); IR

(film): 3420, 3063, 2924, 1733, 1455, 1388, 1109 cm^{-1} ; Calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.11; H, 6.90; N, 4.56. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 1.00 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.63-1.71 (2H, m, CH_2CH_3), 3.95 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.64 (1H, m, CHOH), 4.83 (1H, bs, CHPh), 4.90 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.90 (1H, d, $J=4.5$ Hz, $J_{1,3}=1.0$ Hz, $\text{CH}=\text{C}$), 7.19-7.40 (10H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.2, 30.3, 44.4, 61.3, 71.4, 127.3, 127.8, 128.2, 128.4, 128.5, 128.7, 128.9, 133.8, 136.0, 140.7, 162.7; LC-ESI-MS rt 12.1 min., m/z 308 (M+1), 330 (M+Na), 637 (2M+Na); IR (film): 3421, 3064, 3031, 2963, 1731, 1455, 1353, 1069 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.16; H, 6.85; N, 4.53.

(E)-1-Benzyl-3-(2-hydroxybutylidene)-4-phenylazetididin-2-one (5b). First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.80 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.46 (2H, m, CH_2CH_3), 3.84 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.00 (1H, dt, $J=6.3, 6.6$ Hz, CHOH), 4.89 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.95 (1H, s, CHPh), 6.18 (1H, d, $J=6.6$ Hz, $\text{CH}=\text{C}$), 7.15-7.40 (10H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.2, 29.7, 44.2, 62.2, 70.6, 127.6, 127.7, 127.8, 128.4, 128.9, 129.0, 135.3, 136.5, 142.9, 164.1; LC-ESI-MS rt 11.1 min., m/z 308 (M+1), 330 (M+Na); IR (film): 3432, 2959, 2924, 2853, 1736, 1641, 1454, 1111 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.18; H, 6.94; N, 4.57. Second diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.64 (3H, t, $J=7.4$ Hz, CH_2CH_3), 1.38 (2H, m, CH_2CH_3), 3.72 (1H, d, $J=15.0$ Hz, CH_2Ph), 3.97 (1H, pseudo quartet, $J=6.6$ Hz, CHOH), 4.90 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.99 (1H, s, CHPh), 6.12 (1H, d, $J=6.6$ Hz, $\text{CH}=\text{C}$), 7.17-7.38 (10H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.1, 29.5, 44.1, 62.2, 70.5, 127.5, 127.7, 127.8, 128.4, 128.6, 128.7, 128.8, 128.9, 135.3, 136.7, 142.9, 164.1; LC-ESI-MS rt 11.0 min., m/z 308 (M+1), 330 (M+Na), 637 (2M+Na); IR (film): 3430, 2958, 2953, 2860, 1661, 1453, 1110 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.14; H, 6.88; N, 4.54.

3-((E)-3-(2-Hydroxybutylidene)-2-oxo-4-phenylazetididin-1-yl)propanoic acid (5c). ^1H NMR (300MHz, CDCl_3) δ_{H} 0.80 (3H, t, $J=7.2$ Hz, CH_2CH_3), 1.46 (2H, m, CH_2CH_3), 2.62 (2H, m, CH_2CO), 3.32 (1H, dt, $J=6.6, 14.6$ Hz, NCH_2), 3.75 (1H, dt, $J=7.8, 14.6$ Hz, NCH_2), 4.05 (1H, pseudo quartet, $J=6.2$ Hz, CHOH), 5.17 (1H, bs, CHPh), 6.16 (1H, d, $J=6.2$ Hz, $\text{CH}=\text{C}$), 7.30-7.70 (5H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.0, 29.8, 36.1, 44.7, 60.7, 69.6, 125.4, 128.0, 128.4, 128.8, 129.3, 138.1, 142.0, 164.3, 178.1; Calcd for $\text{C}_{18}\text{H}_{23}\text{NO}_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 68.14; H, 7.31; N, 4.40.

(Z)-1-Benzyl-3-(2-hydroxybutylidene)-4-(4-nitrophenyl)azetididin-2-one 5d. First diastereomer: ^1H NMR (300MHz, CDCl_3) δ_{H} 0.97 (3H, t, $J=7.2$ Hz, CH_2CH_3), 1.54-1.67 (2H, m, CH_2CH_3), 4.05 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.53 (1H, dt, $J=4.5, 5.7$ Hz, CHOH), 4.89 (1H, bs, CHPh), 4.90 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.72 (1H, dd, $J=4.5$ Hz, $J_{1,3}=1.5$ Hz, $\text{CH}=\text{C}$), 7.05-7.12 (2H, m, Ar), 7.14-7.40 (3H, m, Ar), 7.42 (2H, d, $J=8.7$ Hz, Ar), 8.23 (2H, d, $J=8.7$ Hz, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.3, 30.2, 45.3, 60.5, 71.3, 124.2, 126.9, 128.1, 128.2, 128.6, 128.9, 134.3, 135.1, 140.2, 143.7, 163.9; LC-ESI-MS rt 11.8 min., m/z 353 (M+1), 375 (M+Na); IR (film): 3419, 2964, 2926, 2854, 1734, 1654, 1522, 1496, 1349, 1221, 1105 cm^{-1} ; 1110 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.20; H, 5.74; N, 7.98. Second

diastereomer ^1H NMR (300MHz, CDCl_3) δ_{H} 1.00 (3H, t, $J=7.2$ Hz, CH_2CH_3), 1.58-1.70 (2H, m, CH_2CH_3), 4.06 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.51 (1H, dt, $J=4.8, 5.7$ Hz, CHOH), 4.88 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.91 (1H, bs, CHPh), 5.71 (1H, dd, $J=4.8$ Hz, $J_{1,3}=1.5$ Hz, $\text{CH}=\text{C}$), 7.05-7.20 (2H, m, Ar), 7.22-7.40 (3H, m, Ar), 7.42 (2H, d, $J=8.7$ Hz, Ar), 8.23 (2H, d, $J=8.7$ Hz, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.5, 30.3, 45.3, 60.6, 71.3, 123.9, 128.1, 128.2, 128.5, 128.6, 128.9, 134.3, 135.0, 140.3, 142.9, 162.6; LC-ESI-MS rt 11.7 min., m/z 353 (M+1), 375 (M+Na); IR (film): 3399, 2966, 2926, 2847, 1734, 1654, 1522, 1496, 1349, 1262, 1106 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.18; H, 5.70; N, 7.96.

(E)-1-Benzyl-3-(2-hydroxybutylidene)-4-(4-nitrophenyl)azetid-2-one (5d). ^1H NMR (300MHz, CDCl_3) δ_{H} 0.76 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.43-1.54 (2H, m, CH_2CH_3), 3.92 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.01 (1H, q, $J=5.4$ Hz, CHOH), 4.87 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.10 (1H, s, CHPh), 6.22 (1H, dd, $J=5.4$ Hz, $J_{1,3}=1.5$ Hz, $\text{CH}=\text{C}$), 7.12-7.15 (2H, m, Ar), 7.30-7.42 (3H, m, Ar), 7.43 (2H, d, $J=8.4$ Hz, Ar), 8.21 (2H, d, $J=8.4$ Hz, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 9.2, 30.0, 44.8, 61.7, 70.8, 118.9, 128.0, 128.2, 128.5, 128.8, 129.3, 135.1, 138.1, 142.0, 148.8, 165.4; LC-ESI-MS rt 10.9 min., m/z 353 (M+1), 375 (M+Na); IR (film): 3421, 2962, 2925, 2854, 1739, 1638, 1522, 1496, 1348, 1126 cm^{-1} ; Calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.17; H, 5.69; N, 7.92.

Oxidation of alcohol 5 to carbonyl derivative 6 or 7

Compound **5** (1 mmol) and resin supported chromic acid (3 mmol, 3 equiv., 1.5 g. of resin with loading 2 mmol/g) were refluxed in benzene (10 mL) for 24h. The resin was then filtered and solvent removed under reduced pressure. The carbonyl derivative was purified by flash chromatography on silica gel (cyclohexane/ethyl acetate 8/2 as eluant).

(Z)-2-(1-Benzyl-2-oxo-4-phenylazetid-3-ylidene)acetaldehyde (6^a). ^1H NMR (300MHz, CDCl_3) δ_{H} 3.99 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.98 (1H, bs, CHPh), 5.00 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.88 (1H, dd, $J=7.8$ Hz, $J_{1,3}=0.9$ Hz, $\text{CH}=\text{C}$), 7.05-7.50 (10H, m, Ar), 10.42 (1H, d, $J=7.8$ Hz, $\text{CH}=\text{O}$); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 44.8, 61.4, 126.1, 126.4, 127.4, 127.8, 128.2, 128.6, 129.0, 134.2, 134.5, 140.8, 161.5, 189.5; LC-ESI-MS rt 11.3 min., m/z 278 (M+1), 300 (M+Na); Calcd for $\text{C}_{18}\text{H}_{15}\text{NO}_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.95; H, 5.41; N, 5.09.

(E)-2-(1-Benzyl-2-oxo-4-phenylazetid-3-ylidene)acetaldehyde (6^a). ^1H NMR (300MHz, CDCl_3) δ_{H} 3.93 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.98 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.23 (1H, d, $J_{1,3}=1.5$ Hz, CHPh), 6.42 (1H, dd, $J=7.3$ Hz, $J_{1,3}=1.5$ Hz, $\text{CH}=\text{C}$), 7.05-7.20 (2H, m, Ar), 7.20-7.40 (6H, m, Ar), 7.40-7.50 (2H, m, Ar), 9.47 (1H, d, $J=7.3$ Hz, $\text{CH}=\text{O}$); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 44.8, 62.3, 120.1, 127.5, 128.8, 128.6, 129.0, 129.4, 129.6, 134.1, 134.9, 141.8, 160.9, 189.1; LC-ESI-MS rt 10.9 min., m/z 278 (M+1), 300 (M+Na); Calcd for $\text{C}_{18}\text{H}_{15}\text{NO}_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.92; H, 5.46; N, 5.02.

(E)-1-Benzyl-3-(2-oxobutylidene)-4-phenylazetid-2-one (7b). ^1H NMR (300MHz, CDCl_3) δ_{H} 0.90 (3H, t, $J=7.2$ Hz, CH_3CH_2), 2.43 (2H, m, CH_3CH_2), 3.85 (1H, d, $J=15.0$ Hz, CH_2Ph), 4.86 (1H, d, $J=15.0$ Hz, CH_2Ph), 5.17 (1H, s, CHPh), 6.60 (1H, s, $\text{CH}=\text{C}$), 7.10-7.50 (10H, m, Ar); ^{13}C NMR (75MHz, CDCl_3) δ_{C} 8.6, 31.7, 45.2, 60.8, 127.1, 128.0, 128.3, 128.5, 128.7,

128.9, 129.4, 135.1, 138.3, 143.8, 164.9, 198.2; Calcd for C₂₀H₁₉NO₂: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.63; H, 6.27; N, 4.60.

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