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# SYNTHESIS OF NOVEL CARBO- AND HETEROPOLYCYCLES. 17.[1] INTRAMOLECULAR 1,3-DIPOLAR CYCLOADDITION REACTION OF 3-ENDO-AZIDOBICYCLO[3.3.1]NON-6-ENE. A FACILE ROUTE TO 5-AZAPROTOADAMANT-4-ENE.†

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Abstract——The intramolecular 1,3-dipolar cycloaddition of 3-endo-azidobicyclo[3.3.1]non-6-ene **1** proceeded on heating in toluene under reflux to afford regioselectively very unstable 1,2,3-triazoline derivative **2**, which decomposed spontaneously in MeOH to give exclusively 5-azaprotoadamant-4-ene **6**.

The use of intramolecular 1,3-dipolar cycloaddition reactions in organic synthesis has been increasing quite rapidly in recent years.[2] The utilization of azides has been explored, in particular, for the regioselective construction of nitrogen heterocycles as well as alkaloid skeletons.[3,4] Recently, we have reported a convenient synthesis of 2-amino-4-hydroxy derivatives and 2-hydroxy-5-aza analogues of tricyclo-nonane, -decane, -undecane, and -dodecane derivatives via intramolecular 1,3-dipolar cycloaddition reactions of appropriate C- and N-bicycloalkenylnitrones.[5] As an extension of these studies, we report in this paper a facile route to 5-azaprotoadamant-4-ene (5-azatricyclo[4.3.1.0$^{3,8}$]dec-4-ene) **6** via the intramolecular 1,3-dipolar cycloaddition reaction of 3-endo-azidobicyclo[3.3.1]non-6-ene **1**, followed by nitrogen-extrusion and rearrangement of the initial cycloadduct **2**.

The starting 3-endo-azidobicyclo[3.3.1]non-6-ene **1** was readily prepared from the corresponding carboxylic acid[6] by our method previously reported.[7] Azide **1** in toluene was heated to reflux under argon for 10 h to afford very unstable product as a colorless solid after evaporation of the solvent. This product revealed no azide absorption band but a weak C=N absorption band at 1640 cm$^{-1}$ in the ir (KBr) spectrum (presumably due to formation of an imine by decomposition).

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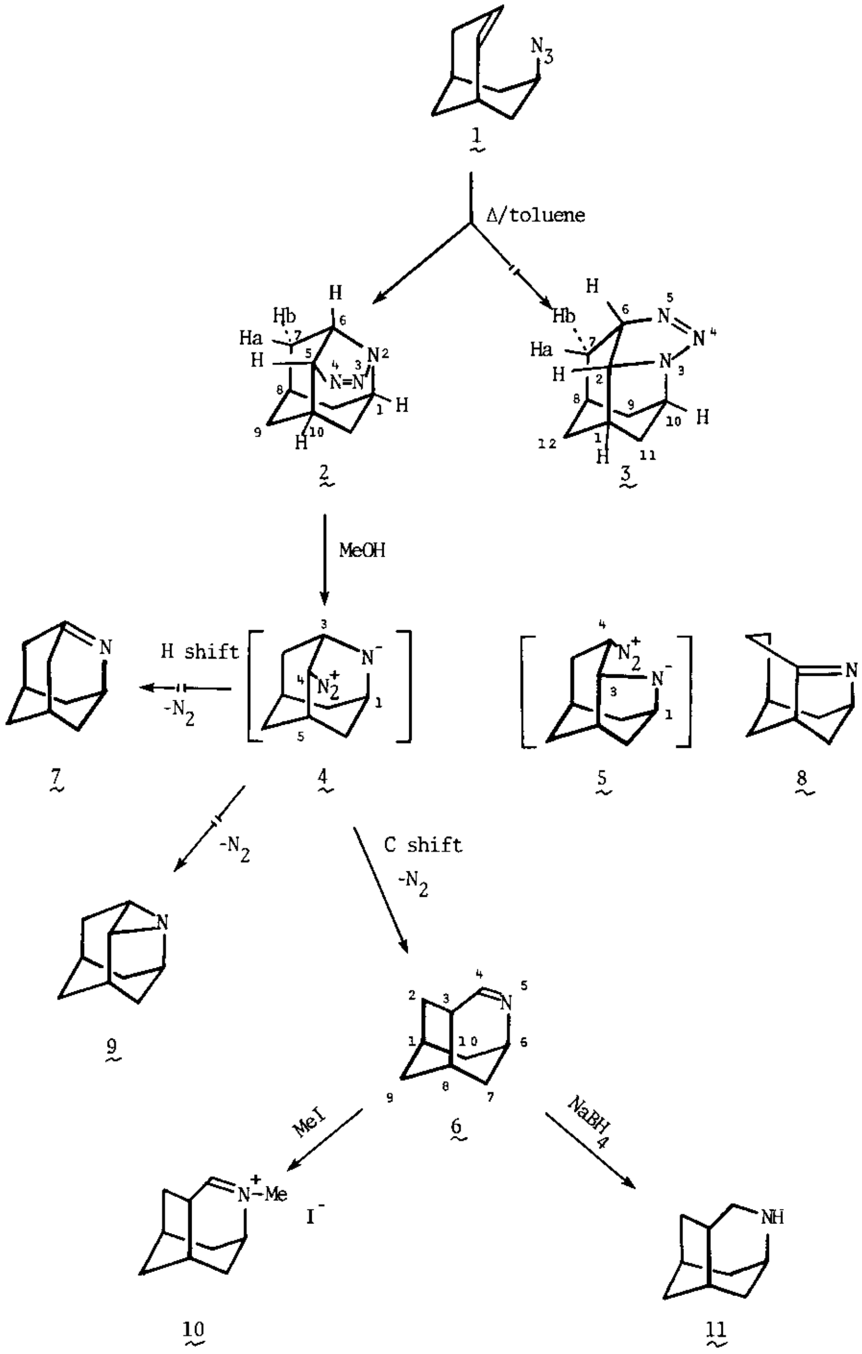
† Dedicated to the late Professor Dr. Tetsuji Kametani.

This product decomposed spontaneously in $CDCl_3$ to afford a complex mixture. Therefore, the initial adduct was treated with MeOH to afford a new product as a colorless solid quantitatively, mp 164-165 °C. The structure of this product was determined as 5-azatricyclo[4.3.1.0$^{3,8}$]dec-4-ene (trivial 5-azaprotoadamant-4-ene) 6 based on analysis[8] and the following spectral data: Ir(KBr) 1640 cm$^{-1}$; $^1$H nmr[9] δ 8.18 (d, *J*=4.4 Hz, 1H), 4.10-3.80 (m, 1H), 3.05-2.60 (m, 1H), 2.60-1.20 (m, 8H); $^{13}$C nmr[9] δ 172.6 (d, 1), 55.1 (d, 1), 43.0 (t, 1), 39.0 (d, 1), 38.7 (d, 1), 37.4 (t, 2), 31.8 (d, 1), 30.6 (t, 1); ms *m/z*(%) 136 (33), 135 (36, $M^+$), 69 (52), and 66 (100). Other structures such as highly strained bridgehead imines 7 and 8 as well as aziridine 9 derivable from the initial cycloadducts 2 and/or 3 were not compatible with these spectral data. However, two regioisomeric triazolines 2 and 3 can be a precursor of the stable imine 6 as explained in Scheme. In order to determine the regioselectivity of this intramolecular cycloaddition, 1 in $C_6D_6$ was heated under argon at 115 °C and the reaction was followed by $^1$H nmr spectroscopy at 200 MHz. After heating for 55 h, the signals of azide 1 disappeared completely, and two sets of new signals appeared at δ 8.04 (d, *J*=4.0 Hz), 4.06 (m) and at δ 4.15 (dt, *J*=8.2 and 5.3 Hz), 3.76 (m), 3.18 (t, *J*=7.7 Hz) in a ratio of 0.79:0.79:0.21:0.21:0.21. The former set of signals was apparently due to formation of imine 6, and the latter was assignable to the intermediate triazoline because of its disappearance on treatment with $CD_3OD$. The coupling pattern of the triazoline ring protons allowed us to assign structure 2 rather than 3, on the basis of the calculated coupling constants (Lemieux-Lown equation).[10,11] Thus, the characteristic doublet, triplet signals at δ 4.15, multiplet signals at δ 3.76, and triplet signals at δ 3.18 were assignable to $H_6$, $H_1$, and $H_5$ of 2, respectively. The relative ratio of 1, 2, and 6 was 35:33:33 after 17 h, and 14:38:48 after 30 h, respectively, and, no other characteristic signals were detectable during the heating. The simultaneous formation of imine 6 during the reaction indicates instability of 2. All of these results indicate that intramolecular cycloaddition of 1 proceeded rather sluggishly but regioselectively to afford triazoline 2 which decomposed rapidly in polar solvents to give exclusively novel imine 6 (Scheme).[12] Imine 6 gave the corresponding methiodide 10 (5-methyl-5-azaprotoadamant-4-enium iodide) as a colorless solid by standard procedure (78%), mp >300 °C: Ir(KBr) 1670 cm$^{-1}$; $^1$H nmr δ 9.75 (dd, *J*=6.0 and 1.0 Hz, 1H), 4.20-3.90 (m, 1H), 3.80 (d, *J*=1.0 Hz, 3H), 3.90-3.40 (m, 1H), and 3.10-1.60 (m, 10H). Reduction of 6 with $NaBH_4$ in MeOH gave amine 11 as a colorless solid (73% after sublimation), mp 123-124 °C: Ir(KBr) 2920, 1540, 1410 cm$^{-1}$; $^1$H nmr δ 5.27 (s, 1H, $D_2O$ exchangeable), 3.50-3.20 (m, 1H), 3.20-2.60 (m, 2H), 2.60-1.10 (m, 11H); ms *m/z*(%) 138 (35), 137 (42, $M^+$), 136 (37), 108 (32), 94 (85), 80 (100), and 56 (52).

As described above, the intramolecular cycloaddition of bicycloalkenylazide 1 provides a facile

Scheme



1
Δ/toluene
2
3
MeOH
H shift
$-N_2$
7
4
5
8
$-N_2$
C shift
$-N_2$
9
6
MeI
$NaBH_4$
10
11

route to 5-azaprotoadamant-4-ene 6 that may be useful for the synthesis of related azaheteropolycycles.

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12. For the decomposition modes of 1,2,3-triazolines via diazonium betaines, see (a) ref. 2a, pp. 568-621; (b) ref. 3c; (c) ref. 3d, pp. 329-330 etc.

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