AZABICYCLO[3.2.0]HEPTANE-3,4-DIONE (10): A THERMAL AZONIA 1,3-SHIFT OF 2-AZABICYCLO[3.2.0]HEPT-2-ENES TO 2-AZANORBORN-2-ENES[1]

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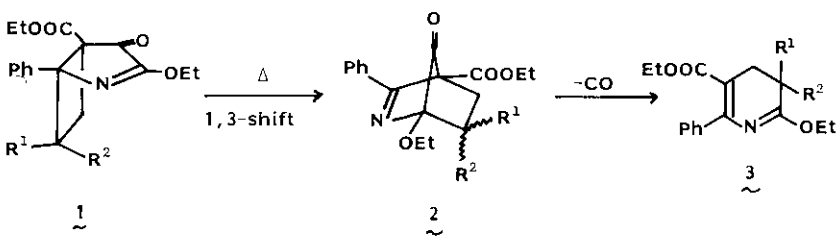
Abstract—— Thermolysis of 2-azabicyclo[3.2.0]hept-2-enes caused azonia 1,3-shift in non-stereospecific manner to give 2-azanorborn-2-enes. This rearrangement reaction was greatly affected by the stereochemistry of the substituent at the migrating center.

Previously we showed that the imidic esters 1, on thermolysis, afforded dihydropyridines 3, and suggested that the reaction proceeded in a thermal (azonia) 1,3-shift followed by a cheletropic elimination of CO from the intermediary 2-azanorborn-2-en-7-one 2 (Chart 1).[2] This paper concerns with the isolation of the intermediate, 2-azanorborn-2-ene which is the compound of very few precedents.[3]

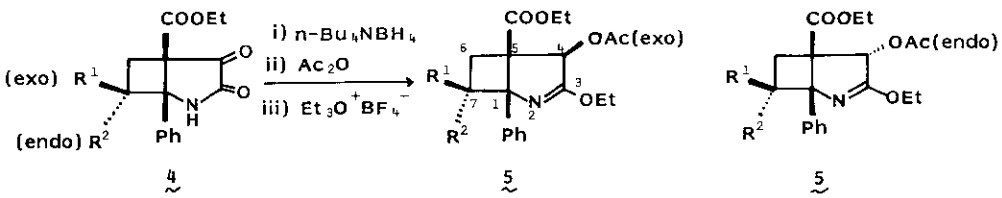


1 2 3

Chart 1

To avoid cheletropic loss of CO from the intermediate, we chose 4-acetoxy derivatives 5 as the subustrates which were prepared from 2-azabicyclo[3.2.0] heptane-3,4-diones 4[4] by hydride reduction, acetylation, and imidation.[5]

Stereochemistry of the 4-acetoxy group of the resulting product was elucidated on the basis of γ-effect[6] in ^{13}C-NMR spectrum. The 4-endo-acetoxy isomer (such as 5b) always gave the C_6-signal at higher field and the 4-exo-acetoxy isomer (such as 5a) gave that signal at lower field than that of the corresponding 4-oxo derivative (such as 4; R^1=Ph, R^2=H), respectively.



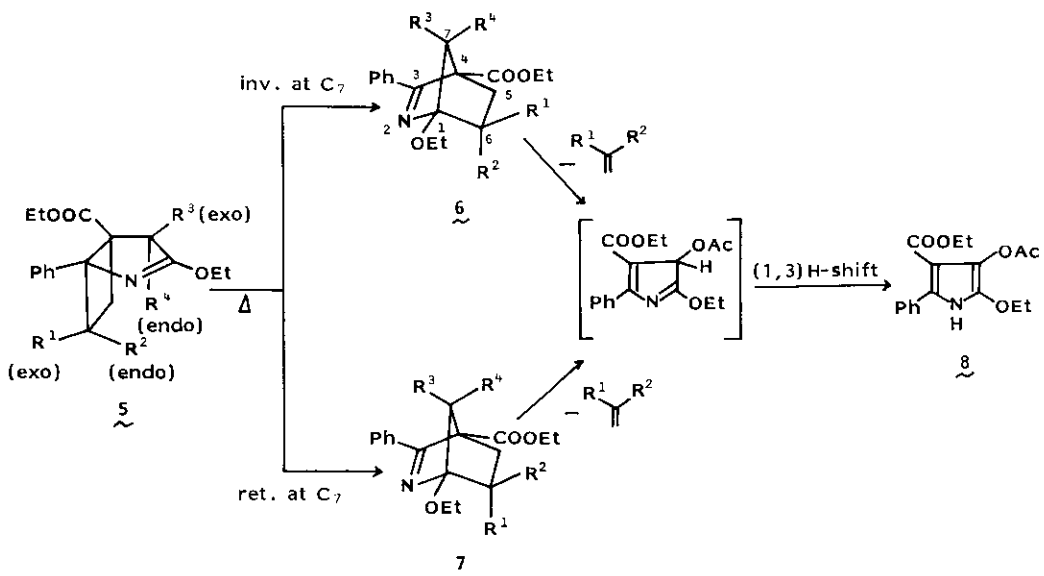
4 5 5

(a, d, g, h, i, j,) (b, c, e, f, k, l, m)

structures see Table 1

Chart 2

Heating of the 4-exo-acetoxy-7-exo-phenyl derivative 5a in toluene at 160°C for 8 h yielded two 2-azanorborn-2-enes 6a, mp 119-120°C and 7a, mp 116-118°C in 29 and 23% yields, together with the pyrrole 8, mp 126-130°C (λmax 304 nm) in 1% yield (Chart 3). The structures of 6a and 7a account well for their UV (λmax 240 nm, Ph-C=N-) and the other spectroscopic data. The stereochemistry of 6-phenyl group in each product was established as shown in Chart 4 by analyses of their ^{1}H-NMR spectra comparing with those of 5-endo-deuterium labelled compounds 10 and 11 which were prepared

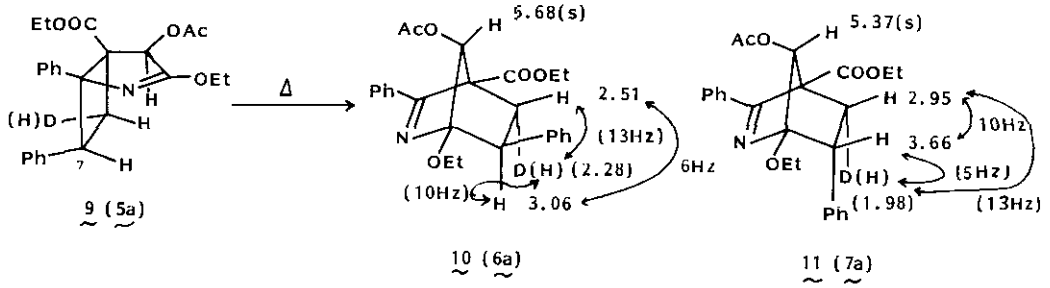


5 6 7 8

Chart 3

by a similar thermolysis of the 6-exo-deuterium-7-exo-phenyl derivative 9.[7] Thus, 6a is the 1,3-shift product with inversion of configuration at the migrating center (C_7) and 7a is the product with retention of configuration at C_7. The pyrrole 8 should be the product of retro-Diels-Alder reaction of 6a and 7a, since on pyrolysis of a mixture of 6a and 7a at 300°C for 2 h, it was produced quantitatively.[8]

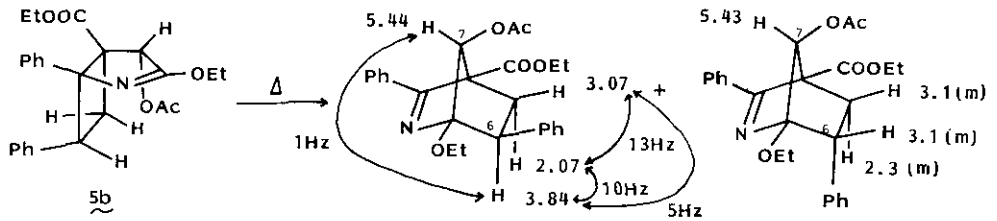
Thermolysis of the 4-endo-acetoxy isomer 5b, though required higher temperature (180°C for 8 h), similarly gave 2-azanorborn-2-enes, 6b and 7b, and the pyrrole 8 in 24, 47 and 1% yields, respectively. Presence of a long range coupling (1 Hz) between C_7-syn-H and C_6-endo-H in 6b established its stereochemistry at C_6 as 6-exo-phenyl configuration. Therefore 6b is the product of C_7-inversion and 7b is that of C_7-retention.



9 (5a)

10 (6a)

11 (7a)



5b

6b

7b

Chart 4

On the other hand, the 7-endo-phenyl-4-endo-acetoxy isomer 5c was stable under the similar condition. It decomposed only at 300°C. The only isolable product, pyrrole 8 (21%), again suggested the intermediary formation of the 2-azanorborn-2-ene under the forced condition.

Thermolysis of both the 4-exo and 4-endo isomers of the 7-exo-phenyl-7-endo-methyl derivative (5d and 5e) again required forced conditions (180°C, 3 h for 5d and 180°C, 18 h for 5e), and yielded a single 2-azanorborn-2-ene, 7d and 7e, in 30 and 25% yield together with the pyrrole 8 in 35 and 30% yield, respectively.

Table 1 Thermolysis of 2-Azabicyclo[3.2.0]hept-2-enes 5

	Azabicycloheptenes 5						Product (Yield, %) 2-Azanorbornenes		pyrrole	others
	R^1	R^2	R^3	R^4	Temp.(°C)	Time(h)	6(inv.)	7(ret.)	8	
a	Ph	H	OAc	H	160	8	29	23	1	—
b	Ph	H	H	OAc	180	8	24	47	1	—
c	H	Ph	H	OAc	300	5.5	—	—	21	—
d	Ph	Me	OAc	H	180	3	—	30[c]	35	—
					200	4	—	—	96	—
e	Ph	Me	H	OAc	180	18	—	25[c]	30	33[a]
					200	15	—	—	63	—
f	Me	Ph	H	OAc	250	3.5	—	—	88	—
g		H	OAc	H	180	2	42	36	—	—
h		H	OAc	H	180	1	40	23	—	—
i		H	OAc	H	180	2	39	39	—	—
j		Me	OAc	H	140[d]	0.3[d]	—	20	—	48[a]
k		Me	H	OAc	180	2	—	—	—	88[b]
l	H	OEt	H	OAc	350	5	—	—	—	80[a]
m	Me	OAc	H	OAc	350	1	—	9[c]	—	67[a]

a: Starting material b: 1,3-Shift product 12

c: Assignment of the stereochemistry at C_6 is tentative.

d: Higher temperature and prolonged reaction gave a complex mixture.

At higher temperature (200°C) the pyrrole 8 was an only isolable product (96% from 5b and 63% from 5e).

The 7-endo-phenyl-7-exo-methyl derivative with the 4-endo-acetoxy group (5f) resisted to the reaction under the similar condition and gave the pyrrole 8 at elevated temperature (250°C).

These and previously reported results[2] are consistent with the Berson's observation[9] that 7-endo-substituent retards the thermal 1,3-shift in bicyclo[3.2.0] heptene system, where the symmetry allowed process (suprafacial 1,3-shift with inversion of configuration at migrating center) becomes difficult to occur for sterical reasons. He concluded that in such cases the reaction proceeds through the symmetry forbidden process (suprafacial 1,3-shift with retention of configuration at migrating center) rather than through the biradical process.

The 7-endo-ethoxy-4-endo-acetoxy compound 5l was thermally stable. It was recovered unchanged (80%) at 350°C for 5 h, in contrast to the 4-oxo-compound 1 (R^1=H, R^2=OEt) which gave the dihydropyridine 3 (R^1=H, R^2=OEt) in 75% yield.[2] The 7-exo-methyl-4,7-endo-diacetoxy derivative 5m gave a rearranged product 7m in only 9% yield with recovery of the starting material (67%), while the 4-oxo-compound 1 (R^1=Me, R^2=OAc) gave the dihydropyridine 3 (R^1=Me, R^2=OAc) in 47% yield.[2] Comparing the present results with those previously obtained for the oxo-compounds[2], it is apparent that sp^3 configuration at C_4 retards the reaction and this retardation is more significant for the 4-endo-acetoxy isomer which apparently has greater steric interaction than that in the 4-exo isomer at the transition state of suprafacial rearrangement.

Thermolysis of the 7-exo-vinyl derivative is supposed to be complicated, since three reactions (paths A, B, and C in Chart 5) which were observed for the 4-oxo-compounds[10] are expected to occur competitively. The 7-exo-vinyl-4-exo-acetoxy derivative 5g, on heating at 180°C, gave the 2-azanorborn-2-enes, 6g and 7g (path A products), in 42 and 36% yield, respectively, whose structures and stereochemistries were elucidated in the same manner as described above. Thermolysis of the 7-exo-(E) and (Z)-propenyl derivatives, 5h and 5i, also exclusively formed the path A products, 6h-i and 7h-i, respectively. Paths B and C were not observed for these compounds.

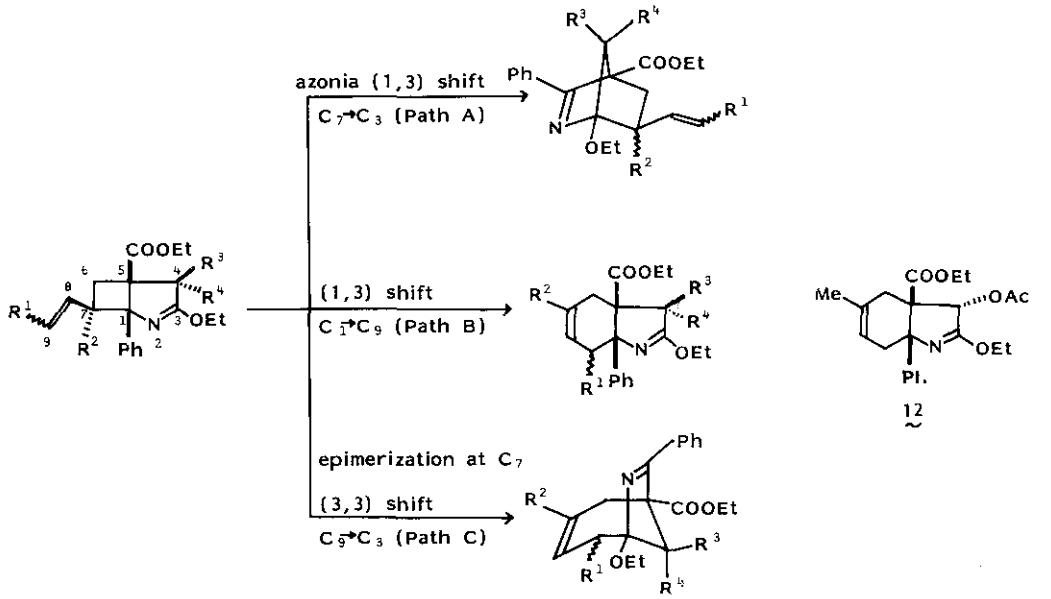


Chart 5

However, thermolytic behavior of two C_4-stereoisomers of the 7-exo-vinyl-7-endo-methyl derivative was remarkably different. The 4-exo-acetoxy isomer 5j gave the azanorborn-2-ene 7j (path A), while the 4-endo-acetoxy isomer 5k gave the hydroindole 12 (path B). The result again confirms that increase of the steric interaction in the transition state retards the path A reaction.

REFERENCE AND NOTES

1) Dioxopyrrolines XXXIII: Part XXXII: Azabicyclo[3.2.0]heptane-3,4-dione (9): T. Sano, J. Toda, K. Yamaguchi, and S. Sakai, Chem. Pharm. Bull., 32, 3258 (1984).

2) T. Sano, Y. Horiguchi, and Y. Tsuda, Heterocycles, 16, 889 (1981).

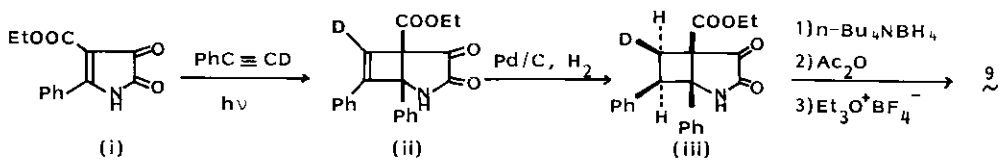
3) 2-Azanorborn-2-enes were previously prepared by intramolecular Diels-Alder reactions of sulfonyl cyanides and cyclopentadiene [J. C. Jagt and A. M. van Leusen, J. Org. Chem., 39, 564 (1974)], and of olefins and pentacyclro-1-azapentadiene [M. E. Jung and J. J. Sharpiro, J. Am. Chem. Soc., 102, 7862 (1980), B. K. Rammash, C. M. Gladstone, and J. L. Wong, J. Org. Chem., 46, 3036 (1981)].

4) T. Sano, Y. Horiguchi, and Y. Tsuda, Heterocycles, 16, 359 (1981).

5) Details will be reported in a full paper.

6) A. P. Marchand, "Stereochemical Applications of NMR Studuies in Rigid Bicyclic System," Berglag Chemie International Inc., Florida, 1982, p59.

7) 9 was prepared via the photocycloaddition of i to deuterated phenylacetylene as follows. Details will be reported elsewhere.



8) This experiment will eliminate the possibility of the direct formation of 8 by the fragmentation of cyclobutane ring in 5a.

9) J. A. Berson, Acc. Chem. Res., 5, 406 (1972).

10) T. Sano, Y. Horiguchi, S. Kambe, J. Toda, J. Taga, and Y. Tsuda, Heterocycles, 16, 893 (1981).

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