

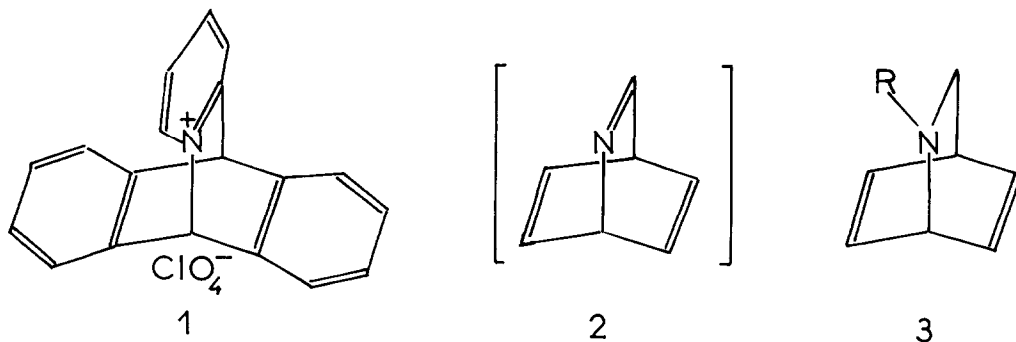
AN APPROACH TO 2-AZABARRELENE :
SYNTHESIS OF AN UNSTABLE 2-AZABICYCLO[2.2.2]5,7-OCTADIENE

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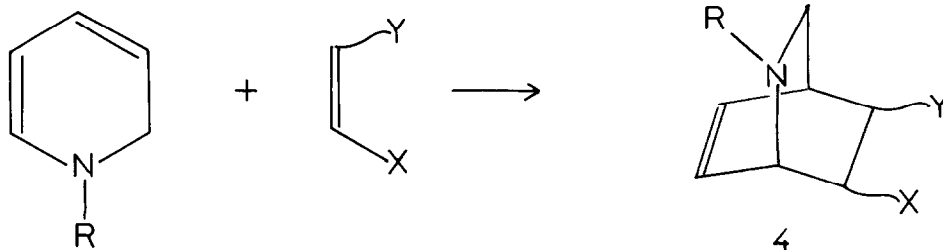
(Received in UK 20 September 1977; accepted for publication 3 October 1977)

Although some compounds such as 1¹ possess in their structure the interesting 2-azabarrelene system which is stabilized in this case by insertion of its double bonds in aromatic cycles, the bicyclic parent 2 is still unknown, despite attempts to synthesize such derivatives². Nevertheless, theoretical calculations predict some stability for 2-azabarrelene, as a result of a positive balance between the stabilizing through bonds interactions and the destabilizing through space ones³.



As an approach to this fundamental structure and in order to get insight into the relative stability of bicyclo[2.2.2]octadienes and their aza analogs 3 which exhibit homoallyl type interaction between the nitrogen lone pair and the monadjacent π bonds⁴, we have performed the synthesis of a 2-azabicyclo[2.2.2]5,7-octadiene (3 : R=CO₂CH₃).

In order to find a practical synthetic route to these derivatives we looked at a method for introduction of a second double bond in compounds such as 4 which are readily available from Diels-Alder cycloadditions on 1,2-dihydropyridines⁵.

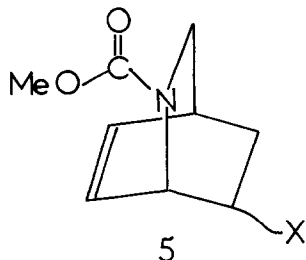


R=CO₂Me ; n : endo ; x : exo

4a : X = CN, Y = H

4b : X = CO₂Me, Y = H

The thermal condensation of acrylonitrile and methyl acrylate with N-carbomethoxy-1,2-dihydropyridine occurs in a regioselective manner yielding only the C-7 substituted products as it can be inferred from frontier orbital theory applied to cycloaddition of a 1-heterosubstituted diene with a dienophile bearing an electron-withdrawing group⁶. The endo and exo isomers have been separated and classical transformations involving a Curtius rearrangement have been performed on the methyl esters 4b_n and 4b_x, leading to the primary amines 5a_n and 5a_x⁷. These latter were converted into the quaternary hydroxides 5b_n and 5b_x and the N-oxides 5c_n and 5c_x⁸.



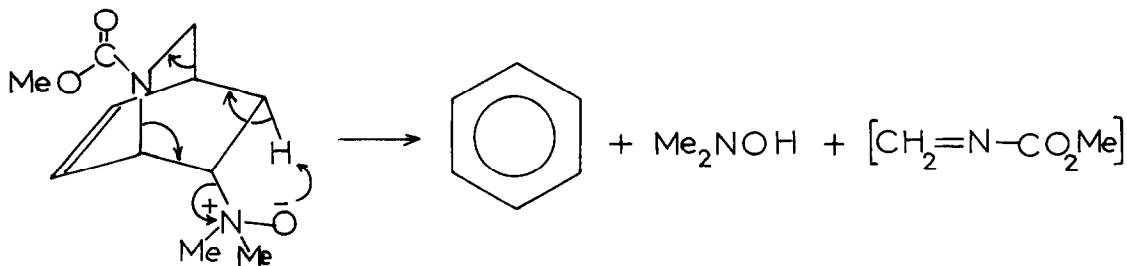
n : endo ; x : exo

5a X = NH₂

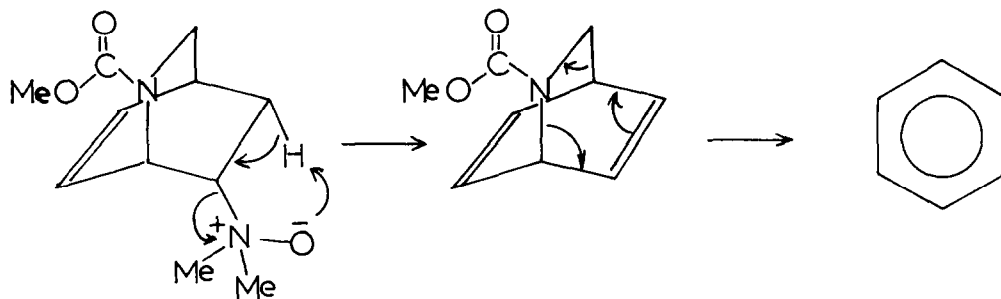
5b X = N⁺(Me)₃, OH⁻

5c X = Me₂N⁺-O⁻

These compounds were submitted either to Hofmann or Cope eliminations, but the expected azabicyclooctadiene was not obtained. Nevertheless dimethylhydroxylamine was produced when 5c_n was subjected to the Cope elimination in refluxing benzene ; furthermore in refluxing carbon tetrachloride formation of benzene was evidenced by nmr. Thus, the elimination took place but led to benzene, either directly through a 10 electrons pericyclic path (scheme I) or in a step-wise manner : the normal Cope elimination being followed by a Diels-Alder retroversion which would occur on the azabicyclooctadiene produced in the first step (scheme II).

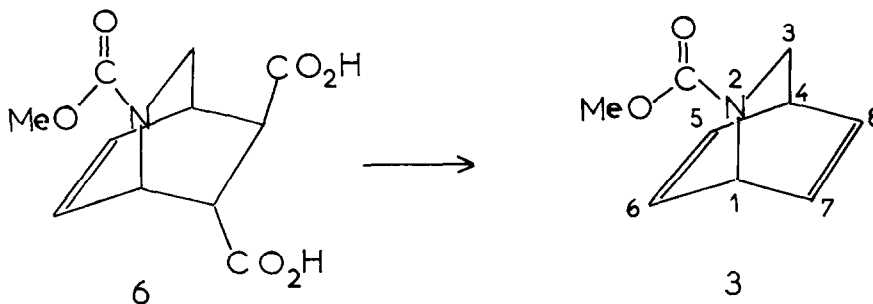


Scheme I



Scheme II

The creation of a double bond by anodic oxidation of vicinal dicarboxylic acids⁹ appeared as a way to produce the diene under milder conditions. Thus we prepared the diacid **6** by condensation of methyl fumarate with N-carbomethoxy-1,2 dihydropyridine followed by saponification. The oxidative decarboxylation was performed by electrolysis of a cold solution (0°) of the trans diacid⁸ (7-endo, 8-exo ; 2.55 g) in a mixture of pyridine (190 cc), water (20 cc) and triethylamine (2.5 cc) with Pt electrodes under a constant intensity of 50mA. Work up including ether extraction from water solution, acidic washings, MgSO₄ drying, evaporation and chromatography on basic alumina afforded a 17 % yield of N-carbomethoxy-1 azabicyclo[2.2.2] 5,7-octadiene **3** which was characterized by the following spectral data : ir (film, cm⁻¹) 3060 (ν_{C-H}), 1695 (ν_{C=O} carbamate), 1615 (ν_{C=C}), 800, 770, 735, 720, 680, 660 (out of plane δ_{C-H} cis) ; pmr (CDCl₃, δ, TMS) 6.63 (m, 4 ethylenic H), 5.50 (m, H-1), 3.75 (m, H-4), 3.68 (s, CH₃), 2.93 (d, CH₂, J₃₋₄ = 3Hz).



Slow decomposition of **3** occurred in chloroform solution as shown by the appearance of the benzene signal in nmr after 12 hours, whereas the neat liquid was totally decomposed by overnight standing at room temperature. This spontaneous transformation evidences the instability of the 2-azabicyclo[2.2.2] 5-7 octadiene structure which undergoes a very easy retrograde Diels Alder reaction yielding the highly stabilized benzene molecule. Such decomposition does not occur so easily on bicyclooctadienes¹⁰. Of course, the greater fragility of the C-N bond as compared to the C-C one is an important cause of this different behaviour, but the question

arises to know if the interaction of the nitrogen lone pair with the two double bonds in homoallylic position does not play a part in this destabilization¹¹.

Although unstable, N-carbomethoxy-2 azabicyclo[2.2.2]5,7-octadiene represents the first example of a 2-azabicyclo[2.2.2]octadiene structure possessing two nonstabilized ethylenic linkages.

References and Notes

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7. In order to avoid isomerisation, the acyl azides have been prepared through the intermediary hydrazides and not from the acids.
8. All these new compounds, which give correct analytical results and show pmr spectra in accordance with the assigned structures, will be described in a further paper.
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10. For instance bicyclo[2.2.2]2,5-octadiene can be prepared by Hofmann or Cope reaction performed at 150°; C.A. Grob, H. Kny and A. Gagneux, *Helv. Chim. Acta.*, 40, 130 (1957).
11. Although in our compound the nitrogen hybridation is different owing to the presence of the carbamate function, it is worth noting that, while the homoallyl system of 2-azabicyclo[2.2.2]oct-5-ene is rather stabilized by the interaction between n and π electrons^{4,12}, the bishomoallyl interacting system of 7-azanorbornene derivatives is destabilized by this interaction^{12,13}.
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