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THE THERMAL REORGANIZATION OF HOMOAZEPINE DERIVATIVES

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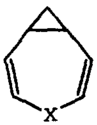
The thermal reorganization of bicyclic hydrocarbons possessing the vinylcyclopropane moiety and their heterocyclic counterparts undergo a variety of rearrangements depending upon the nature of the hetero-substituent. For example, bicyclo[6.1.0]nona-2,4,6-triene rearranges mainly to *cis*-8,9-dihydroindene (1a), but the heterocycles 9-carbethoxy- (1b) and 9-phthalimido-9-azabicyclo[6.1.0]nona-2,4,6-triene (2) rearrange to 4-carbethoxy-4-azabicyclo[5.2.0]nona-2,5,8-triene and 9-phthalimido-9-azabicyclo[4.2.1]nona-2,4,7-triene respectively. In order to gain more insight into the nature of the hetero-atom effect on thermal reorganization pathways, we felt it important to examine the behavior of a number of other bicyclic systems. In this connection, we report on the behavior of the homoazepines 1a and 2a (3), which are the first heterocyclic counterparts of the homotropilidenes 1b and 2b studied earlier by Doering and Roth (4).



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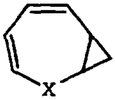

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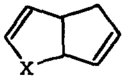

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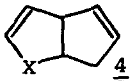


4

a, X = NCOOEt

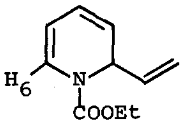
b, X = CH_2

c, X = NCH_3

On heating (220°C) a sample of 1a for 11 hours in a sealed evacuated vessel, a single new isomeric substance assigned structure 3a, 2-carbethoxy-2-azabicyclo[3.3.0]octa-3,7-diene (bp 57-58°/0.15 mm, >95% pure), was produced in nearly quantitative yield. The isomer 3a readily absorbed 1.9 molar equivalents of hydrogen to produce 2-carbethoxy-2-azabicyclo[3.3.0]-

octane, 5, which was identified by direct comparison (nmr, ir, and vpc) with a sample prepared in an independent way (5). The spectral properties of 3a are consistent with the assigned structure: ν_{max}^{film} 1700(s) cm^{-1} (C=O) and 1620 (m) cm^{-1} (N-C=C); τ(60 MHz; CCl_4 with tetramethylsilane; recorded at ~70°C) (6) 3.58 (H_3, dd, J ~2, 4 Hz) 4.2 (H_7 and H_8, m), 4.94 (H_1, d with fine structure, J ~9 Hz), 5.15 (H_4, dd, J ~2, 4 Hz), 5.85 (OCH_2, q, J ~7 Hz), 6.3 (H_5, m), 7.5 ($2H_6$, m), and 8.75 (CH_3, t, J ~7 Hz). The spectral data most readily accommodates 3a and not an isomeric bicyclo[3.3.0]octadiene (7). The formation of 3a is most simply rationalized by the well known vinylcyclopropane rearrangement of 1a (8). It is of interest that 1b also undergoes a similar rearrangement (85% complete at 305°C after 24 hours) to produce only 3b (4). The related isomer 2b, however, does not undergo a vinylcyclopropane rearrangement to produce 4b, but undergoes a much more complex series of rearrangements discussed below.

On pyrolysis of 2a at 220°C for 30 minutes, a mixture (average of four runs) consisting of 50% (±3%) isomer 6, 17% (±3%) of an unknown mixture, and 33% (±7%) starting material was produced. The total isolated and separated yield was >36%.

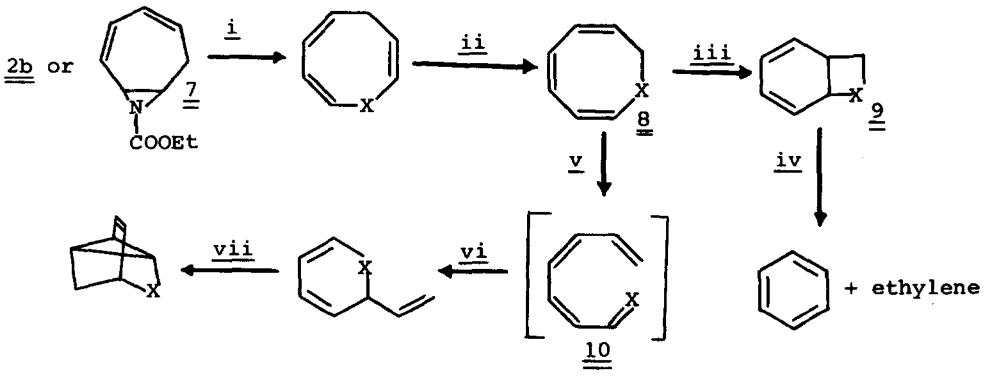


6

The major (50%) component, assigned structure 6, absorbed 2.9 molar equivalents of hydrogen to produce 1-carbethoxy-2-ethylpiperidine, which was identified by direct comparison (nmr, ir, vpc) with an authentic sample. The nmr spectrum (60 MHz; CCl_4 with tetramethylsilane) most readily accommodates structure 6: τ3.43 (H_6, d, J ~7.2 Hz), 4.0-5.2 (7H, complex m), 5.88 (OCH_2, q, J ~7 Hz), and 8.73 (CH_3, t, J ~7 Hz) (9). The minor (17%) component is a mixture of substances, which, upon hydrogenation, produces a new mixture containing mainly 5 (5). The isolation of 5 perhaps suggests that 2a undergoes a vinylcyclopropane reaction to produce (presumably) 4a (7), but mainly a more complex reaction to produce 6 occurs.

The main thermal reorganization pathway for both 2a and 2b is suggested to be strikingly similar and a possible mechanism is depicted in the Chart (4). As a first step, 2b can undergo a 1,5-homodienyl hydrogen migration (12) (step i) followed successively by the 1,5-dienyl hydrogen shift ii (13), the electrocyclic reactions v and vi (14), and the intramolecular Diels-Alder reaction vii (4), as well as the electrocyclic reaction iii (15) and the reverse [2+2] cycloaddition iv (4). We suggest that

Chart



the pathway for 2a is similar, but 2a isomerizes to 7 before undergoing the reactions depicted in the Chart. Other pathways are, of course, conceivable.

In this study, only 6 (of the possible intermediates shown in the Chart) was isolated in the thermolysis of 2a. Small amounts of 8 (X = NCOOEt) have been isolated from the reaction between carbethoxynitrene and cycloheptatriene (2,3). We have found that 8 (X = NCOOEt), which appears to exist only (nmr) as the monocycle and not as 9 (X = NCOOEt), isomerizes cleanly to 6 at 130°C. Professor Paquette has kindly informed us that 9 (X = NSO_2CH_3), which exists only (nmr) in the bicyclic form, isomerizes at somewhat lower temperatures to produce 10 (X = NSO_2CH_3) (16). Doering observed that the hydrocarbon 2b produced all of the components shown in the Chart except cycloocta-1,3,6-triene (which is known to isomerize, >99%, thermally to 8, X = CH_2) (13), 10 (X = CH_2), and ethylene (4).

The results of this study indicate the remarkable similarity of the thermal behavior of the hydrocarbons 1b and 2b with the corresponding N-carbethoxyl derivatives 1a and 2a. We have also thermolyzed the N-methyl derivatives 1c and 2c, which were prepared by lithium aluminum hydride reduction of 1a and 2a respectively, but we have thus far been unable to isolate pure products from what appears to be extensively decomposed reaction mixtures (2).

Acknowledgements

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5. Compound 5, bp 48-49°/0.02 mm, was prepared by hydrogenation (0.98 molar-equivalents uptake) of a mixture of 2-carbethoxy-2-azabicyclo]3.3.0]oct-1(5)-ene and 2-carbethoxy-2-azabicyclo-[3.3.0]oct-8-ene. We thank Dr. Joseph E. Dolfini (Squibb Institute for Medical Research, New Brunswick, N. J.) for the experimental details of this preparation. See also J. D. Simpson, Master's Thesis, Purdue University, June, 1966 and J. E. Dolfini and J. D. Simpson, J. Am. Chem. Soc., 87, 4381 (1965).
6. The carbethoxyl group apparently suffers hindered rotation. For a related example, see R. Garner and W. B. Watkins, Chem. Comm., 386 (1969).
7. Professor L. Paquette (Ohio State University) has informed us that photolysis of the carbomethoxyl derivative of 2a produces the analogous 4a and 5-carbomethoxy-5-aza-1α, 2α, 4α, 6α-tricyclo[4.2.0.$0^{2,4}$]oct-7-ene. Comparison of the spectrum of 3a with Paquette's methyl analog of 4a, the only other reasonable isomer, shows that 3a is correctly assigned.
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9. In view of the low field positions of all of the nmr proton resonances (besides the ethoxyl group) and the hydrogenation experiment, only two other structures besides 7 seem reasonable: 1,2-dihydro-6-vinylpyridine (a) and 1,4-dihydro-2-vinylpyridine (b). The observed doublet at τ3.43 appears to rule out a for which a doublet is also possible for H_5 (see a), but at higher fields (ca. τ5) (10). Structure b is eliminated because its two allylic protons should also appear at higher fields (ca. τ7) (11).
10. For example, see the spectrum of 3a reported above and the spectra of 1a and 2a (3).
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