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FORMATION AND TRAPPING OF 6-AZABICYCLO[3.2.2]NON-5-ENE, A STRAINED BRIDGEHEAD IMINE

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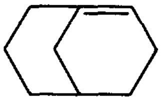
Summary: Photolysis or flash vacuum pyrolysis of 1-bicyclo[3.2.1]octylazide 9 yields 6-azabicyclo[3.2.2]non-5-ene 10, a strained bridgehead imine, which could not be isolated but was trapped with methanol.

Renewed interest in the synthesis and chemistry of bridgehead olefins (Bredt-olefins)[2] has been aroused since the first preparation of bicyclo[3.3.1]non-1-ene 1 fifteen years ago.[3] At that time Wiseman[4] put forward the hypothesis that bridgehead olefins may be compared in strain and reactivity with the corresponding monocyclic (E)-cycloalkenes, from which they are formally derived by bridging.

Bredt's rule and Wiseman's stability criterion should also be applicable to unsaturated bridgehead compounds containing heteroatoms, e.g. bridgehead imines. Indeed, whereas the 2,5-ethylene-bridged (E)-1-azacyclohex-1-ene 2[5] and the (E)-1-azacycloheptenes 3[5], 4[6], and 5[7] cannot be isolated, but may be trapped with methanol, the bridged (E)-1-azacyclooctene 6 is stable at room temperature.[8] A recent report[9] describes the synthesis and reactions of two tricyclic bridgehead imines 7 and 8 with bis-homoadamantane skeleton, both of which are formal bridged (E)-1-azacyclooctenes.[10] Imines 7 and 8 have not been isolated pure, but they seem to survive for a limited period of time at ordinary temperature.



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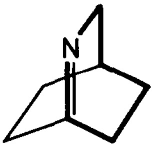

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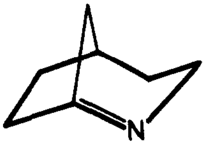

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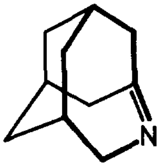

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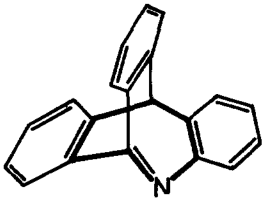

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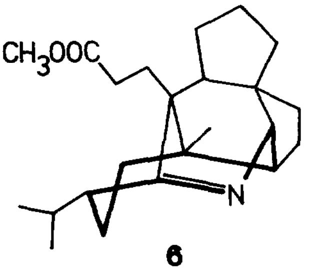

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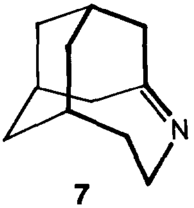

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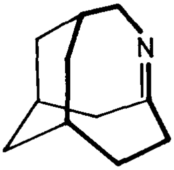

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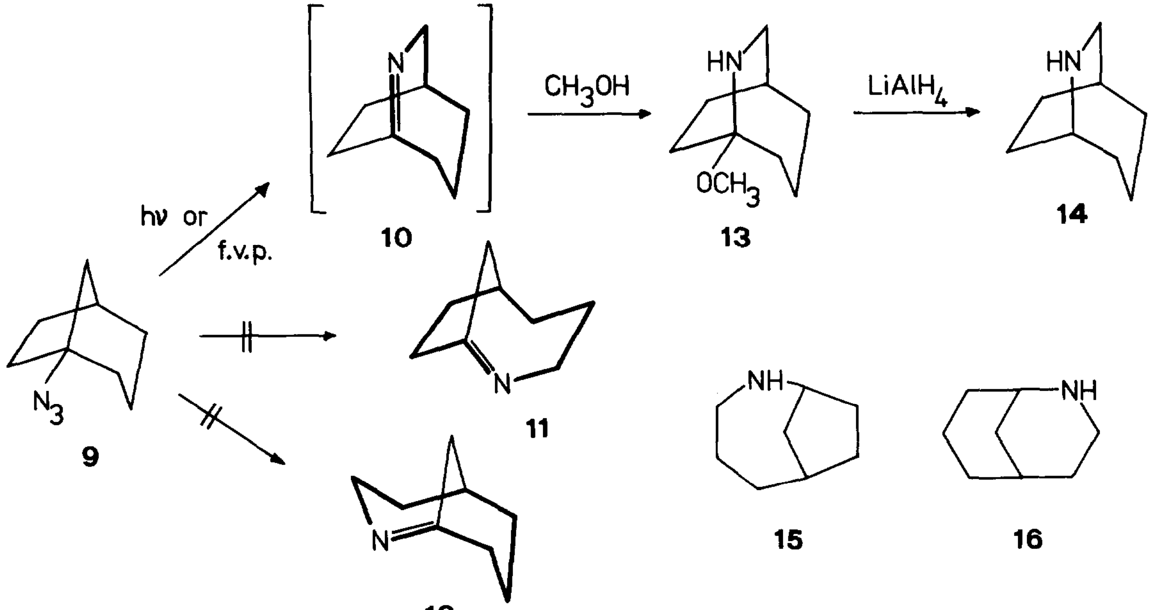
Herein we report our attempts to prepare further bridgehead imines with (E)-1-azacycloheptene and (E)-1-azacyclooctene subunit. Photolysis of 1-bicyclo[3.2.1]octylazide 9 should give rise to a mixture of three isomeric bridgehead imines 10, 11, and 12 in analogy to the rearrangement of related bridgehead azides.[5,6,7,9] A methanol solution of azide 9[11] was irradiated at -5° for 36 h in a high pressure Hg lamp with Pyrex filter. After removal of the solvent and short path distillation, a single compound was isolated in 22% yield, whose spectral characteristics were those of an addition product of methanol to either imine 10, 11, or 12 (IR: 3340 (NH) and 1085 cm^{-1} (OCH_3); ^1H-NMR (CCl_4): δ 3.08 (s, 3 H, OCH_3), 2.7-3.0 (m, 2 H, NCH_2); 1.38 ppm (s, 1 H, NH); ^{13}C-NMR ($CDCl_3$): δ 86.7 (s), 48.2 (t), 47.6 (q), 43.0 (t), 32.8 (t), 30.0 (d), 28.1 (t), 23.3 (t), 19.9 ppm (t)). Structure 13 for this methanol adduct was proved by reduction to the corresponding amine 14 with $LiAlH_4$ and comparison with material prepared by an independent route.[13] Again no trace of an isomeric amine, e.g. 15[15] or 16[17], was found. Photolysis of azide 9 in an inert solvent (e.g. pentane) at low temperature gave only an intractable polymer. Attempts to obtain an adduct of cyanide ion to imine 10 were also futile.



The isolation of methoxy-amine 13 in the photolysis of azide 9 does not yet prove the intermediacy of bridgehead imine 10. In principle, methanol could react directly with the photo-activated azide 9 to give the observed product.[18] However, flash vacuum pyrolysis of 1-bicyclo[3.2.1]octylazide 9 at 418° and 0.01 Torr and condensation of the products formed on a cooling finger (liquid nitrogen) pretreated with methanol again gave methoxy-amine 13 in 30% yield free of isomers. This is clear evidence that the bridgehead imine 10 is indeed formed, although 10 itself could not be isolated and characterized even at -50°.

Imine 10 belongs to the class of bridged (E)-1-azacycloheptenes. In line with Wiseman's postulate and previous experience with related bridgehead imines, compound 10 is therefore not stable, but polymerizes. Dimeric products as in the case of imines 4[6] and 5[7] could not be isolated.

At the moment it is not clear why imine 10 is formed in preference to the isomeric imines 11 and 12, both of which are bridged (E)-1-azacyclooctenes and consequently far less strained. For either a concerted or a two-step reaction via an intermediate nitrene,[19] one would expect that already in the transition state the difference in strain of the possible products should be manifest. It may be interesting to note that a similar regioselectivity leading to the more strained bridgehead olefin was observed in the pyrolysis of the lithium salt of bicyclo[2.2.1]heptane-1-carbaldehyde tosylhydrazone, a reaction proceeding via a carbene.[20]

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10. We do not agree with the authors that 8 is a (E)-1-azacycloheptene. The larger of the two smallest rings incorporating the imine double bond is eight-membered.

11. Azide 9 was prepared from 1-bicyclo[3.2.1]octylamine[12] as the hydrochloride with p-toluenesulfonylazide and potassium t-butoxide in dimethyl sulfoxide in 76% yield. IR: 2095 cm^{-1} (N_3); ^{1}H-NMR: δ 2.1 - 2.5 (m, 1 H, CH), 1.0 - 2.0 ppm (m, 10 H, CH_2); ^{13}C-NMR ($CDCl_3$): δ 67.6 (s), 43.3 (t), 36.9 (t), 35.4 (d), 33.5 (t), 31.4 (t), 28.1 (t), 19.9 ppm (t).

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13. Bicyclo[3.2.1]octan-8-one[14] was transformed into the oxime (hydroxylamine-hydrochloride in ethanol, 86 %), and Beckmann rearrangement (p-toluenesulfonylchloride in pyridine) led to 6-azabicyclo[3.2.2]nonan-7-one (64 %). $LiAlH_4$-reduction and acid work-up gave the hydrochloride of amine 14 (87 %), ^{13}C-NMR ($CDCl_3$): 49.3 (d), 45.1 (t), 33.5 (t), 31.4 (t), 27.5 (d), 21.3 (t), 20.7 (t), 20.2 ppm (t).

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