About 1-Triphenylmethyl-3-*tert*-butylaziridinone and Some of Its Reactions [1].

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A high-yield synthesis of 1-triphenylmethyl-3-*tert*-butylaziridinone (**4**), its physical and spectral properties, the limits of its thermal stability, and reactions with methanol, benzylamine and sodium methoxide in methanol are described.

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Introduction.

The stability of α-lactams (aziridinones) has been shown [2] to be dependent on the substituents at the 1 and 3 positions. To date, all stable pure α-lactams have a tertiary alkyl group attached to the nitrogen (*e.g.*, *tert*-butyl or 1-adamantyl). In addition, there must be at least one tertiary alkyl or aryl group at position 3, although two marginally stable 3,3-dimethylsubstituted α-lactams have been reported [3,4].

In an effort to determine if the triphenylmethyl (trityl) group would be a new stabilizing substituent for α-lactams, we attempted the synthesis of 1-triphenylmethyl-3-*tert*-butylaziridinone (**4**). This project was conceived and carried out independently of the work of Shimazu *et al.* who recently reported [5] that 1-triphenylmethyl-3-*tert*-butylaziridinone (**4**) is an unstable oil (no bp reported).

Results and Discussion.

Differing from the previous report, [5] that 1-triphenylmethyl-3-*tert*-butylaziridinone (**4**) is an oil, we have found that this α-lactam is a crystalline solid, mp 103-104 °C. Also, contrary to the statement by Shimazu *et al*. [5], that α-lactam **4** is thermally unstable and has to be stored at -20°C to prevent decomposition, we find that α-lactam **4** is extremely stable and can be stored under exclusion of moisture at room temperature indefinitely. Thus, over a period of five months at 25 °C, we have intermittently monitored a pure sample of **4** by IR and found no decomposition whatsoever: the 1840 cm^{-1} band (in CCl_4) prevails and no other band appeared in the carbonyl region. Even refluxing **4** in *n*-heptane (bp 98 °C) for one hour induced no decomposition. Only refluxing in *n*-octane (bp 126 °C) for 2.75 hours effected complete thermal decomposition (*vide infra*).

The discrepancies are not limited to those pertaining to the physical state (solid *versus* liquid), physical constants and stability of α-lactam **4**, but also include its precursor **3** and some reaction products. Thus, in contrast to the cited report [5], the reaction of **4** with sodium methoxide in methanol at room temperature, after 24 hours, gives 93% yield of pure crystalline methyl 2-triphenylmethylamino-3,3-dimethylbutanoate (**9**) of mp 108-109 °C, rather than an oil of unknown bp (Scheme 9).

Furthermore, Shimazu *et al*. report [5] that the reaction of α-lactam **4** with benzylamine gives a gum they designate as *N*-benzyl-2-triphenylmethylamino-3,3-dimethylbutanamide (**8b**). In contrast, we obtained a crystalline solid, mp 131-132°C, *N*-triphenylmethyl-2-benzylamino-3,3-dimethylbutanamide (**8a**), Scheme 5. The same product was obtained from the silver oxide-promoted nucleophilic substitution of α-bromoamide **3** with benzylamine, thus confirming structure **8a**.

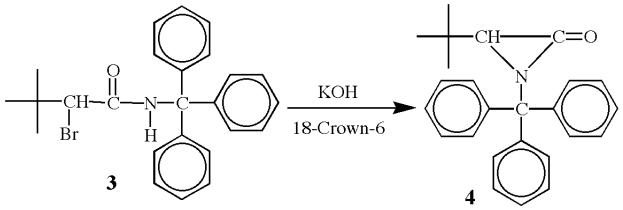
1. Synthesis of α-Lactam **4**.

Commercially available (Lancaster) *tert*-butylacetyl chloride (**1**) was converted to the known [6] 2-bromo-3,3-dimethylbutanoyl chloride (**2**), bp 72 °C/19 mm, in near quantitative yield. The identity of **2** was confirmed by NMR.

α-Bromoacid chloride **2** was converted to *N*-triphenylmethyl-2-bromo-3,3-dimethylbutanamide (**3**) in 54-55% isolated yield, by both the general procedures of Schlesinger and Prill [7] and Lengyel and Aaronson [8], and fully characterized by mp, TLC, IR, ^{1}H-NMR, ^{13}C-NMR, and elemental analysis. Our mp (122-123°C) is at variance with the lit. [5] value (170-170.5 °C).

We devoted a substantial study [9] to finding the best method to synthesize α-lactam **4** from α-bromoamide **3**, and once that was found, to determine the optimal reaction conditions of that method. We examined three different methods: 1) The dehydrohalogenation of *N*-chloro-*N*-triphenylmethyl-3,3-dimethylbutanamide with 1 equivalent of sodium *tert*-butoxide (NaO*t*Bu) in toluene at 5 °C [10], which was found thoroughly unsatisfactory, in that it led to no α-lactam at all. 2) The 1,3-dehydrohalogenation of *N*-triphenylmethyl-2-bromo-3,3-dimethylbutanamide (**3**) with potassium hydroxide (KOH) in benzene at 15 °C in the presence of a catalytic amount of 18-crown-6 ether [11]. This is the procedure used by Shimazu *et al.* [5] for the synthesis of α-lactam **4** (Scheme 1). Even after several modifications, such as increasing the concentration of 18-crown-6 ether or changing the solvent to toluene and carrying out the reaction at –25 °C, this method was found inferior to the third one. and 3) The 1,3-dehydrohalogenation of α-bromoamide **3** with sodium *tert*-butoxide in ether at 0 °C. This is a variation of the method of Sheehan and Lengyel [3] which we found far superior to any other approach tried.

Scheme 1. The phase transfer catalyst (PTC) synthesis of α-lactam **4**.

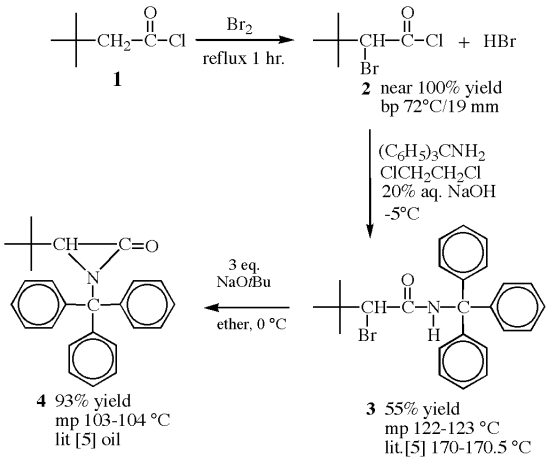


At this point, a variety of reaction conditions were examined to find the optimal ones. The base was changed from NaO*t*Bu to potassium *tert*-butoxide (KO*t*Bu), with a resultant decrease in the yield of **4**. We now prefer NaO*t*Bu over KO*t*Bu because the former, while still a strong enough base to effect smooth and fast 1,3-dehydrobromination, is much less hygroscopic, and therefore easier to handle. The amount of the base was varied too, and 3 equivalents was found to give the highest yield of **4** (93%).

Before we came to the conclusion that dry diethyl ether is the best solvent in this synthesis, we also tried tetrahydrofuran, diisopropyl ether, and mixtures of solvents, such as diethyl ether/tetrahydrofuran (2:1), diethyl ether/tetrahydrofuran (3:1), and diethyl ether/*tert*-butyl alcohol (83:17). Finally, the reaction was carried out at different temperatures, varying from -50 °C to +30 °C, with 0 °C being the optimal one.

The final outcome of these efforts was a synthesis of 1-triphenylmethyl-3-*tert*-butylaziridinone (**4**) from *N*-triphenylmethyl-2-bromo-3,3-dimethylbutanamide (**3**) with sodium *tert*-butoxide in ether at 0 °C, in 93% yield. Full characterization was achieved again by mp, TLC, IR, ^{1}H-NMR, ^{13}C-NMR, and elemental analysis (see Experimental). The synthesis of α-lactam **4** is outlined in Scheme 2.

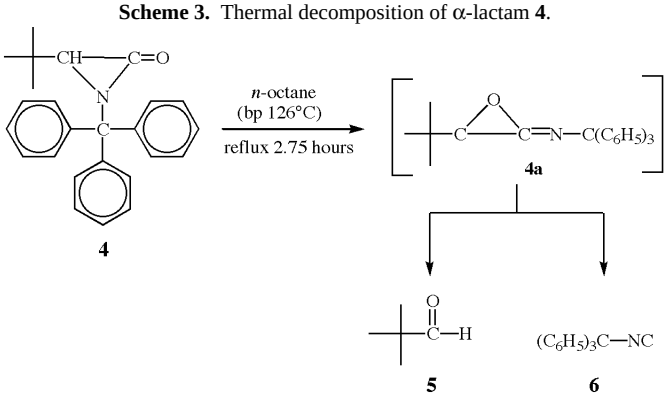
Scheme 2. Our synthesis of α-lactam **4**.



2. Thermal Decomposition of α-Lactam **4.**

Refluxing α-lactam **4** in *n*-pentane (bp 36 °C), *n*-hexane (bp 69 °C), or *n*-heptane (bp 98 °C) for one hour caused no decomposition whatsoever. Only refluxing in *n*-octane (bp 126 °C) for 2.75 hours brought about complete thermal decomposition (Scheme 3), and the products were, as expected, pivalaldehyde (**5**) and triphenylmethyl isonitrile (**6**), in quantitative yield. This astounding thermal stability contradicts the statement of Shimazu *et al*. [5]. It is assumed [12] that this thermal fragmentation of α-lactams occurs *via* an imino-oxirane intermediate, such as **4a**. After separation and isolation, characterization of the products was achieved by GC-MS and FT-IR. The IR and MS of the two thermal decomposition products were identical with those of authentic pivalaldehyde (Lancaster) and trityl isonitrile, synthesized by a modification [13] of Hofmann's "carbylamine" method [14].

Scheme 3. Thermal decomposition of α-lactam **4**.



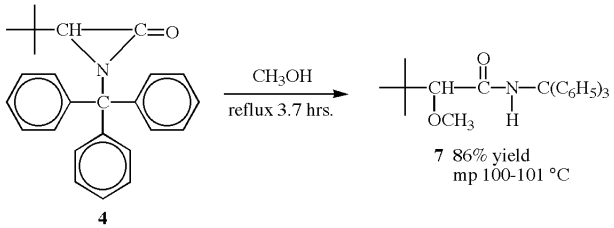
3. Reactions of α-Lactam **4**.

It has been learned early [2,3] that non-ionic protic nucleophiles such as water, alcohols, thiols, and amines open the α-lactam ring with exclusive or predominant cleavage of the C_3-N bond, while ionic aprotic nucleophiles such as alkoxide ions, *etc.*, open it with exclusive or predominant cleavage of the C_2-N bond. Since the early 1960's, few exceptions have been reported.

a) Reactions with Non-Ionic Nucleophiles.

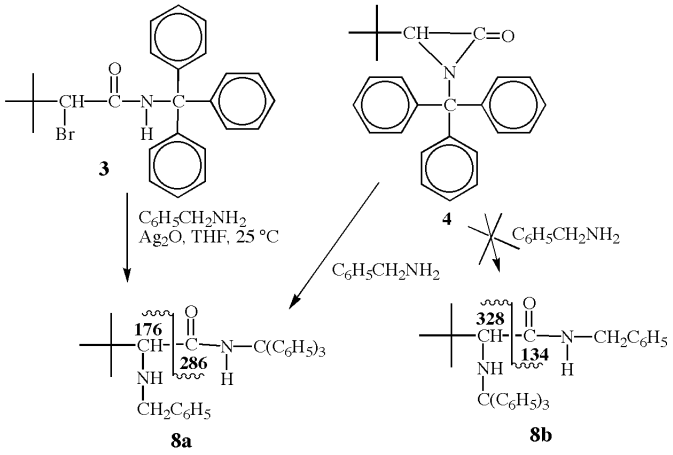
We chose to perform two reactions on **4** with protic non-ionic nucleophiles: with methanol (Scheme 4) and with benzylamine (Scheme 5). When α-lactam **4** was refluxed in methanol (bp 65 °C) for 3.7 hours, *N*-triphenylmethyl-2-methoxy-3,3-dimethylbutanamide (**7**) was formed in 86% yield, mp 100-101 °C (lit. [5] 101 °C). The product was also characterized by TLC, IR, ^{1}H-NMR, ^{13}C-NMR, GC-MS, and elemental analysis.

Scheme 4. Reaction of α-lactam **4** with methanol.



When α-lactam **4** was treated with four equivalents of benzylamine in THF at room temperature for 40 hours, the same procedure as used by Shimazu *et al.* [5], *N*-triphenylmethyl-2-benzylamino-3,3-dimethylbutanamide (**8a**) was isolated in 92% yield, mp 131-132 °C (lit. [5] 95%, colorless gum). The product was fully characterized by TLC, IR, ^{1}H-NMR, ^{13}C-NMR, MS, and elemental analysis. This is in contrast to the claim of Shimazu *et al*. [5] that α-lactam **4** reacts with benzylamine to give *N*-benzyl-2-triphenylmethylamino-3,3-dimethylbutanamide (**8b**). The authors describe the benzylamine reaction product as a "gum", without mp or elemental analysis. In addition, they did not fully characterize reaction product **8**. In their ^{1}H-NMR data, Shimazu *et al.* [5] account for only 33 of the 34 hydrogens, and did not report N-H/N-D exchange. They also do not provide ^{13}C-NMR or mass spectral data. There is no discussion of even the *mere possibility* of an alternative structure (**8a**).

Scheme 5. Reaction of α-lactam **4** with benzylamine and an independent synthesis of **8a**.

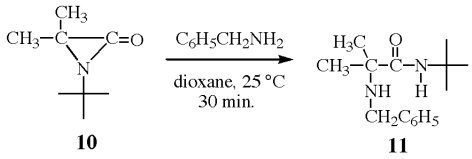


These two isomeric structural alternatives (**8a** and **8b**) are so closely related, both are α-*N*-alkylaminoamides, that they are indeed difficult to distinguish without having both structural isomers at hand; albeit it is possible to distinguish them with confidence by a combination of NMR and mass spectrometry.

This has been demonstrated first by Sheehan and Lengyel [3], who, in 1962, reacted 1-*tert*-butyl-3,3-dimethylaziridinone (**10**) with one equivalent of benzylamine in dioxane at room temperature, for 30 minutes, and after freeze-drying and chromatography, obtained 71.5% yield of *N*-*tert*-butyl-2-benzylamino-2-methylpropanamide (**11**), Scheme 6.

The product had been fully characterized, by mp (85-86°C), IR (CCl_4): 3350, (N-H), 1680 (amide C=O), 1515 (amide II), ^{1}H-NMR (benzylic CH_2 signal at 3.71 δ), a correct elemental analysis, and mass spectrometric molecular weight determination (M^+ at m/z 249). Its structure (**11**)

Scheme 6. Reaction of 1-*tert*-butyl-3,3-dimethylaziridinone with benzylamine.



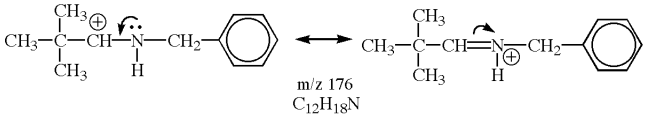
was assigned on the basis of the above evidence and a prominent fragment ion at m/z 148 in the mass spectrum (Scheme 7). An ion of this mass cannot be derived from the alternative α-*tert*-butylamino *N*-benzylamide structure.

Scheme 7. An abundant resonance-stabilized immonium type fragment ion in the mass spectrum of **11**.

In a similar fashion, an unequivocal choice can be made between structures **8a** and **8b** based on NMR and the same mass spectrometric argument. If either or both the m/z 176 and 286 ions are present in the mass spectrum, then the structure is **8a**. Alternatively, if either or both the m/z 328 and 134 fragment ions are present, then the structure is **8b** (Scheme 5). Since the mass spectrum of our benzylamine reaction product exhibits an abundant fragment ion at m/z 176, we consider the structure confirmed as **8a**. We had recorded mass spectra of our benzylamine product on different instruments using different ionization methods and sample injection conditions, to obtain both an abundant molecular ion and abundant structure-proving fragment ions (see Experimental).

The EI high resolution mass spectrum of our benzylamine reaction product exhibited a very intense ion at m/z 176.14415 (83.45% relative abundance), best elemental composition fit (within 1.3 ppm of the calculated exact mass) $C_{12}H_{18}N$, depicted in Scheme 8.

Scheme 8. An abundant resonance-stabilized immonium type fragment ion in the high resolution mass spectrum of **8a**.



As more representatives of both types of isomers (**8a** and **8b**) have been synthesized, both from α-lactams [5] and from α-bromoamides [15], it became evident, that the benzylic methylene signal of α-benzylaminoamides (**8a**

type) occurs around 3.5-3.9 δ, confirming the earlier report [3], while the benzylic methylene signal of *N*-benzylamides (**8b** type) appears at 4.1-4.5 δ. In ^{13}C-NMR, the benzylic methylene carbon signal for type **8a** structures is at 53 δ, but at 43 δ for type **8b** structures. Why some α-lactams, for example **4** and **10**, react with benzylamine to give α-benzylaminoamides, while others give *N*-benzylamides [5], is not known at present.

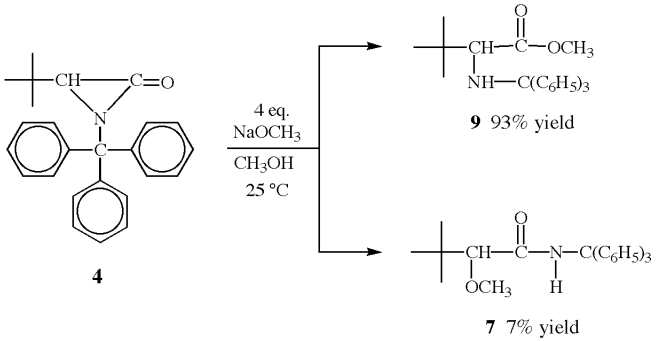
The 400 MHz high-resolution ^{1}H-NMR spectrum of our benzylamine reaction product clearly indicates that the two benzylic methylene protons are diastereotopic, that is they are stereochemically and magnetically non-equivalent. This diastereotopicity prevails even after the N-H hydrogens have been removed from the molecule by $CDCl_3$/CF_3COOD N-H→N-D exchange, indicating that mutual geminal coupling does not depend on the presence of an adjacent N-H which is the connecting link between the benzylic CH_2 and the chiral center in structure **8a**. *N*-Benzyl-*trans*-2,6-dimethylpiperidine [16], in which the two diastereotopic benzylic methylene protons are also three bonds removed from the chiral center, and are connected by a nitrogen atom, represents a closely related analogue.

The 400 MHz ^{1}H-NMR spectrum of our benzylamine reaction product is very similar to that reported by Shimazu *et al*. [5] for their impure benzylamine reaction product. We therefore suggest that these two products are identical, and both have structure **8a**. We obtained the ultimate proof of structure **8a** by an independent synthesis from α-bromoamide **3** and benzylamine, in the presence of silver oxide, using a modification of the procedure reported by D'Angeli *et al*. [15,17] (Scheme 5).

b) Reaction of α-Lactam **4** with Sodium Methoxide in Methanol.

According to the report published by Shimazu *et al*. [5], the reaction of 1-triphenylmethyl-3-*tert*-butylaziridinone (**4**) with 2.3 equivalents of sodium methoxide in methanol yields exclusively methyl 2-triphenylmethylamino-3,3-dimethylbutanoate (**9**), a colorless oil, in 68% yield. At room temperature the reaction took 24 hours.

Scheme 9. Reaction of α-lactam **4** with sodium methoxide in methanol.



In contrast, we noted that 4 equivalents of $NaOCH_3$ were necessary for the reaction to go to completion at 25 °C. The reaction yielded (Scheme 9), as expected [2,3], the corresponding methyl ester, methyl 2-triphenylmethylamino-3,3-dimethylbutanoate (**9**) as the major product, in 93% yield, mp 108-109 °C, accompanied by 7% of the α-methoxyamide, *N*-triphenylmethyl-2-methoxy-3,3-dimethylbutanamide (**7**). The physical and spectral properties of product **7** were identical with those of the methanolysis product.

EXPERIMENTAL

General Remarks.

Melting points were determined on a Thomas Hoover Capillary Melting Point Apparatus and are uncorrected. ^{1}H and ^{13}C-NMR spectra were recorded on either a 400 or 500 MHz Bruker instrument with tetramethylsilane as internal standard. Chemical shifts are reported in ppm (δ). IR spectra were measured on a Perkin Elmer Spectrum 1000 FT-IR. Microanalyses were performed by Atlantic Microlab Inc., Norcross, GA. Mass spectra were recorded either on a Hewlett Packard GC-MS GCD system, a Hewlett Packard 5890 gas chromatograph equipped with a 5971A mass selective detector, or a Fisons double focusing high resolution mass spectrometer with direct injection into the EI ion source. The ESI tandem mass spectrometry was performed on a Finnigan LCQ quadrupole ion trap mass spectrometer at the Scripps Research Institute, La Jolla, CA. For column chromatography, JT Baker Silica gel (40 microns) was used. Thin layer chromatography (TLC) was performed with Analtech Silica gel glass backed plates (250 microns).

2-Bromo-3,3-dimethylbutanoyl Chloride (**2**).

The procedure of Homeyer *et al*. [6] was followed. *tert*-Butylacetyl chloride (Lancaster, 100g, 0.742 mol) was refluxed for one hour with bromine (130 g, 0.8162 mol). A near-quantitative yield of the product was obtained by distilling the crude product at reduced pressure; bp 72 °C/19 mm (lit. [6] bp 93-97 °C/37 mm). ^{1}H-NMR ($CDCl_3$): δ 1.2 (s, 9H, *tert*-butyl), 4.5 (s, 1H, C*H*).

N-Triphenylmethyl-2-bromo-3,3-dimethylbutanamide (**3**).

Both the general procedures of Schlesinger and Prill [7] and Lengyel and Aaronson [8] were performed. Both give about 54-55% yield. To a solution of triphenylmethylamine (Lancaster, 10.0g, 0.0386 mol) in 1,2-dichloroethane (50 ml) at –5 °C, 2-bromo-3,3-dimethylbutanoyl chloride (**2**) (8.24 g, 0.0386 mol) and 20% aqueous NaOH (8.0 mL) were added separately and simultaneously from two addition funnels over a period of 20 minutes. The reaction mixture was then stirred overnight at room temperature. The organic layer was then washed with 5% aqueous HCl (50 mL), 5% aqueous $NaHCO_3$ (50 mL), and distilled water (50 mL). The organic layer was dried over anhydrous sodium sulfate and the solvent evaporated under reduced pressure to give a quantitative yield of crude **3**. Purification by flash chromatography (90% *n*-hexane/10% ethyl acetate) yielded pure amide **3**, 9.28 g (55.2%), mp 122-123°C; lit. [5] 80%, mp 170-170.5 °C. TLC: (90% *n*-hexane/10% ethyl acetate) R_f=0.44; IR (CCl_4): 3410 (N-H), 3062 (aromatic C-H), 2970 (aliphatic C-H), 1688 cm^{-1} (amide C=O); ^{1}H-NMR ($CDCl_3$): δ 1.11 (s, 9H, *tert*-

butyl), 4.27 (s, 1H, C*H*-Br), 7.23 (m, 16H, N-H and 15 aromatic protons); ^{13}C-NMR ($CDCl_3$): δ 27.88 (methyl carbons in *tert*-butyl group), 35.51 (quaternary carbon in *tert*-butyl group), 65.51 (*C*-Br), 71.00 (quaternary carbon in trityl group), 127.31 (*p*-carbons of phenyl groups), 128.20 (*m*-carbons of phenyl groups), 128.70 (*o*-carbons of phenyl groups), 144.41 (C_1-carbons of phenyl groups), 166.59 (carbonyl carbon).

Anal. Calcd. for $C_{25}H_{26}BrNO$: C 68.81; H 6.01; Br 18.31; N 3.21; Found C 68.90; H 6.03; Br 18.30; N 3.16.

1-Triphenylmethyl-3-*tert*-butylaziridinone (**4**).

A variation of the procedure of Sheehan and Lengyel [3] was used. *N*-Triphenylmethyl-2-bromo-3,3-dimethylbutanamide (**3**) (1.00 g, 0.0023 mol) was dissolved in 100 mL of dry diethyl ether and cooled to 0 °C in an ice bath. Sodium *tert*-butoxide (0.66 g, 0.0069 mol) was added to the solution in one portion, and the resulting suspension was stirred for 2.5 hours. Then the reaction mixture was washed with distilled water (100 mL). The organic layer was dried over anhydrous sodium sulfate and the ether removed on a rotary evaporator under reduced pressure. The residual crude α-lactam **4** was dissolved in 5 mL of hexane and cooled to –23 °C for 3 days. Pure 1-triphenylmethyl-3-*tert*-butylaziridinone (**4**) precipitated as a white crystalline solid and was collected, 0.75 g (93%), mp 103-104 °C; lit. [5] 76%, colorless oil; TLC: (90% *n*-hexane/ 10% ethyl acetate) R_f = 0.71; IR (CCl_4): 3100-3000 (aromatic C-H), 2980-2850 (aliphatic C-H), 1840 cm^{-1} (α-lactam C=O); ^{1}H-NMR ($CDCl_3$): δ 0.90 (s, 9H, *tert*-butyl), 2.14 (s, 1H, C*H*); 7.28-7.46 (m, 15H, phenyl protons in the trityl group); ^{13}C-NMR ($CDCl_3$): δ 27.66 (methyl carbons in *tert*-butyl group), 32.20 (quaternary carbon in *tert*-butyl group), 56.18 (methine carbon in α-lactam ring), 78.12 (quaternary carbon in trityl group), 127.72 (*p*-carbons in phenyl groups), 128.26 (*m*-carbons in phenyl groups), 128.95 (*o*-carbons in phenyl groups), 142.73 (C_1-carbons in phenyl groups), 162.09 (carbonyl carbon).

Anal. Calcd. for $C_{25}H_{25}NO$: C 84.47; H 7.09; N 3.94; Found C 84.59; H 7.09; N 3.98.

Thermal Decomposition of α-Lactam **4**.

α-Lactam **4** (0.1 g, 0.028 mol) was dissolved in *n*-octane (4 mL, bp 126 °C) and refluxed for 2.75 hours. Then the mixture was cooled to room temperature and subjected to analysis by FT-IR and GC-MS. The reaction yielded pivalaldehyde (**5**) and triphenylmethyl isonitrile (**6**) as the only products, in agreement with prior observations [2,12]; IR (octane): 2124 cm^{-1} (N=C); 1732 cm^{-1} (aldehyde C=O); GC-MS: two components; first peak molecular ion at m/z 86 (pivalaldehyde), second peak molecular ion at m/z 269 (triphenylmethyl isonitrile).

The IR and GC-MS of the two thermal decomposition products were identical with those of authentic pivalaldehyde (Lancaster) and trityl isonitrile. The latter was synthesized [13] in our laboratory for comparison, from tritylamine by a modified Hofmann "carbylamine" synthesis [14].

Reaction of α-Lactam **4** with Methanol.

α-Lactam **4** (0.2 g, 0.56 mmol) was dissolved in methanol (3 mL) and refluxed (65 °C) for 3.7 hours. The methanol was removed on a rotary evaporator to yield 0.19 g of an oily residue, which was taken up in boiling *n*-hexane. Upon cooling, *N*-triphenylmethyl-2-methoxy-3,3-dimethylbutanamide (**7**) precipitated and was collected on a Büchner funnel, 0.19 g (86%), mp 100-101°C; lit. [5] 84%, mp 101 °C; TLC: (90% *n*-hexane/ 10% ethyl acetate) R_f = 0.62; IR (CCl_4): 3410 (N-H), 3100-3000 (aromatic C-H), 2980-2850 (aliphatic C-H), 1692 cm^{-1} (amide C=O); ^{1}H-NMR ($CDCl_3$): δ 1.01 (s, 9H, *tert*-butyl), 3.18 (s, 1H C*H*), 3.42 (s, 3H, OC*H*$_3$), 7.28 (s, 15H, aromatic protons), 7.70 (s, 1H, N-H exchangeable in $CDCl_3$/CF_3COOD). ^{13}C-NMR ($CDCl_3$): δ 26.63 (methyl carbons in *tert*-butyl group), 35.35 (quaternary carbon in *tert*-butyl group), 59.87 (-O*C*H$_3$), 70.13 (quaternary carbon in trityl group), 91.37 (*C*H-OCH$_3$), 127.18 (*p*-carbons in phenyl groups), 128.12 (*m*-carbons in phenyl groups), 128.80 (*o*-carbons in phenyl groups), 144.96 (C_1-carbons in phenyl groups), 170.54 (carbonyl carbon);GC-MS: single peak, with molecular ion at m/z 387; significant fragment ions: m/z 330 [M-C_4H_9·]$^+$; 243 ($(C_6H_5)_3C^+$); 165 ($C_{13}H_9^+$); 101, base peak, [$(C_4H_9CH\text{-}OCH_3)^+$ or $(C_4H_9\text{-}CH{=}O\text{-}CH_3)^+$], 69 ($C_5H_9^+$), and 41 ($C_3H_5^+$).

Anal. Calcd. for $C_{26}H_{29}NO_2$: C 80.59; H 7.54; N 3.61; Found C 80.81; H 7.64; N 3.71.

Reaction of α-Lactam **4** with Benzylamine.

α-Lactam **4** (0.355 g, 1 mmol) was dissolved in 3 mL of dry THF, and freshly distilled benzylamine (0.428 g, 4 mmol, 4 equivalents) was added. After stirring at room temperature for 40 hours the THF and excess benzylamine were removed under reduced pressure, the latter at 0.1 mm. The white crystalline residue, 0.461 g (100%) showed one spot on TLC (80% *n*-hexane/ 20% ethyl acetate). It was chromatographed on silica gel, with 70% *n*-hexane/25% chloroform/5% 2-propanol as eluent, to yield 0.43 g (92%) of pure *N*-triphenylmethyl-2-benzylamino-3,3-dimethylbutanamide (**8a**), mp 131-132 °C; lit. [5] 95%, colorless gum; TLC: (80% *n*-hexane/ 20% ethyl acetate) R_f = 0.50; IR (CCl_4): 3440 (amide N-H), 3334 (amine N-H), 3063, 3029 (aromatic C-H), 2959, 2868 (aliphatic C-H), 1690 (amide C=O), 1520 cm^{-1} (amide II); ^{1}H-NMR ($CDCl_3$): δ 1.02 (s, 9H, *tert*-butyl), 1.76 (s, 1H, amine N-H exchangeable in D_2O), 2.13 and 2.79 (d, 1H, C*H*-C=O), 3.57 (d, 1H benzylic methylene proton) 3.71 (d, 1H benzylic methylene protons), 7.07-7.30 (m, 20H, trityl and benzylic phenyl protons); 8.74 (s, 1H, amide N-H); ^{13}C-NMR ($CDCl_3$): interpreted with the aid of the Attached Proton Test (APT) 27.46 δ (*C*H$_3$- carbons in *tert*-butyl group), 34.22 (quaternary carbon in *tert*-butyl group), 53.73 (benzylic *C*H$_2$- carbon), 70.06 (quaternary carbon in trityl group), 72.68 (N-*C*H-C=O), 126.91 (*p*-carbon in benzylic phenyl), 127.27 (*p*-carbons in trityl group), 127.87 (*m*-carbons in benzylic phenyl), 128.21 (*m*-carbons in trityl group), 128.50 (*o*-carbons in benzylic phenyl), 128.76 (*o*-carbons in trityl group), 139.42 (C_1 in benzylic phenyl), 145.02 (three C_1-carbons in trityl group), 171.45 (carbonyl carbon); MS (EI): m/z of the major fragment ions, their relative abundance (%), elemental composition and structure: m/z 357, 17.12% ($C_{25}H_{27}NO^+$, M-$NCH_2C_6H_5^+$); 243, 100% ($C_{19}H_{15}^+$, the trityl group); 182, 93.26% ($C_{13}H_{12}N^+$, $[(C_6H_5)_2C{=}NH_2]^+$); 176, 83.45% ($C_{12}H_{18}N^+$, $[(CH_3)_3CCH{=}NHCH_2C_6H_5]^+$); 174, 38.77% ($C_{12}H_{16}N^+$, $[(CH_3)_3CCHN{=}CHC_6H_5]^+$); 165, 40.35% ($C_{13}H_9^+$, the fluorenyl ion); 106, 4.71% ($C_7H_8N^+$, the benzylamino ion); 105, 6.57% ($C_7H_7N^+$, $[C_6H_5CH{=}NH]^+$); 104, 24.67% ($C_7H_6N^+$, $C_6H_5C{=}NH^+$); 91, 49.60% ($C_7H_7^+$, the tropylium ion); and 77, 13.33% ($C_6H_5^+$, the phenyl ion); MS/MS (ESI & CID): $(MNa)^+$ at m/z 485.3; $(MH)^+$ at 463.3; fragment ions at m/z 243.1 ($C_{19}H_{15}^+$, the trityl group); 221.2 ($C_{13}H_{21}N_2O^+$, $[(CH_3)_3CCH(NHCH_2C_6H_5)CONH_3]^+$); 165.0 ($C_{13}H_9^+$, the fluorenyl ion).

Anal. Calcd. for $C_{32}H_{34}N_2O$: C 83.08; H 7.41; N 6.06; Found C 83.04; H 7.37; N 5.66.

An Independent Synthesis of *N*-Triphenylmethyl-2-benzylamino-3,3-dimethylbutanamide (**8a**) from *N*-Triphenylmethyl-2-bromo-3,3-dimethylbutanamide (**3**).

The general procedure of D'Angeli *et al.* [15] was followed. To a solution of α-bromoamide **3** (0.873 g, 2 mmol) in 5 mL of dry tetrahydrofuran was added silver oxide (Mallinckrodt, 0.464 g, 2 mmol), vigorously stirred with a magnet bar, then benzylamine (Sigma, 0.643 g, 6 mmol, 3 equivalents) was added to the suspension and the stirring continued for ten hours. After this period, starting α-bromoamide (**3**) (R_f = 0.60) almost completely disappeared, as shown by TLC in 85% *n*-hexane/15% ethyl acetate as solvent system, and a new spot appeared, R_f = 0.43. The suspension was filtered over 0.5 g of Celite, and washed five times with 5 mL of ethyl acetate. The clear filtrate was evaporated to constant weight *in vacuo*. The residue was 1.56 g of an oil, which was flash chromatographed with 90% *n*-hexane/10% ethyl acetate as eluent, to yield 0.79 g (85.4%) of pure *N*-triphenylmethyl-2-benzylamino-3,3-dimethylbutanamide (**8a**), mp 131-132 °C; TLC: (80% *n*-hexane/20% ethyl acetate) R_f = 0.50; (85% *n*-hexane/15% ethyl acetate) R_f = 0.43. This product is identical with that obtained from the reaction of α-lactam **4** with benzylamine in all physical and spectroscopic properties.

Anal. Calcd. for $C_{32}H_{34}N_2O$: C 83.08; H 7.41; N 6.06; Found C 83.38; H 7.41; N 5.77.

The starting material, *N*-triphenylmethyl-2-bromo-3,3-dimethylbutanamide (**3**) (0.083 g) was also recovered from the column in pure form.

Reaction of α-Lactam **4** with Sodium Methoxide in Methanol.

To a solution of α-lactam **4** (0.4 g, 1.13 mmol) in methanol (12 mL) was added sodium methoxide (0.244 g, 4.5 mmol). After 24 hours at room temperature, the methanol was removed under reduced pressure. The residue was taken up in methylene chloride (200 mL) and washed with water (100 mL). The organic layer was dried over anhydrous Na_2SO_4, and the solvent removed under reduced pressure to yield 0.43 g (98%) of an oily residue, which crystallized upon standing. This product was flash chromatographed (97% *n*-hexane/3% ethyl acetate) to obtain 0.41 g (93%) pure crystalline methyl 2-triphenylmethylamino-3,3-dimethylbutanoate (**9**), mp 108-109 °C; lit. [5] 68%, colorless oil; TLC: (95% *n*-hexane/ 5% ethyl acetate) R_f = 0.33; IR (CCl_4): 3321 (N-H), 3062 (aromatic C-H), 2959, 2878 (aliphatic C-H), 1738 cm^{-1} (ester C=O); ^{1}H-NMR ($CDCl_3$): δ 1.06 (s, 9H, *tert*-butyl), 2.61 (d, 1H, N-H) exchangeable in $CDCl_3/D_2O$), 3.11 (s, 3H, -COOCH_3), 3.23 (d, 1H, methine proton), 7.25 (t, 3H, 3 *p*-hydrogens in trityl group), 7.27 (3 *m*-hydrogens in trityl group), 7.56 (3 *o*-hydrogens in trityl group); ^{13}C-NMR ($CDCl_3$): δ 27.58 (methyl carbons in *tert*-butyl group), 35.93 (quaternary carbon in *tert*-butyl group), 50.86 (-COO*C*H_3), 63.71 (methine carbon), 70.77 (quaternary carbon in trityl group), 126.50 (*p*-carbons in trityl group), 127.78 (*m*-carbons in trityl group, 129.43 (*o*-carbons in trityl group), 146.20 (C_1-carbons in trityl group), 174.29 (carbonyl carbon of ester); GC-MS: exhibits the following major ions: M^+ at m/z 387; 372 $(M\text{-}CH_3)^+$; 355 $(M\text{-}CH_3OH)^+$; 330 $(M\text{-}C_4H_9\cdot)^+$; 328 $(M\text{-}COOCH_3\cdot)^+$; 310 $(M\text{-}C_6H_5\cdot)^+$; 250 $(328\text{-}C_6H_6)^+$; 244 ($C_{19}H_{16}^+$, triphenylmethane); 243 ($C_{19}H_{15}^+$, the trityl group); 241 ($C_{19}H_{13}^+$); 239 ($C_{19}H_{11}^+$); 228 $(C_{18}H_{12})^+$; 215; 202; 193; 182 ($C_{13}H_{12}N^+$, $[(C_6H_5)_2C{=}NH_2]^+$); and 165, base peak, ($C_{13}H_9^+$, the fluorenyl cation); MS/MS (ESI & CID): $(MNa)^+$ at m/z 410.2; 409 $(MNa\text{-}H)^+$; 350, base peak, $(409\text{-}COOCH_3\cdot)^+$, $[(CH_3)_3CCH{=}N(Na)C(C_6H_5)_3]^+$; 340 $(MNa\text{-}C_5H_{10})^+$; 317.2 $(340\text{-}Na)^+$; 243.1 ($C_{19}H_{15}^+$, the trityl group); and 166 ($C_{13}H_{10}$, fluorene).

Anal. Calcd. for $C_{26}H_{29}NO_2$: C 80.59; H 7.54; N 3.61; Found C 80.66; H 7.58; N 3.63.

A second fraction was eluted from the column, pure crystalline *N*-triphenylmethyl-2-methoxy-3,3-dimethylbutanamide (**7**), as a minor product, 0.03 g (7%), mp 100-101 °C; TLC: (90% *n*-hexane/ 10% ethyl acetate) R_f = 0.54; IR (CCl_4): 3410 (N-H), 3100-3000 (aromatic C-H), 2980-2850 (aliphatic C-H), 1692 cm^{-1} (amide C=O). This compound is identical with the methanolysis product.

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