Isolation and Stability of an α-Lactam with a New Substitution Pattern: 3-Phenyl-1,3-di-t-butylaziridin-2-one

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Summary The isolation of 3-phenyl-1,3-di-t-butylaziridin-2-one the first example of a trisubstituted α-lactam having two t-alkyl substituents, is described, and its stability and mass spectrum are compared with those of other known aziridinones

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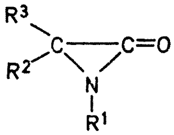
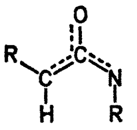
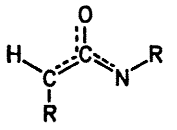
OF the aziridinones so far isolated, the most stable ones have a t-alkyl group at positions 1 and 3, and no other substituent at C-3 (Ia)[1] The reason suggested by Sheehan and his co-workers[2] for the low reactivity and high thermal stability of these aziridinones is steric destabilization of a (IIa) or (IIb) involved in the ring-opening reactions The failure of all investigators to isolate the corresponding common acyclic, planar or quasi-planar, and charge-delocalized intermediate or transition state of the type of

(Ia) $R^1 = R^2 =$ t alkyl $R^3 = H$
(Ib) $R^1 = R^2 = Ph$ $R^3 = H$
(Ic) $R^1 = R^2 = R^3 = Ph$
(Id) $R^1 = R^2 = Bu^t$ $R^3 = Ph$
(Ie) $R^1 = Bu^t$, $R^2 = Ph$, $R^3 = H$
(If) $R^1 = Bu^t$, $R^2 = R^3 = Ph$
(Ig) $R^1 = R^2 = Bu^t$, $R^3 = H$

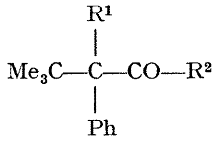


diphenylaziridinone (Ib) or the triphenylaziridinone (Ic) was then attributed to charge delocalization in (II) by the aromatic substituents to such an extent that the acyclic form is stable and cyclization does not occur If this is so, then the relative importance of these two factors should determine whether further substitution by an aryl group in aziridinones of type (Ia) will increase or decrease the stability, and, if so, to what extent We now report the isolation of the first example of an α-lactam (Id) with this substitution pattern No trisubstituted α-lactam having two t-alkyl substituents has so far been isolated or detected


(IIa)


(IIb)

2,2-Dimethyl-1-phenylpropan-1-ol was purified *via* its acid phthalate derivative and treated with purified thionyl chloride to give α phenylneopentyl chloride [3] Conversion of this chloride in tetrahydrofuran solution into the Grignard reagent under argon followed by treatment of the resulting solution with carbon dioxide under pressure, afforded pure 3,3-dimethyl-2-phenylbutanoic acid (IIIa)[4] in 72% yield


$$\mathrm{Me_3C{-}\overset{\displaystyle R^1}{\underset{\displaystyle Ph}{C}}{-}CO{-}R^2}$$

(IIIa) $R^1 = H$ $R^2 = OH$
(IIIb) $R^1 = H$, $R^2 = Cl$
(IIIc) $R^1 = Br$, $R^2 = Cl$
(IIId) $R^1 = Br$, $R^2 - NHCMe_3$

This acid was heated under reflux with purified thionyl chloride for 45 min and the acid chloride (IIIb) obtained was treated with bromine in boiling carbon tetrachloride until conversion into (IIIc) was complete (disappearance of the n m r peak at τ 8 93 and appearance of a peak at τ 8 82) Treatment of the crude bromo-acid chloride with t-butylamine furnished in 52% yield [from (IIIa)], the bromo-amide (IIId) [m p 60 0—60 5° (from hexane), i r (CCl_4) ν_{max} *ca* 3450 and 1690 cm $^{-1}$, ^{1}H n m r (CCl_4) τ 8 79 (s, 9H), 8 67 (s, 9H) 3 78 (s, 1H), 2 11—2 8 (m, 5H)] Ring closure to the desired α-lactam (Id) was then achieved by the reaction of (IIId) with potassium t-butoxide in ether at ice-salt temperatures Unlike the more stable α-lactams (Ia), where the ring closure could be driven to completion at many concentrations by the use of an excess of base,[1a,1b,1f] the present reaction requires a very careful control of the reagents and experimental conditions in order to effect complete conversion of (IIId) into (Id) However, even from an impure sample of the α-lactam, we isolated crystals of the pure α-lactam (Id) by low-temperature crystallization from pentane, m p 39·5—41·5° The slow decomposition of this compound, even at room temperature, precluded elemental analysis Its structure is confirmed by its i r and n m r spectra, which exhibit features similar to those reported for other aziridinones [i r (CCl_4) ν_{max} *ca* 1835 cm^{-1}, no N–H absorption in the 3400 cm^{-1} region, ^{1}H n m.r. (CCl_4) τ 8 93 (s, 9H), 8 78 (s, 9H), 2·18—2·77 (m, 5H)] The two t-butyl groups in (Id) are presumably *trans*

In view of the statement made by Lengyel and Sheehan[2b] that "under otherwise identical conditions, C-3 disubstituted α-lactams are more stable than C-3 monosubstituted ones," we compared the thermal and chemical stability of the series of α-lactams, (Id)—(Ig) Whereas (Ig)[1a] decomposes only slowly at 140°, (Id) requires only about 2 5 hr for complete decomposition in dry benzene (50 mg /3 ml) at 45°, and in ice-cold methanol (50 mg /3 ml), (Id) requires approximately 3 5 hr for complete decomposition, in contrast to (Ig) which requires several days in refluxing methanol (Ie) decomposes in methanol at 5° within 20 min ,[5a] and (If) has been reported to be "much more reactive chemically "[5b] Although the published data on the thermal stability[5] of (Ie) and (If) do not permit an accurate comparison with (Id), it appears that (Id) is less stable thermally than (Ie) or (If), which are alike in this respect [5b] Thus, thermal and chemical stability do not parallel each other in the above four α-lactams, and this conclusion points out the need for some revision in the factors listed by Sheehan and his co-workers[2] in determining the stability of α-lactams

The sharp difference noted above between (Id) and compounds of type (Ia) is also observed in their mass spectra The primary step in the electron impact-induced fragmentation of (Ia, $R^1 = R^2 =$ 1-adamantyl or Bu^t, $R^3 = H$) is ejection of carbon monoxide from the molecular ion,[1e,6] and the ($M-28$) ion constitutes the strongest peak in these spectra above *m/e* 135 In contrast to this behaviour, we have not observed any significant peak corresponding to either M or ($M-28$) in the mass spectrum of (Id) at 23° at all voltages up to 80 ev, whereas the mass spectrum of (If) contains "a reasonably strong molecular ion peak ' [5b]

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