

PHYSICO-CHEMICAL STUDY OF INDOLE ALKALOIDS MODELS.
VI. RELATIVE THERMODYNAMIC STABILITY OF ENDO- AND
SEMI-CYCLIC OLEFINS IN THE BICYCLO[2,2,2]OCTANE SYSTEM (1)

G. Van Binst and Y. Merck

Service de Chimie Organique
Faculté des Sciences
Université Libre de Bruxelles

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Many alkaloids contain a semi-cyclic double bond on a 1-azabicyclo[2,2,2]octane system. In order to study the relative stability of such olefins, we have prepared ethylidenebicyclo[2,2,2]octane and 2-ethylbicyclo[2,2,2]oct-2-ene as model compounds and measured the equilibrium constant between them by acid catalysis.

Starting from bicyclo[2,2,2]octanone we obtained in two steps a mixture of ethylidenebicyclo[2,2,2]octane and of 2-ethylbicyclo[2,2,2]oct-2-ene (ratio 57/43) with an overall yield of 69 %.

The olefinic isomers have been separated by gas-liquid chromatography on a SE 30 column. Identification of the pure compounds has been made by I.R. and N.M.R. spectroscopies.

We have isomerised the pure olefins in acid medium in presence of *p*-toluenesulfonic acid as catalyst. Cope and co-workers (2) have observed on monocycloalkenes the formation of tertiary alcohols and acetates as by-products resulting from the addition of water to the double bond. To avoid these side reactions we worked with glacial acetic acid containing 10 % of acetic anhydride.

The equilibria were approached starting from both isomers and equilibrium was considered to be reached when the compositions obtained from both sides did not differ for more than 2 %. The concentrations of the isomerised compounds were measured by gas chromatography after extraction of the bicyclic products with hexane.

In order to verify the response of the flame-ionisation detector (apparatus Aerograph 1525 B) for the two olefins, we injected solutions of known concentrations. A factor of 1.040 was used to correct the ratio of

the surfaces $S_{\text{semi}}/S_{\text{endo}}$ obtained by planimetry.

The results we obtained are summarised in the following table.

Equilibria between 2-ethylbicyclo[2,2,2]oct-2-ene and ethylidenebicyclo[2,2,2]octane :

- from 2-ethylbicyclo[2,2,2]oct-2-ene :

| T (°K) ^a | % endo ^b | % semi ^b | K _{semi/endo} | ln K ^c | ΔF ^o _{endo+semi} ^d (cal/mole) |
|---------------------|---------------------|---------------------|------------------------|-------------------|---|
| 298.18 | 18.18 | 81.82 | 4.501 | 1.504 | -891 |
| 323.18 | 20.33 | 79.67 | 3.919 | 1.366 | -877 |
| 323.18 | 20.30 | 79.70 | 3.926 | 1.368 | -878 |
| 348.18 | 23.40 | 76.60 | 3.274 | 1.186 | -820 |
| 348.18 | 22.90 | 77.10 | 3.367 | 1.214 | -840 |

- from ethylidenebicyclo[2,2,2]octane :

| T (°K) ^a | % endo ^b | % semi ^b | K _{semi/endo} | ln K ^c | ΔF ^o _{endo+semi} ^d (cal/mole) |
|---------------------|---------------------|---------------------|------------------------|-------------------|---|
| 298.18 | 17.78 | 82.22 | 4.624 | 1.531 | -907 |
| 323.18 | 20.06 | 79.94 | 3.986 | 1.383 | -888 |
| 323.18 | 20.53 | 79.47 | 3.871 | 1.354 | -869 |
| 348.18 | 22.82 | 77.18 | 3.382 | 1.218 | -843 |

^a Temperature stabilised within 0.05°. ^b Values corrected.

^c The relative deviation of the concentrations being 1%, the values of ln K are known within 0.046.

^d Values obtained using $\Delta F^{\circ}_{\text{endo+semi}} = -R.T.\ln K$ with $R = 1.9865$ cal.mole⁻¹.degree⁻¹.

From our values of ΔF^o we have calculated ΔH^o and ΔS^o :

$$\Delta H^{\circ}_{\text{endo+semi}} = -1304 \pm 32 \text{ cal/mole}$$

$$\Delta S^{\circ}_{\text{endo+semi}} = -1.3 \pm 0.1 \text{ e.u.}$$

In conclusion, it is established that in the bicyclo[2,2,2]-octane system a semi-cyclic double bond is thermodynamically more stable compared to an endocyclic double bond.

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