REACTIVITY OF 1,3-DI-*tert*-BUTYLAZIRIDINONES WITH PHENYL SUBSTITUENTS. A NEW FRAGMENTATION OF α-LACTAMS

Masako Shimazu, Yasuyuki Endo,* and Koichi Shudo

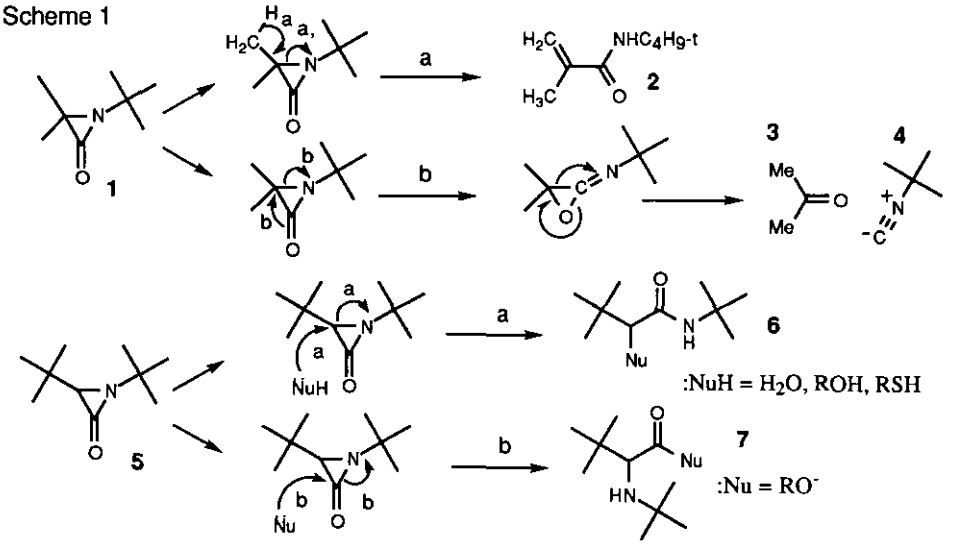
Faculty of Pharmaceutical Sciences, University of Tokyo,
7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan

Abstract- Several isolable aziridinones with bulky substituents were prepared and their reactions with nucleophiles, *i.e.*, methanol, sodium methoxide and benzylamine, were investigated. A novel fragmentation of aziridinones having a phenyl group on the C3 moiety was found.

Aziridinone is one of the smallest heterocycles,[1] and has been postulated as an intermediate in numerous processes. Since the isolation of the first aziridinone, *N-tert*-butyl-3-phenylaziridinone,[2] attempts have been made to find more stable aziridinones. So far, less than twenty aziridinones have been isolated and fully characterized. The fundamental reactivities of aziridinones are self-fragmentations and ring-opening by nucleophilic reagents. Two pathways of decomposition have been reported for thermolysis of aziridinones.[3] 1-*tert*-Butyl-3,3-dimethylaziridinone (**1**) which possesses β-hydrogen for elimination undergoes slow decomposition even at room temperature to give *N-tert*-butylmethacrylamide (**2**) as the major product. Acetone (**3**) and *tert*-butyl isocyanide (**4**) are obtained as the minor products. It is assumed that the aziridinone rearranges to an iminolactone, which fragments further to give the ketone and the isocyanide. In aziridinones having no β-hydrogen, the isomerization to **2** cannot take place. The relative stability of 1,3-di-*tert*-butyl- aziridinone (**5**)[4] among the synthesized compounds is noteworthy. Aziridinones smoothly react with various nucleophiles and the reaction has been investigated in the case of relatively stable **5**.[4] Depending on the nucleophile, a strong selectivity is observed in the type of ring opening.[4] Reactions with proton-containing nucleophiles such as water, alcohols and thiols, lead exclusively to the amides (**6**)

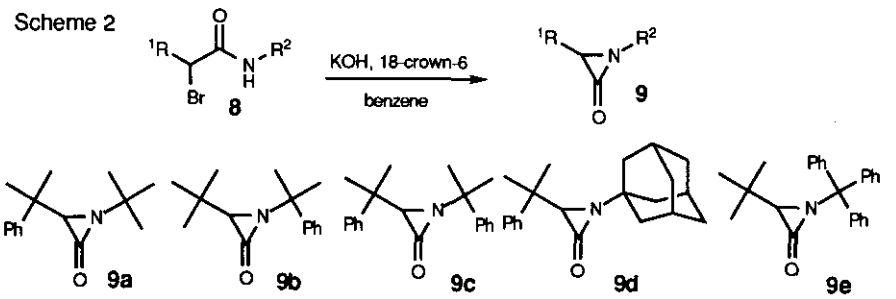
corresponding to N-C3 bond cleavage. On the other hand, reactions of aziridinones with nucleophiles such as alkoxides give amino acid derivatives (**7**), corresponding to ring opening at the N-acyl bond. Bulky substituents on the lactam ring may prevent nucleophilic attack on the lactam. Indeed, all the aziridinones so far isolated have an *N-tert*-butyl group (or equivalent tertiary alkyl: adamantyl).[5] The stereochemical features of the nucleophilic ring opening have been reported. The results demonstrate that the N-C3 bond of aziridinone is cleaved by nucleophiles with a high degree of stereospecificity and with inversion of configuration.[6] In this paper, we report the preparation and nucleophilic reactions of 1,3-di-*tert*-butyl-aziridinones substituted with phenyl groups, and the particular fragmentations of those possessing a γ-phenyl group on the C-3 moiety.

Scheme 1



The title compounds were synthesized by means of dehydrohalogenation of *N*-alkyl-α-haloamides, which were prepared from the corresponding acyl chlorides by α-bromination, followed by condensation with amines. The acyl precursor 3-methyl-3-phenylbutyric acid was prepared from 2-methyl-2-phenyl-3- chloropropane.[7]

Scheme 2



The amine precursor α,α-dimethylbenzylamine was prepared from α,α-dimethylbenzyl cyanide.[8] Treatment

of *N*-alkyl-α-haloamides (**8a-8e**) with powdered potassium hydroxide in benzene in the presence of a catalytic amount of 18-crown-6[9] gave 1,3-di-*tert*-butylaziridinones substituted with phenyl groups (**9a-9e**) in yields of 58-95%.

These aziridinones are relatively stable; they can be stored at -20°C for a few weeks without decomposition. These compounds were characterized on the basis of their ^{1}H-NMR and IR spectra, which showed a carbonyl band at about 1840 cm^{-1}. In the reactions of the aziridinones with acidic proton-containing nucleophiles (the results are summarized in Table 1), two aziridinones (**9b** and **9e**) reacted in refluxing methanol to give 2-methoxy-3,3-dimethyl-*N*-substituted butyramides (**10b** and **10e**) as the sole products in accordance with other reported aziridinones. The stability of **9b** in refluxing methanol is comparable to that of **5**. However, the reactions of aziridinones with a phenyl group on the C3 moiety (**9a**, **9c** and **9d**) differed from those of the other aziridinones. In these cases, the formations of the correspondig 2-methoxybutyramidse (**10a**, **10c** and **10d**) were depressed and the same product, 2-methyl-1-phenylpropene (**11**) was isolated in all cases.

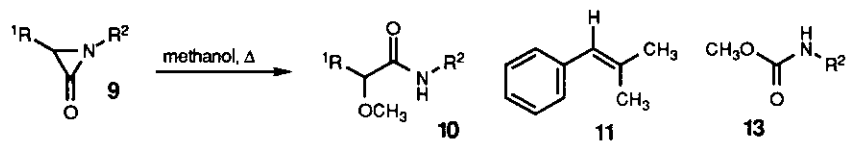
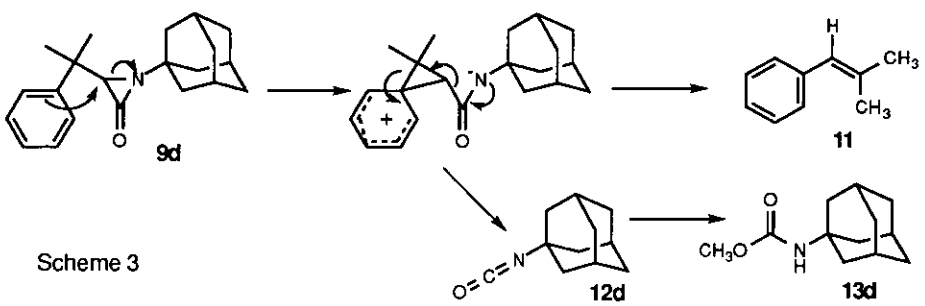


Table 1 Reactions of Aziridinones in Refluxing Methanol

reactant	R^1	R^2	reaction period (h)	yields (%) 10	11	13
9a	2-methyl-2-phenylethyl	*tert*-butyl	48	14	12	-
9b	*tert*-butyl	2-methyl-2-phenylethyl	23	73	0	0
9c	2-methyl-2-phenylethyl	2-methyl-2-phenylethyl	48	19	34	41
9d	2-methyl-2-phenylethyl	adamantyl	51	30	26	28
9e	*tert*-butyl	triphenylmethyl	4.5	84	0	0



Scheme 3

The formation of **11** seemed to involve molecular rearrangement with participation of the phenyl group, implying a new fragmentation pathway of aziridinones as illustrated in Scheme 3. The other fragments of the

reactions were the corresponding isocyanates (**12**) which were isolated as the methyl carbamates (**13c** and **13d**).

The reactions of the aziridinones (**9a-9e**) with sodium methoxide in methanol (anionic nucleophile) afforded amino acid derivatives (**14a-14e**) as the sole products, as are the cases with other reported aziridinones. The results are summarized in Table 2. The reactions of **9a-9d** were completed in less than 1 h at 20°C, while the reaction of **9e** with the triphenylmethyl group on N1 required 24 h. Although the reactions of aziridinones with amines have been reported to give α-substituted amides such as **6**, the reactions of our aziridinones (**9a-9e**) with benzylamine in THF at 20°C gave amino acid derivatives (**15a-15e**) as the sole products (Table 3). However, the reaction of 1,3-di-*tert*-butylaziridinone (**5**) has not been thoroughly examined. Our investigation on the reaction of **5** with benzylamine in THF showed that the amino acid derivative was produced in 97% yield.

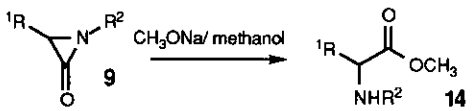


Table 2 Reactions of Aziridinones with Sodium Methoxide at 20°C

reactant	R^1	R^2	reaction period (h)	yields (%) **14**
9a	2-methyl-2-phenylethyl	*tert*-butyl	0.25	76
9b	*tert*-butyl	2-methyl-2-phenylethyl	1	93
9c	2-methyl-2-phenylethyl	2-methyl-2-phenylethyl	1	99
9d	2-methyl-2-phenylethyl	adamantyl	1	85
9e	*tert*-butyl	triphenylmethyl	24	68

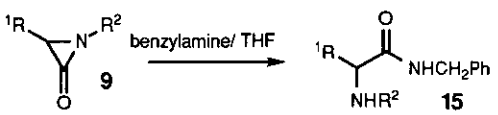


Table 3 Reactions of Aziridinones with Benzylamine at 20°C

reactant	R^1	R^2	reaction period (h)	yields (%) **15**
9a	2-methyl-2-phenylethyl	*tert*-butyl	5	35
9b	*tert*-butyl	2-methyl-2-phenylethyl	48	95
9c	2-methyl-2-phenylethyl	2-methyl-2-phenylethyl	48	93
9d	2-methyl-2-phenylethyl	adamantyl	44	89
9e	*tert*-butyl	triphenylmethyl	44	95

The thermal stability and chemical reactivity of aziridinones as a function of substitution patterns have been reviewed.[1] The greater the steric requirement of the substituents on N1 and on C3, the greater the thermal

stability and the lower the reactivity towards nucleophiles. Properties of aziridinones are determined not only by the steric factor but also in part by the electronic factor. Although the two phenyl groups on C3 are bulkier than two methyl groups and there is no β-hydrogen, 1-*tert*-butyl-3,3-diphenylaziridinone is difficult to prepare.[10] Our design and synthesis of new aziridinones with a phenyl group on the C3 moiety were intended to investigate substituent effects of the detached phenyl group. The aziridinones described in this paper have almost the same stability as 1,3-di-*tert*-butylaziridinone (**5**). Introduction of a trimethylphenyl group to N1 increased the stability in the case of the reaction with methoxide. In the case of methanolysis, a novel fragmentation of aziridinones with phenyl group participation was found.

EXPERIMENTAL

General Remarks Melting points were obtained on a Yanagimoto micro hot stage apparatus without correction. ^{1}H-Nmr spectra were measured with a JEOL JMN-GX-400 spectrometer (400 MHz) with TMS as an internal standard, and the chemical shifts are given in ppm as δ values from TMS. Mass spectra were recorded on a JEOL JMS-D-300 instrument for DI-Mass and on a JMS-DX-300 for high resolution analysis. Ir spectra were recorded with a Shimadzu IR-408 and the data are presented in cm^{-1}. Flash column chromatography was performed on silica gel (Merck 9385).

***N*-*tert*-Butyl-2-bromo-3-methyl-3-phenylbutanamide (8a) (general procedure)**: 3-Methyl-3-phenylbutyric acid (3.0 g, 17.0 mmol) was added to thionyl chloride (3.5 g, 29.4 mmol). The mixture was refluxed for 1 h, then thionyl chloride was removed under reduced pressure. The residue was dissolved in CCl_4, and 0.94 mL of Br_2 was added. The resulting solution was refluxed until the bromine color disappeared (about 3.5 h). The solution was then added to an ice-cold solution of 3.6 mL (34 mmol) of *tert*-butylamine in CH_2Cl_2 (50 mL). The mixture was diluted with water, and washed with dilute hydrochloric acid, 5% aqueous sodium hydroxide, and water. The organic layer was dried over sodium sulfate and concentrated to give a crude residue, which was purified by silica gel column chromatography (CH_2Cl_2/hexane =2:1) to give **8a** (3.58 g, 68%). The product was recrystallized from hexane; **8a**: mp 129-130 °C, IR (KBr): 1650 cm^{-1} (-CONH-), ^{1}H-NMR (400 MHz, $CDCl_3$) 7.37 (dd, 2H, J=8.0, 1.2 Hz), 7.28 (dt, 2H, J=8.0, 1.2 Hz), 7.19 (dt, 1H, J=8.0, 1.2 Hz), 5.24 (bs, 1H, NH), 4.35 (s, 1H), 1.57 (s, 6H), 1.16 (s, 9H). Anal. Calcd for $C_{15}H_{22}NOBr$: C, 57.70; H, 7.10; N, 4.49. Found: C, 57.67; H, 7.15; N, 4.16.

***N*-(1-Methyl-1-phenylethyl)-2-bromo-3,3-dimethylbutanamide (8b)**: Yield 80%. mp 173.5-174.0

°C; IR (KBr): 1655 cm^{-1} (-CONH-); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.40 (dt, 2H, J=8.1, 1.5 Hz), 7.34 (tt, 2H, J=8.1, 1.5 Hz), 7.25 (tt, 1H, J=8.1, 1.5 Hz), 6.34 (br s, 1H), 4.04 (s, 1H), 1.74 (s, 3H), 1.68 (s, 3H), 1.15 (s, 9H). Anal. Calcd for $C_{15}H_{22}NOBr$: C, 57.70; H, 7.10; N, 4.49. Found: C, 57.90; H, 7.14; N, 4.31.

***N*-(1-Methyl-1-phenylethyl)-2-bromo-3-methyl-3-phenylbutanamide (8c)**: Yield 84%. mp 140.8 - 141.0 °C; IR (KBr): 1655 cm^{-1} (-CONH-); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.41 (d, 2H, J=7.3 Hz), 7.33 (t, 2H, J=7.3 Hz), 7.23 (t, 3H, J=7.0 Hz), 7.18 (d, 1H, J=7.3 Hz), 7.10 (d, 2H, J=7.3 Hz), 5.66 (br s, 1H), 4.21 (s, 1H), 1.60 (s, 3H), 1.57 (s, 3H), 1.56 (s, 3H), 1.47 (s, 3H). Anal. Calcd for $C_{20}H_{24}NOBr$: C, 64.18 ; H, 6.46 ; N, 3.74. Found: C, 63.98 ; H, 6.41 ; N, 3.60.

***N*-(1-Adamantyl)-2-bromo-3-methyl-3-phenylbutanamide (8d)**: Yield 80%. mp 170-170.5 °C; IR (KBr): 1655 cm^{-1} (-CONH-); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.43 (dt, 2H, J=7.0, 1.5 Hz), 7.35 (tt, 2H, J=7.3, 1.8 Hz), 7.28 (tt, 1H, J=7.3, 1.8 Hz), 5.15 (br s, 1H), 4.34 (s, 1H), 1.81 (s, 6H), 1.61-1.56 (m, 15H). Anal. Calcd for $C_{21}H_{28}NOBr$: C, 64.61; H, 7.23 ; N,3.59. Found: C, 64.64 ; H, 7.24 ; N, 3.64.

***N*-Triphenylmethyl-2-bromo-3,3-dimethylbutanamide (8e)**: Yield 80%. mp 170-170.5 °C; IR (KBr): 1660 cm^{-1} (-CONH-); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.32-7.23 (m, 15H), 4.12 (s, 1H), 1.11 (s, 9H). HR-MS Calcd for $C_{25}H_{26}NOBr$: 435.1198. Found: 435.1197.

1-*tert*-Butyl-3-(1-methyl-1-phenylethyl)aziridinone (9a) (general procedure): 2-Bromo-carboxamide (**8a**, 620 mg, 2.0 mmol) in anhydrous benzene (20 mL) was treated with 18-crown-6 (80 mg, 0.30 mmol) and powdered potassium hydroxide (410 mg, 7.3 mmol). The suspension was stirred for 12 h at rt, then filtered. The filtrate was washed with water (30 ml x 3), dried over sodium sulfate, and evaporated to dryness to give **9a** as a colorless oil (264 mg, 58%). **9a**: IR (KBr): 1850 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$) 7.37 (dd, 2H, J=1.2, 8.0 Hz), 7.28 (dt, 2H, J=1.2, 8.0 Hz), 7.19 (dt, 1H, J=1.2, 8.0 Hz), 3.03 (s, 1H), 1.45 (s, 3H), 1.27 (s, 3H), 1.21 (s, 9H). HR-MS Calcd for $C_{15}H_{21}NO$: 231.1623. Found: 231.1619.

1-(1-Methyl-1-phenylethyl)-3-*tert*-butylaziridinone (9b): Colorless oil; Yield 95%. IR (KBr): 1840 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.45 (dt, 2H, J=7.3, 1.5 Hz), 7.37 (tt, 2H, J=8.1, 1.8 Hz), 7.28 (tt, 1H, J=7.3 Hz), 2.60 (s, 1H), 1.70 (s, 3H), 1.66 (s, 3H), 0.92 (s, 9H). HR-MS Calcd for $C_{15}H_{21}NO$: 231.1623, Found: 231.1639.

1-(1-Methyl-1-phenylethyl)-3-(1-methyl-1-phenylethyl)aziridinone (9c): Gummy colorless oil. yield 82%. IR (KBr): 1840 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.33 (m, 4H), 7.28 (m, 5H), 7.18 (m, 1H),

2.83 (s, 1H), 1.60 (s, 3H), 1.55 (s, 3H), 1.28 (s, 3H), 1.22 (s, 3H). HR-MS Calcd for $C_{20}H_{23}NO$: 293.1780. Found: 231.17847.

1-(1-Methyl-1-phenylethyl)-3-(1-adamantyl)aziridinone (9d): Colorless cubes (from hexane) mp 72.5-73.0 °C. yield 86%. IR (KBr): 1840 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.43 (dt, 2H, J=7.3, 1.1 Hz), 7.36 (tt, 2H, J=7.3, 2.2 Hz), 7.23 (tt, 1H, J=7.3, 2.2 Hz), 3.10 (s, 1H), 2.08-1.58 (m, 15H), 1.45 (s, 3H), 1.25 (s, 3H). Anal. Calcd for $C_{21}H_{27}NO$: C, 81.51 ; H, 4.53 ; N, 8.79. Found: C, 81.60 ; H, 4.24 ; N, 8.90.

1-Triphenylmethyl-3-*tert*-butylaziridinone (9e): Colorless oil ; yield 76%. IR (KBr): 1840 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.44 (dt, 6H, J=7.0, 1.5 Hz), 7.33 (tt, 6H, J=7.0, 1.8 Hz), 7.28 (tt, 3H, J=7.0, 1.8 Hz), 2.11 (s, 1H), 0.92 (s, 9H) . HR-MS Calcd for $C_{25}H_{25}NO$: 355.1936. Found: 355.1933.

Reaction of aziridinones in refluxing methanol: An aziridinone (0.225 mmol) was dissolved in 50 mL of methanol, and the solution was refluxed until the reaction was completed. Methanol was removed under reduced pressure, and the residue was separated by silica gel column chromatography (hexane/ ethyl acetate).

2-Methoxy-3-methyl-3-phenyl-*N*-*tert*-butylbutyramide (10a): IR (KBr): 1650 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.41 (dt, 2H, J=7.3, 1.5 Hz), 7.30 (t, 2H, J=7.3 Hz), 7.21 (t, 1H, J=7.3 Hz), 5.65 (br s, 1H, NH), 3.43 (s, 1H), 3.24 (s, 3H), 1.45 (s, 3H), 1.44 (s, 3H), 1.15 (s, 9H). HR-MS Calcd for $C_{16}H_{25}NO_2$: 263.1885. Found: 263.1924.

2-Methoxy-3,3-dimethyl-*N*-(1-methyl-1-phenylethyl)butyramide (10b): White needles, mp 97.0-97.2 °C. IR (KBr): 1655 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.42 (dt, 2H, J=8.1, 1.5 Hz), 7.34 (tt, 2H, J=8.1, 1.8 Hz), 7.24 (tt, 1H, J=8.1, 1.8 Hz), 6.69 (br s, 1H, NH), 3.41 (s, 3H), 3.12 (s, 1H), 1.76 (s, 3H), 1.72 (s, 3H), 0.98 (s, 9H). Anal. Calcd for $C_{16}H_{25}NO_2$: C:72.97, H:9.57, N:5.32. Found: C:72.75, H:9.45, N:5.03.

2-Methoxy-3-methyl-3-phenyl-*N*-(1-methyl-1-phenylethyl)butyramide (10c): IR (KBr): 1655 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.44 (dd, 2H, J=7.3, 1.5 Hz), 7.33 (t, 2H, J=7.3 Hz), 7.26 (t, 2H, J=7.3 Hz), 7.21 (q, 2H, J=7.3 Hz), 7.13 (dd, 2H, J=7.3, 1.8 Hz), 6.23 (br s, 1H), 3.46 (s, 1H), 3.30 (s, 3H), 1.59 (s, 3H), 1.59 (s, 3H), 1.48 (s, 3H), 1.46 (s, 3H), 1.43 (s, 3H). HR-MS Calcd for $C_{21}H_{27}NO_2$: 325.2042. Found: 325.2078.

2-Methoxy-3-methyl-3-phenyl-*N*-(1-adamantyl)butyramide (10d): White powder, mp 91-92 °C.

IR (KBr): 1655 cm^{-1} ;^{1}H-NMR (400 MHz, $CDCl_3$): 7.41 (dt, 2H, J=8.1, 1.5 Hz), 7.30 (t, 2H, J=8.1 Hz), 7.21 (t, 1H, J=7.3 Hz), 5.56 (br s, 1H), 3.41 (s, 1H), 3.23 (s, 3H), 2.01-1.43 (m, 15H). Anal. Calcd. for $C_{22}H_{31}NO_2$: C:77.38, H:9.15, N:4.10. Found. C:77.15, H:9.26, N:4.17

2-Methoxy-3-methyl-3-phenyl-*N*-triphenylmethylbutyramide (10e): White powder, mp 101 °C. IR (KBr): 1645 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.68 (br s, 1H), 7.31-7.22 (m, 15H), 3.39 (s, 3H), 3.16 (s, 1H), 0.98 (s, 9H). Anal. Calcd for $C_{26}H_{29}NO_2$: C:80.59, H:7.54, N:3.61. Found. C:80.85, H:7.70, N:3.91.

2-Methyl-1-phenyl-1-propene (11): bp 188 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.31 (t, 2H, J=7.3 Hz), 7.22 (d, 2H, J=7.0 Hz), 7.17 (t, 1H, J=7.0 Hz), 6.27 (br s, 1H), 1.90 (d, 3H, J=1.1 Hz), 1.86 (d, 3H, J=1.1 Hz).

Methyl *N*-(1-methyl-1-phenylethyl)carbamate (13c): ^{1}H-NMR (400 MHz, $CDCl_3$): 7.41 (d, 2H, J=7.3 Hz), 7.34 (t, 2H, J=7.7 Hz), 7.25 (tt, 1H, J=7.3, 1.5 Hz), 5.09 (br s, 1H), 3.59 (s, 1H), 1.67 (s, 6H). HR-MS Calcd for $C_{11}H_{15}NO_2$: 193.1103. Found: 193.1147.

Methyl *N*-(1-adamantyl)carbamate (13d): White powder; mp 118-119 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.52 (br s, 1H), 3.60 (s, 3H), 2.07-1.65 (m, 15H). Anal. Calcd for $C_{12}H_{19}NO_2$: C:68.87, H:9.15, N:6.69. Found. C:68.89, H:9.45, N:6.73

Reaction of aziridinones with sodium methoxide in methanol: An aziridininone (0.19 mmol) was dissolved in 2 mL of methanol, and 24 mg (0.44 mmol, 2.3 eq) of sodium methoxide was added. The mixture was stirred at 20 °C. After the reaction was completed, the solution was poured into 40 mL of CH_2Cl_2, and the whole was washed with water. The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ ethyl acetate).

Methyl 2-*tert*-butylamino-3-methyl-3-phenylbutyrate (14a): Yield 76%. Colorless oil. IR (KBr): 1720 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$): 7.35 (dd, 2H, J=1.4, 8.0 Hz), 7.28 (dt, 2H, J=1.4, 8.0 Hz), 7.18 (dt, 1H, J=1.4, 8.0 Hz), 3.41 (s, 3H), 3.29 (s, 1H), 1.39 (s, 3H), 1.34 (s, 3H), 0.90 (s 9H). HR-MS Calcd for $C_{16}H_{25}NO_2$: 263.1885. Found: 263.1845.

Methyl 2-(1-methyl-1-phenylethyl)amino-3,3-dimethylbutyrate (14b): Yield 93%. Colorless oil. IR (KBr): 1735 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$): 7.44 (d, 2H, J=7.3 Hz), 7.29 (t, 2H, J=7.3 Hz), 7.19 (t, 1H, J=7.3 Hz), 3.45 (s, 3H), 2.69 (s, 1H), 1.97 (br s, 1H), 1.41 (s, 6H), 0.85 (s, 9H). HR-MS Calcd for

$C_{16}H_{25}NO_2$: 263.1885. Found: 263.1858.

Methyl 2-(1-methyl-1-phenylethyl)amino-3-methyl-3-phenylbutyrate (14c): Yield 99%. Colorless oil. IR (KBr): 1735 cm-1, ^{1}H-NMR (400 MHz, $CDCl_3$): 7.23-7.13 (m, 10H), 3.25 (s, 3H), 3.04 (s, 1H), 1.93 (br s, 1H), 1.34 (s, 3H), 1.30 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H). HR-MS Calcd for $C_{21}H_{27}NO_2$: 325.2042. Found: 325.2029.

Methyl 2-(1-adamantyl)amino-3-methyl-3-phenylbutyrate (14d): Yield 85%. White powder. IR (KBr): 1730 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37 (d, 2H, J=7.3 Hz), 7.31 (t, 2H, J=7.3 Hz), 7.19 (t, 1H, J=7.3 Hz), 3.48 (s, 1H), 3.39 (s, 3H), 1.96-1.33 (m, 15H). Anal. Calcd for $C_{22}H_{31}NO_2$: C:77.38, H:9.15, N:4.10. Found. C:77.15, H:9.26, N4.17.

Methyl 2-triphenylmethylamino-3,3-dimethylbutyrate (14e): Yield 68%. Colorless oil. IR (KBr): 1730 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$): 7.53 (dt, 6H, J=7.0, 1.5 Hz), 7.24 (tt, 6H, J=7.0, 1.5 Hz), 7.17 (tt, 3H, J=7.0, 1.1 Hz), 3.18 (d, 1H, J=1.1 Hz), 3.08 (s, 3H), 2.55 (d, 1H, J=1.7 Hz), 1.03 (s, 9H). HR-MS Calcd for $C_{26}H_{29}NO_2$: 387.2198. Found: 387.2202.

Reaction of aziridinones with benzylamine: An aziridinone (0.216 mmol) was dissolved in 0.5 mL of THF, and 46.3 mg (0.432 mmol, 2.0 eq) of benzylamine in 0.5 mL of THF was added at 20°C. After the reaction was completed, THF was removed under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ ethyl acetate).

2-*tert*-Butylamino-3-methyl-3-phenyl-*N*-benzylbutyramide (15a): Yield 35 %. White powder (from hexane); mp 63-64 °C. IR (KBr):1655 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$): 7.38 (dd, 2H, J=1.2, 8.0 Hz), 7.31 (dt, 2H, J=1.2, 8.0 Hz), 4.45 (dd, 1H, J=14.1, 5.5 Hz), 4.30 (dd, 1H, J=14.1, 5.8 Hz), 3.25 (s,1H), 1.59 (s, 3H), 1.48 (s, 3H), 0.68 (s, 9H). Anal. Calcd for $C_{22}H_{30}N_2O$: C:78.06, H:8.93, N:8.28. Found. C:77.93, H:9.22, N:8.25.

2-(1-Methyl-1-phenylethyl)amino-3,3-dimethyl-*N*-benzylbutyramide (15b): Yield 95%. White powder (from hexane); mp 124.5-125.0 °C. IR (KBr): 1640 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$): 7.41-7.19 (m, 10H), 6.89 (br s, 1H), 4.35-4.32 (m, 2H), 2.69 (s, 1H), 1.71 (br s, 1H), 1.40 (s, 3H), 1.37 (s, 3H), 0.86 (s, 9H). Anal. Calcd for $C_{22}H_{30}N_2O$: C:78.06, H:8.93, N:8.28. Found. C:78.13, H:9.23, N:8.26.

2-(1-Methyl-1-phenylethyl)amino-3-methyl-3-phenyl-N-benzylbutyramide (15c): Yield 93%. White powder (from hexane); mp 95-96 °C. IR (KBr): 1640 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$): 7.32-7.07

(m, 15H), 6.50 (br s, 1H), 4.31 (dd, 1H, J=14.7, 5.9 Hz), 4.12 (dd, 1H, J=14.7, 5.8 Hz), 3.08 (s, 1H), 1.72 (br s, 1H), 1.37 (s, 3H), 1.30 (s, 3H), 1.20 (s, 3H), 1.11 (s, 3H); HR-MS Calcd for $C_{27}H_{32}N_2O$: 400.2515. Found: 400.2500. Anal. Calcd for $C_{27}H_{32}N_2O$: C:80.96, H:8.03, N:6.99. Found. C:81.03, H:8.23, N:6.72.

2-(1-Adamantyl)amino-3-methyl-3-phenyl-N-benzylbutyramide (15d): Yield 89%. White powder (from hexane); mp 120-121 °C. IR (KBr): 1650 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$): 7.38-7.20 (m, 10H), 4.47 (dd, 1H, J=14.3, 6.2 Hz), 4.32 (dd, 1H, J=14.3, 6.2 Hz), 3.41 (s, 1H), 1.84-1.27 (m, 16H). HR-MS Calcd for $C_{28}H_{36}N_2O$: 416.2828. Found: 416.2831. Anal. Calcd for $C_{28}H_{36}N_2O$: C:80.73, H:8.71, N:6.72. Found. C:80.87, H:8.85, N:6.53.

2-Triphenylmethylamino-3,3-dimethyl-N-benzylbutyramide (15e): Yield: 95%. Colorless gum. IR (KBr): 1645 cm^{-1}, ^{1}H-NMR (400 MHz, $CDCl_3$) 7.45-7.05 (m, 20H), 3.85 (dd, 1H, J=14.3, 5.5 Hz), 3.78 (dd, 1H, J=14.6, 5.1 Hz), 2.93 (d, 1H, J=6.6 Hz), 2.88 (d, 1H, J=6.9 Hz), 0.95 (s, 9H). HR-MS Calcd for $C_{32}H_{34}N_2O$: 462.2673. Found: 462.2701.

REFERENCES AND NOTES

1. For reviews: I. Lengyel and J. C. Sheehan, *Angew. Chem., Int. Ed. Engl.*, **1968**, *7*, 25; G. L'Abbe, *Bull. Soc. Chim. Fr.*, **1975**, 1127.
2. H. E. Baumgarten, *J. Am. Chem. Soc.*, **1962**, *84*, 4975.
3. J. C. Sheehan and J. H. Beeson, *J. Am. Chem. Soc.*, **1967**, *89*, 362.
4. J. C. Sheehan and I. Lengyel, *J. Am. Chem. Soc.*, **1964**, *86*, 1356.
5. Examples: 1-*tert*-butyl-3,3-dimethyl: ref. 4; 1-*tert*-butyl-3,3-diphenyl: H. E. Baumgarten, R. D. Clark and L. S. Endres, *Tetrahedron Lett.*, **1967**, 5033; 1-(1-adamantyl)-3-*tert*-butyl: E. R. Talaty, E. Dupuy and T. H. Golson, *Chem. Commun.*, **1969**, 49; 1,3-bis(1-adamantyl): E. R. Talaty, E. Dupuy and A. E. Cancienne, *J. Heterocycl. Chem.*, **1967**, *4*, 657.
6. H. Quast and H. Leybach, *Chem. Ber.*, **1991**, *124*, 2105.
7. J. E. Leffler and J. T. Barbas, *J. Am. Chem. Soc.*, **1981**, 103, 7768.
8. K. Sato, T. Honma and S. Sugai, *Agric. Biol. Chem.*, **1985**, 49, 3563.
9. P. S. Scrimin, F. D'Angeli and A. C. Veronese, *Synthesis*, **1982**, 586.
10. G. Simig and K. Lempert, *Tetrahedron*, **1975**, 31, 1195.

Received, 9th January, 1997