Intramolecular 1,3-Dipolar Cycloaddition of Alkylazide-enones and Rearrangements of the Triazoline Intermediates†

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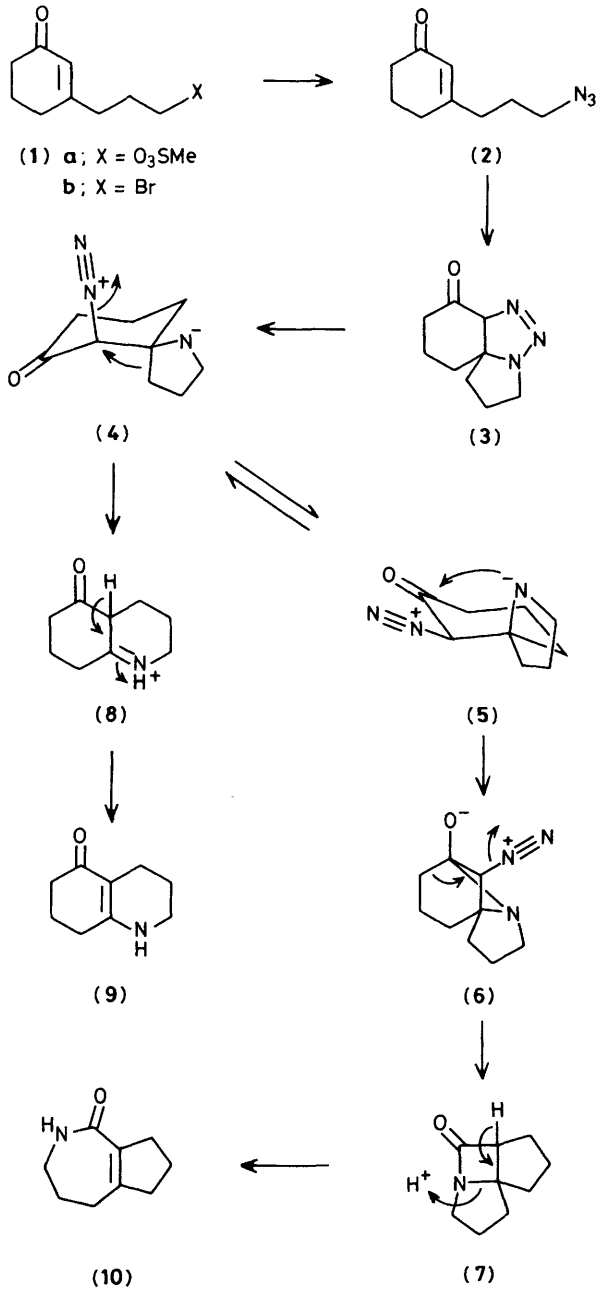
The intramolecular 1,3-dipolar cycloaddition of alkylazide-enones is followed by several novel rearrangements.

The 1,3-dipolar cycloaddition reaction between alkylazides and olefins has been extensively studied. The intramolecular version of this cycloaddition has been investigated by few workers.[1] Recently, Schultz and coworkers reported some interesting results with emphasis on their application to practical synthetic methods.[2] In the course of our studies on the synthesis of perhydrohistrionicotoxin alkaloids, we explored this attractive synthetic approach and encountered some novel rearrangements of the reaction intermediates.

† The work described here was presented at the 9th International Congress of Heterocyclic Chemistry, Tokyo, August 1983.



Scheme 1

Treatment of the bromide (**1b**)[3] with sodium azide in aqueous methanol at 80 °C gave the products (**9**) and (**10**) in 24 and 63% yield, respectively. Alternatively, heating the methanesulphonate (**1a**)[3] with sodium azide in dry dimethylformamide at 80 °C gave the same result. A reasonable mechanism was proposed and is shown in Scheme 1. Intramolecular 1,3-dipolar cycloaddition of (**2**) would give the triazoline (**3**). The unstable triazoline (**3**) could decompose to form the zwitterionic intermediate of conformation (**4**) or (**5**). Conformation (**5**) has a nitrogen anion in the axial position, which could easily attack the carbonyl group to give (**6**). Structure (**6**) could rearrange to give (**10**), presumably *via* the intermediate (**7**). On the other hand, conformation (**4**) could undergo a 1,2-alkyl shift and give the product (**9**) *via* (**8**).

The structure of (**10**) was confirmed by a single crystal *X*-ray analysis. *Crystal data*: $C_9H_{13}NO$, $M = 151.209$, monoclinic,

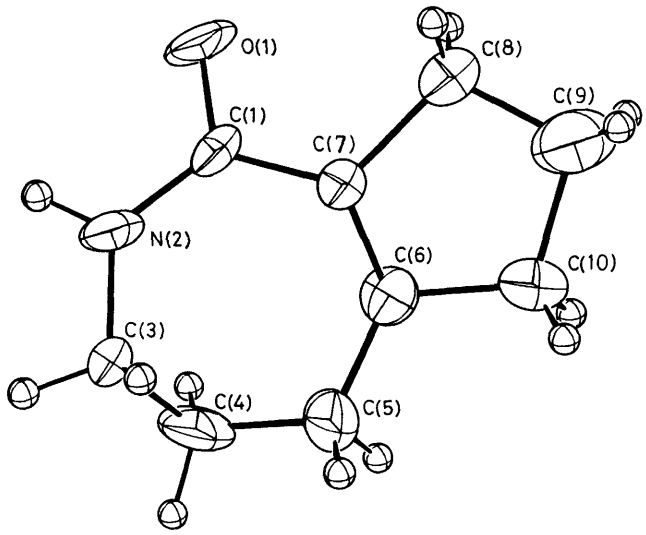
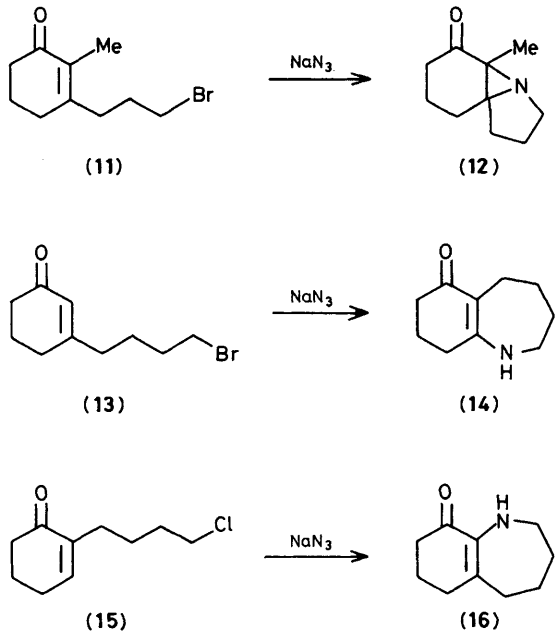


Figure 1. Crystal structure of (**10**) Bond lengths: C(1)–O(1) 1.172(14); C(1)–C(7) 1.364(17); C(1)–N(2) 1.377(15); C(3)–N(2) 1.365(17); C(3)–C(4) 1.547(18); C(4)–C(5) 1.543(22); C(5)–C(6) 1.450(18); C(6)–C(7) 1.278(18); C(6)–C(10) 1.512(22); C(7)–C(8) 1.566(19); C(8)–C(9) 1.445(24); C(9)–C(10) 1.517(21) Å.



Scheme 2

space group $P2_1/n$, $a = 5.478(2)$, $b = 11.485(4)$, $c = 12.831(9)$ Å, $\beta = 94.72(5)°$, $Z = 4$. 1733 Independent reflections were measured of which 816 were considered observed [$I > 2\sigma(I)$]. The structure was solved by direct methods to a present R value of 0.094. An ORTEP drawing of the molecular structure of (**10**) is shown in Figure 1.‡

In order to understand the reaction mechanism, a methyl group was introduced to C(2) of the enone (**1b**). The enone

‡ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

(**11**)§ was prepared and treated with sodium azide in dry dimethylformamide at 80 °C. The aziridine (**12**) was obtained in 57% yield. The bromide (**13**),[4] with a longer side chain, was treated with sodium azide under the same conditions and the product (**14**) was isolated in 64% yield. On the other hand, when the chloride (**15**)[5] was treated with sodium azide in aqueous methanol, we obtained the product (**16**) in 10—15% yield (Scheme 2). The lower yield in this case may be due to the slow intramolecular cycloaddition owing to the regiochemistry of the dipole and dipolarophile. Detailed studies of this reaction and its applications to natural products synthesis will be reported in due course.

§ Compound (**11**) was prepared by the same method of ref. 3, but starting with 2-methyl-3-ethoxycyclohexanedione.

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