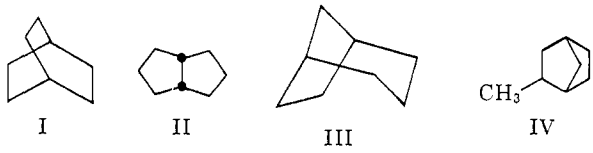
PREDOMINANT IMPORTANCE OF ENTROPY ON RELATIVE STABILITIES OF BICYCLOÖCTANE ISOMERS

Sir:

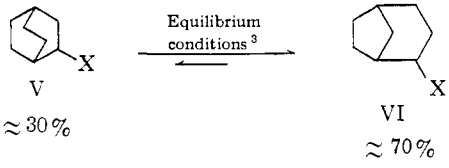
Aluminum bromide converts C_8H_{14} bicyclic hydrocarbons to their three most stable saturated isomers: bicyclo[2.2.2]octane (I), *cis*-bicyclo[3.3.0]octane (II) and bicyclo[3.2.1]octane (III). *Entropy* rather than enthalpy differences are shown here to have decisive importance on the relative stabilities of these compounds.



Barrett and Linstead[1] reported that II was largely rearranged into III with $AlCl_3$; heat of combustion measurements established that *trans*-bicyclo[3.3.0]-octane was 6 kcal./mole less stable than the *cis* isomer II. The same catalyst was said to transform the 2-methylnorbornane stereoisomers IV into III at 75°, but no mention was made of the possible presence of I or II in the product.[2]

In recent years numerous reports of the interconversion of simple monofunctional derivatives of I–IV by carbonium ion processes have appeared,[3–6] but there have been no quantitative investigations of the relative stabilities of these ring systems. Such information, which we supply in the present report, is needed for a better understanding of rearrangements involving these systems. The rigidity of I and III further makes them ideal for testing predictions of quantitative conformational analysis.

Recent experiments under thermodynamic conditions have confirmed the generally held belief that derivatives VI are more stable than V; an approximate $-\Delta F$ of isomerization of 0.5 kcal./mole can be estimated from data of Goering and Sloan.[3] Because of heightened ring strain, norbornane derivatives are much less stable than ring expanded products, but it is not clear from the available literature[1,6] whether derivatives of II or of III are the more stable.



Compounds I–IV were equilibrated with aluminum bromide at various temperatures in the 23–72° range and the product compositions determined by capillary gas chromatography (Table I).[7] Moderate quantities of methylnorbornanes and fragmentation products also were present (these will be discussed in the full paper), but *trans*-bicyclo[3.3.0]octane could not be detected. From the composition data (Table I) the free energies, enthalpies and entropies of isomerization were calculated for each pair of isomers (Table II).[7]

TABLE I

RELATIVE EQUILIBRIUM CONCENTRATIONS OF BICYCLOÖCTANE ISOMERS

Temp., °K.	Percentage composition: Bicyclo[2.2.2]-octane, I	*cis*-Bicyclo-[3.3.0]octane, II	Bicyclo[3.2.1]-octane, III
296.8	3.66	32.95	63.35
317.4	3.41	37.20	59.35
321.8	3.36	37.85	58.78
331.7	3.33	39.78	56.86
345.4	3.11	42.34	54.50

TABLE II

THERMODYNAMIC VALUES FOR BICYCLOÖCTANE ISOMERIZATIONS

Reactant	Product	ΔF^{298} (kcal./mole)	ΔH (kcal./mole)	ΔS^{298} (e.u.)
I	II	-1.31 ± 0.10	$+1.94 \pm 0.45$	$+10.9 \pm 1.6$
II	III	-0.38 ± 0.06	-1.89 ± 0.25	-5.0 ± 0.8
I	III	-1.69 ± 0.12	$+0.06 \pm 0.45$	$+5.5 \pm 2.5$

For the temperatures investigated, the stability order was III > II > I. An analysis of the thermodynamic data (Table II) is highly interesting. The enthalpy difference between bicyclo[2.2.2]octane (I) and bicyclo[3.2.1]octane (III) is indistinguishable from zero; *the considerably greater stability of III over I is due entirely to more favorable entropy.* Both I and III are less strained than *cis*-bicyclo[3.3.0]octane (II) by a substantial amount, $\Delta H = -1.9$ kcal./mole, but this is counterbalanced by the very high entropy of II; in fact, above 378°K. II should be the most stable of the three isomers.

The major source of strain in bicyclo[2.2.2]octane (I) is torsional; three eclipsed ethane interactions yield an estimate of $2.8 \times 3 = 8.4$ kcal./mole strain for this molecule. Cyclopentane is known to be strained to the extent of 6.3 kcal./mole.[8] The five-membered ring in bicyclo[3.2.1]octane (III) is distorted further by valency requirements. It is not hard to understand why the total strain in III due to angular and torsional deviations and to non-bonded repulsions should equal the total strain in I. *cis*-Bicyclo[3.3.0]octane possesses eight cyclopentanoid carbons, each strained roughly to the extent of $6.3/5 = 1.26$ kcal. The total strain in II, estimated in this crude way, is $1.26 \times 8 = 10.1$ kcal./mole or 1.7 kcal./mole greater than that estimated for I. This difference is in good agreement with the experimentally determined heat of isomerization of I to II, 1.9 kcal./mole.[9]

The high entropy of II must be associated with the extreme flexibility of the *cis* ring juncture, as noted for other fused-ring bicyclic compounds,[10] and with the many possible cyclopentane conformations of equal energy.[8,9] The entropy differences between the much more rigid isomers I and III appear to be due primarily to symmetry considerations.[8] If bicyclo[2.2.2]octane (I) possesses D_{3h} symmetry,[11] it then has a symmetry number of six. The entropy of I should therefore be lowered by $R \ln 6$, or 3.6 e.u.[8] Since III has a sym-

(1) J. W. Barrett and R. P. Linstead, *J. Chem. Soc.*, 611 (1936).

(2) M. B. Turova-Polyak, I. E. Sosnina, I. G. Golutvina and T. P. Yudkina, *Zh. Obshch. Khim.*, **29**, 1078 (1959); *Chem. Abstr.*, **54**, 1356 (1960).

(3) A good summary of the somewhat conflicting earlier literature on I–III derivative interconversions has been given by H. L. Goering and M. F. Sloan, *J. Am. Chem. Soc.*, **83**, 1397 (1961); in addition, see ref. 4.

(4) H. L. Goering and M. F. Sloan, *ibid.*, **83**, 1992 (1961); H. M. Walborsky, M. E. Baum and A. A. Youssef, *ibid.*, **83**, 988 (1961); A. F. Bickel, J. Knotnerus, E. C. Kooyman and G. C. Vegter, *Tetrahedron*, **9**, 230 (1960).

(5) Ring expansion of norbornane systems: K. Alder and R. Reubke, *Ber.*, **91**, 1525 (1958); J. A. Berson and D. Willner, *J. Am. Chem. Soc.*, **84**, 675 (1962); J. A. Berson and P. Reynolds-Warnhoff, *ibid.*, **84**, 682 (1962); R. R. Sauers and R. J. Tucker, *J. Org. Chem.*, **28**, 876 (1963), and earlier references therein cited.

(6) Interconversions of bicyclo[3.3.0]octyl and bicyclo[3.2.1]octyl systems: A. C. Cope, J. M. Grisar and P. E. Peterson, *J. Am. Chem. Soc.*, **82**, 4299 (1960), and C. S. Foote, Ph.D. Thesis, Harvard University, 1961.

(7) The general procedure used has been described in detail; K. R. Blanchard and P. von R. Schleyer, *J. Org. Chem.*, **28**, 247 (1963).

(8) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962; also see K. S. Pitzer and W. E. Donath, *J. Am. Chem. Soc.*, **81**, 3213 (1959).

(9) Computer calculations of the strain present in bicycloöctane isomers are in progress, J. B. Hendrickson, personal communication. See J. B. Hendrickson, *ibid.*, **83**, 4537 (1961); **84**, 3355 (1962).

(10) N. L. Allinger, *J. Org. Chem.*, **21**, 915 (1956); N. L. Allinger and J. L. Coke, *J. Am. Chem. Soc.*, **81**, 4080 (1959); **82**, 2553 (1960).

(11) For a literature summary and a discussion, see P. von R. Schleyer and R. D. Nicholas, *ibid.*, **83**, 2700 (1961), especially J. J. MacFarlane and I. G. Ross, *J. Chem. Soc.*, 4169 (1960).

metry number of one, there is no symmetry effect of its entropy and $\Delta S_{I \rightarrow III}$ should be +3.6 e.u., a value in approximate agreement with that found experimentally (Table II). The high symmetry of I is destroyed in its derivatives, such as V, and such derivatives should be favored to a greater extent than the parent hydrocarbon, I, in equilibration processes, *e.g.*, V with VI.[3]

It is novel to find that the course of some organic reactions can be governed largely by symmetry and entropy factors.

Acknowledgment.—The gas chromatography apparatus was purchased with a Grant-In-Aid from the FMC Corporation.

(12) Alfred P. Sloan Research Fellow.
(13) National Science Foundation Predoctoral Fellow.
(14) A. B. Thesis, Princeton University, 1957.

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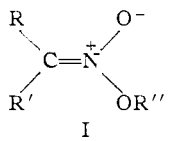
THE SYNTHESIS AND CHARACTERIZATION OF NITRONIC ESTERS

Sir:

Hitherto there has been no generally useful way of synthesizing nitronic esters (I).



I

R, R′ = H, alkyl or aryl
R″ = alkyl

Indeed, those derived from strictly aliphatic nitro compounds are unknown.

We now report a new and general synthesis of nitronic esters which involves treating the salts of nitro compounds with trialkyloxonium fluoroborates[1] at 0°; the reaction is rapid and pure nitronic esters are generally obtained in yields of excess of 90% (*cf.* Table I).

$$RR'CNO_2^-Na^+ + R_3''O^+BF_4^- \longrightarrow I + NaBF_4 + R_2''O$$

TABLE I

NITRONIC ESTERS PREPARED FROM OXONIUM FLUOROBORATES AND NITRO SALTS[a,b]

Nitronic ester	Yield, %
$CH_3CH{=}NO_2CH_3$	90–95
$CH_3CH{=}NO_2C_2H_5$	94
$CH_3CH_2CH{=}NO_2C_2H_5$	79
$CH_3CH_2CH_2CH{=}NO_2C_2H_5$	95
p-Br—C_6H_4—$CH{=}NO_2C_2H_5$	95
p-O_2N—C_6H_4—$CH{=}NO_2C_2H_5$	92
$(CH_3)_2C{=}NO_2C_2H_5$[c]	75–80
CH_3—CH_2—$C(CH_3){=}NO_2C_2H_5$[c]	90–95

[a] All the nitronic esters mentioned in this Communication exhibit intense absorption in the 6.05 to 6.2-μ region. [b] The yields of sodium fluoroborate usually exceed 95%. [c] Prepared at −65 to −60°.

As a typical example: to a stirred, ice-cold, slurry of 3.00 g. (24.0 mmoles) of the dry, finely powdered, sodium salt of 1-nitrobutane in 25 ml. of methylene chloride is rapidly added an ice-cold solution of 4.05 g. (21.8 mmoles) of triethyloxonium fluoroborate in 15 ml. of methylene chloride. After being stirred under nitrogen for 15 min., the mixture is filtered rapidly and the solid washed with 5 ml. of ice-cold, anhydrous ethyl ether. The combined filtrate and wash are rapidly evaporated *in vacuo* to constant volume at *ca.* 5 to 15°. The resulting very pale yellow liquid is subjected to a vacuum of *ca.* 1 mm. for another 5 min. at 25° and stored at −78°; $n^{20}D$ 1.4468; yield 2.72 g. (95%).

Anal. Calcd. for $C_6H_{13}NO_2$: C, 54.94; H, 9.99; N, 10.68. Found: C, 55.16; H, 9.96; N, 11.02.

In principle, nitronic esters in which R ≠ R′ should exist as *cis–trans* isomers; such stereoisomerism, however, has not been reported. By the use of nuclear magnetic resonance (n.m.r.) we have now found that such stereoisomers do indeed exist. Thus, the ethyl nitronic ester obtained from 1-nitrobutane has an n.m.r. spectrum in which *two* "vinyl" hydrogen[2] quartets appear. One quartet (at 6.04 δ)[3] has an area about seven times greater than the area of the second quartet (at 5.75 δ). In the same way, all the nitronic esters in Table I which derive from primary nitro compounds prove to be mixtures of the *cis–trans* isomers in proportions varying from 1:1 to 7:1.

The realization that *cis–trans* isomerism is exhibited by nitronic esters clarifies some otherwise puzzling facts. Thus, the *crude* ethyl nitronic ester obtained from *p*-nitrophenylnitromethane (92% yield) gives good carbon, hydrogen and nitrogen analyses, but it melts over a wide range (82–88°). Recrystallization raises the m.p. to 100–101°, but the analyses remain unchanged. This anomaly is resolved by n.m.r.; the spectrum of the "crude" nitronic ester has *two* "vinyl" hydrogen singlets (at. 7.22 δ and 6.95 δ, in approximately a 4:1 ratio) whereas the recrystallized ester shows only the "vinyl" hydrogen singlet at 7.22 δ. Recrystallization has simply separated the stereoisomers.

Of the nitronic esters thus far prepared from secondary nitro compounds, only the ethyl nitronic ester derived from 2-nitrobutane (*cf.* Table I) is capable of exhibiting *cis–trans* isomerism. Here again clear evidence of stereoisomerism is obtained; *two* singlets (at 1.94 δ and 2.00 δ) due to two different "vinyl" methyl groups are found in the n.m.r. spectrum.

Both stereoisomeric nitronic esters are also produced when diazomethane reacts with *p*-nitrophenylnitromethane and *p*-bromophenylnitromethane.[4] Quantitative yields of the "crude" nitronic esters are obtained, but although analytically pure, these products melt over wide temperature ranges. As before, n.m.r. studies demonstrate that in each instance mixtures of both possible stereoisomers are at hand; and, as before, recrystallization serves to separate the stereoisomers.

Nitronic esters are stable indefinitely at −78°, but at room temperature they decompose relatively rapidly, particularly in the liquid state or in solution. Furthermore, for a given nitronic ester, the stereoisomer which is produced in minor proportion proves to be less stable than the isomer produced in major proportion. Thus, the more stable isomer of the methyl nitronic ester of *p*-nitrophenylnitromethane,[5] in deuteriochloroform solution, has a half-life of 5 days, whereas the less stable isomer has a half-life of only several hours. In general, the ethyl nitronic esters

(1) H. Meerwein, E. Battenberg, H. Gold, E. Pfeil and G. Willfang, *J. prakt. Chem.*, **154**, 83 (1939).

(2) By "vinyl" hydrogen we refer to the hydrogen atom on the unsaturated carbon atom in the compounds listed in Table I.

(3) Chemical shifts from the internal standard, tetramethylsilane, are reported in δ values. The n.m.r. spectra were obtained with a Varian Associates A-60 spectrometer.

(4) F. Arndt and J. D. Rose, *J. Chem. Soc.*, 1 (1935). This reaction is only applicable to nitro compounds which are relatively strong acids. Thus, we have shown that 3-phenyl-1-nitropropane undergoes no reaction whatsoever on treatment with diazomethane even after 5 days.

(5) This is the most stable of the nitronic esters prepared by us. In the crystalline state it only begins to show a lowering of the m.p. after 10 days at room temperature.