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1-TERT-BUTYL-3-PHENYL-3-(TRIFLUOROMETHYL)AZIRIDINONE: AN UNUSUALLY STABLE TRISUBSTITUTED α-LACTAM

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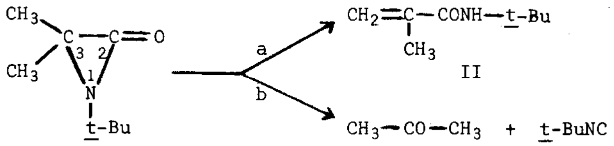
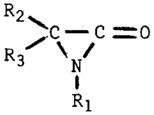
The first trisubstituted aziridinone to be isolated was I. However, this compound undergoes slow decomposition even at room temperature, and complete destruction of the ring can be effected in boiling ether after one hour to afford II as the major product and III and IV as the minor products.[1] One way of blocking the eliminative isomerization reaction (path a) is



I   III   IV

to select tert-alkyl or aryl substituents at C-3. Several examples of the former type of substitution (Va) are known,[2] and these compounds are thermally and chemically the most stable of



Va, R_1 = R_2 = tert-alkyl; R_3 = H

Vb, R_1 = tert-butyl; R_2 = Ph; R_3 = H

Vc, R_1 = tert-butyl; R_2 = R_3 = Ph

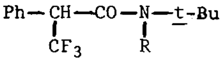
Vd, R_1 = tert-butyl; R_2 = 4-chlorophenyl or 4-bromophenyl; R_3 = H

Ve, R_1 = tert-butyl; R_2 = CF_3; R_3 = Ph

Vf, $R_1 = R_2 =$ *tert*-butyl; R_3 = Ph

all the aziridinones known so far. Of the other type of substitution, only a few examples are known (Vb, [3a-c] Vc, [3d] and Vd [3e]). Although the thermal stability of Vb and Vc is between that of I and Va, the chemical stability of Vb and Vc is very poor and similar to that of I. We now report the first example of an aziridinone (Ve) in which the substitution pattern is not restricted to one involving only aryl or unsubstituted alkyl groups, and its remarkable stability, which is superior to that of any other trisubstituted aziridinone known to date.

3,3,3-Trifluoro-2-phenylpropanoic acid[4] was converted *via* its acid chloride into its *N-tert*-butylamide (VIa) [63%; mp 138.5-139.0° (from hexane-benzene); ir (CCl_4) ν_{max} *ca.* 3420 and 1705 cm^{-1}; ^1H nmr (CCl_4) τ 8.70 (s, 9H), 5.90 (q, 1H, *J* 9 Hz), 4.50 (broad s, 1H), 2.47-2.73 (m, 5H)]. Ring closure to the desired aziridinone (Ve) was accomplished by the reaction of



$$\text{Ph}-\underset{\text{CF}_3}{\text{CH}}-\text{CO}-\underset{\text{R}}{\text{N}}-\underline{\text{t}}\text{-Bu}$$

VIa, R = H; VIb, R = Cl

VIa with purified *tert*-butyl hypochlorite and potassium *tert*-butoxide in dry toluene at ice-salt temperatures without the isolation of VIb, the presumed intermediate. However, the proportion of the base as well as that of *tert*-butyl hypochlorite required, relative to that of VIa, was far in excess (factor of about three) of the stoichiometric 1:1:1 molar ratio, and led to contamination of Ve by other products. Baumgarten and his co-workers prepared the disubstituted aziridinones Vb and Vd by a similar route and mentioned[3b] the distinctly different amounts of base and *tert*-butyl hypochlorite required for each aziridinone; however, they failed to prepare the trisubstituted aziridinone Vc by the same procedure.[3e] Isolation of Ve from the crude reaction mixture was attempted by filtration of the mixture under nitrogen, followed by removal of the toluene at 0° and low-temperature crystallization of the residue from pentane. However, the α-lactam was still impure. A much purer sample was obtained by distillation of the crude product in a high vacuum (less than 0.05 mm) at a bath temperature of 105-120°C. Although complete purification was still not achieved, the presence of Ve in the distillate is suggested by the following spectral characteristics: ir (CCl_4) *ca.* 1870 (shoulder at 1890) cm^{-1}; nmr (CCl_4) τ 8.72 (s), 2.6 (center of m), and absence of the quartet at τ 5.90 found in the spectrum of VIa; mass spectrum, *m/e* 257 ($M^{+\cdot}$). Furthermore, treatment of VIa with potassium *tert*-

butoxide alone did not result in the formation of the ir band at 1870 cm^{-1}.

The ability of Ve to survive the purification process involving distillation above 100° attests to its remarkable thermal stability, and this conclusion is reinforced by the observation that complete decomposition of Ve at 90° requires about 3.5 hours. The chemical stability of Ve is even more striking, since some of this α-lactam could be detected even after its solution in absolute methanol was refluxed for 24 hours. Thus, the stability of Ve approaches that of compounds of the type of Va.

Besides some spiro-α-lactams,[2d,5] the only other trisubstituted aziridinones known are I, Vc, and Vf.[6] In view of the statement made by Lengyel and Sheehan[7] that "under otherwise identical conditions, C-3 disubstituted α-lactams are more stable than C-3 monosubstituted ones," we are comparing the thermal and chemical stability of the series of α-lactams Vb, Vc, Ve, and Vf. The first three compounds are similar to one another in thermal stability, but the last compound is markedly unstable in this regard. The chemical stability (reaction with methanol) of Ve is superior to that of any of the others, and the relative order of chemical stability among the other compounds is Vf>Vb>Vc. Thus, thermal and chemical stability do not parallel each other in the above series of compounds, and this conclusion points out the dangers inherent in a discussion of the thermal and chemical stability of α-lactams in terms of common intermediates or transition states.[7] Furthermore, steric factors of the type discussed by Lengyel and Sheehan[7] cannot be solely responsible for the relative order of stabilities observed in the above series of compounds. In fact, further work is needed before any reliable predictions concerning the change in stability of α-lactams with structure can be made.

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