The Synthesis of 1-Cyclohexyl-2-phenyl-3-nitroaziridine and the Stereochemistry of Cyclization

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The title compound was synthesized by the cyclization of α,β-dibromonitrostyrene with three moles of cyclohexylamine. Evidence for the steric course of the cyclization reaction is also reported.

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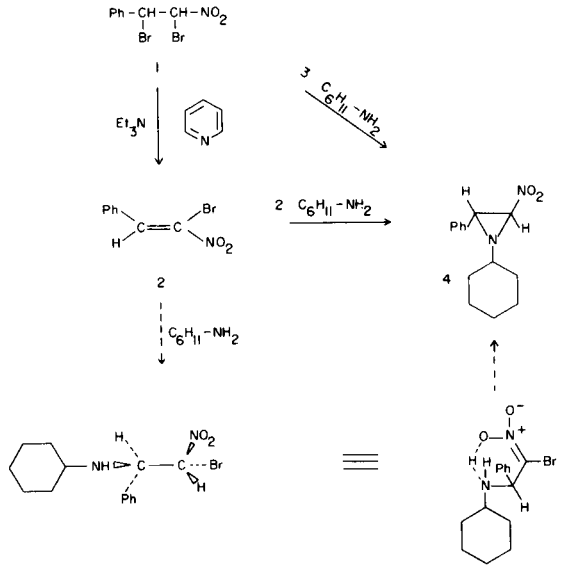
Sir:

Several carboaziridines were synthesized in this laboratory by the cyclization of α,β-dibromo carbonyl compounds with three moles of primary amines (1). The same reaction mechanism (2) is found to follow here in the synthesis of 1-cyclohexyl-2-phenyl-3-nitroaziridine **4** not known in the literature to date. α,β-Dibromonitrostyrene **1** on treatment with three moles of cyclohexylamine gives exclusively *trans*-1-cyclohexyl-2-phenyl-3-nitroaziridine in very high yield. The first mole of amine does not undergo nucleophilic substitution, but acts as a base causing an elimination reaction to afford *trans*-β-bromo-β-nitrostyrene **2**. *trans*-β-Bromo-β-nitrostyrene (3,4) was previously prepared by treating α,β-dibromonitrostyrene in cyclohexane with one equivalent of pyridine or triethylamine. Treatment of **2** with two moles of cyclohexylamine also gave the same *trans*-1-cyclohexyl-2-phenyl-3-nitroaziridine. The *cis*-β-bromo-β-nitrostyrene would be expected to give *cis*-1-cyclohexyl-2-phenyl-3-nitroaziridine. Southwick has reported earlier (5) that the conjugate addition of primary amines, like benzylamine and cyclohexylamine, to (2-nitropropenyl)benzene gives only one racemic form of the adduct. With secondary amines he has suggested the kinetically favored formation of the erythro adduct from the chelated acinitro intermediate. Nitroolefines are known to be excellent Michael acceptors and add numerous functional groups (6,7). Thus, the second step of our synthesis involves the stereospecific Michael addition of the second mole of amine to give the *erythro*-α-amino-β-bromo-β-nitrostyrene **3** as evidenced by the isolation of only the *trans*-aziridine (based on (8) nmr: $^3J_{H\text{-}H} \leq 2$ Hz). The third mole of amine acts as a base in the internal S_N2 type ring closure to give the *trans*-1-cyclohexyl-2-phenyl-3-nitroaziridine.



EXPERIMENTAL

To a 5.0 g. (16.2 mmoles) sample of α,β-dibromonitrostyrene dissolved in 25 ml. of dry acetonitrile, was added dropwise a solution of 5.6 ml. (48.54 mmoles) of cyclohexylamine in 10 ml. of dry acetonitrile over a period of 30 minutes. The solution was maintained at 0-10° during addition of the amine, and then stirred for an hour and left in the refrigerator for two days. The acetonitrile was removed by blowing nitrogen and the residue was stirred with dry benzene. Afterwards, 5.6 g. (96.6%) of cyclohexylamine hydrobromide was recovered. Removal of benzene left an oil which was identified as *trans*-1-cyclohexyl-2-phenyl-3-nitroaziridine, ir (carbon tetrachloride): ν NO_2 1650 cm^{-1} (s), 1550 cm^{-1} (vs), 1360 cm^{-1} (vs); ^1H nmr (deuteriochloroform): δ = 7.3-7.5 (m, 5H, aromatic), 5.0 (d, 1H, C_3H), 3.76 (d, 1H, C_2-H), 1.0-2.0 (m, 11H, cyclohexyl). The high resolution mass spectrum shows a major peak corresponding to the molecular ion minus a nitro group as in the case of *N*-phthalimido nitroaziridine prepared by a completely different method (9).

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