would obviously be desirable to confirm this value and to shed further light on the structure.

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Isomerization of Alkylbicyclo[2.2.1]heptanes over Palladium Catalysts

Sir:

Exchange reactions of cycloalkanes with deuterium catalyzed by transition metals, especially palladium, often show substantial amounts of replacement of hydrogen atoms on both faces of the ring in the initial product distributions.[1,2] In appropriate compounds deuterium–hydrogen exchange is associated with racemization at tertiary carbon centers[2] and with *cis–trans* isomerization.[3] Although the mechanisms of these reactions are still controversial, it is widely accepted that interconversion of adsorbed alkyl and alkene intermediates is a general surface reaction (α,β process) which is limited to *cis* elimination and *cis* addition. The α,β process alone cannot therefore explain the observed distributions for deuterium–hydrogen exchange and isomerization in cycloalkanes of ring size C_4–C_7. Two additional processes have been proposed. Process A: olefinic intermediates desorb, turn over, and readsorb, and the α,β process then continues on the other face of the ring; Schrage and Burwell[4] have suggested that the turnover step may occur while the olefinic intermediates are still attached to the metal surface. Process B: π-bonded olefinic intermediates interconvert with π-allyl complexes during which *trans* addition or elimination of hydrogen (or deuterium) to or from one of the terminal carbon atoms of the allylic system may occur.[5]

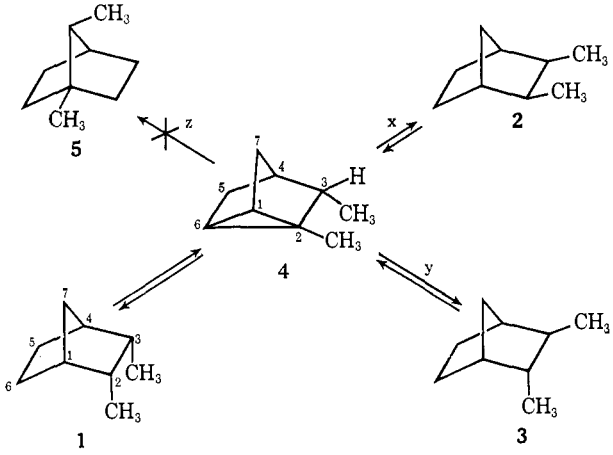
In an effort to distinguish between processes A and B isomerization reactions of di-*endo*-, di-*exo*-, and *exo*,-*endo*-2,3-dimethylbicyclo[2.2.1]heptane (**1–3**) were investigated. Experiments were carried out using a flow system using a large excess of hydrogen and a 2% palladium on silica catalyst.[6] Some results for **1** are given in Table I.

Up to high conversions **2** and **3** are formed from **1** in equal amounts. At the higher temperatures, where equilibrium is approached, **3** largely predominates. In separate experiments it was found that the order of reactivity is **1** > **2** > **3** since comparable reactivity was shown at *ca.* 120, 140, and 180° for the three compounds,

Table I. Isomerization of **1**

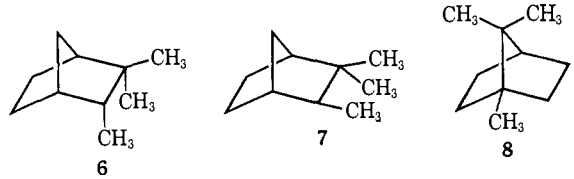
Temp, °C	1, %	2, %	3, %	3/2
116	72	9	9	1.0
126	55	25	20	0.8
135	19	41	40	1.0
146	2	8	90	11.3
162	3	9	88	9.8

respectively. These results cannot be explained by mechanism B, a detailed consideration of which shows that only sequential formation of **2** from **3** is allowed. Process A is also unsatisfactory since it requires the appropriate olefinic intermediates from **2** and **3** to form, turn over, readsorb, and hydrogenate off at nearly equal rates.



An intermediate which can explain the results and also the isomerizations described below is a nortricyclene derivative, such as **4** (2,3-dimethylnortricyclene), which can be formed reversibly from **1** by *trans* elimination–addition of hydrogen at C_2 and C_6. Cleavage of C_1–C_2 by process x and of C_2–C_6 by y with concurrent hydrogen addition gives **2** and **3**, respectively. Cleavage of C_1–C_6 by process z should give 1,7-dimethylnorbornane (**5**), a product not observed at these temperatures (but see below). At this stage details of the mechanism of formation and the nature of the bonding to the surface of intermediates such as **4** are unknown.

A mixture containing 74% of 2-*endo*-3,3-trimethylnorbornane (**6**) and 26% of 2-*exo*-3,3-trimethylnorbornane (**7**) was treated under similar conditions. These structures preclude *endo–exo* isomerization by process B, but again isomerization occurred (see Table II). At higher temperatures 1,7,7-trimethylnorbornane



(**8**) was also formed, together with some products resulting from fragmentation. The formation of **8** is obviously inexplicable in terms of either process A or B but could arise *via* a reaction similar to z from a nortricyclene intermediate similar to **4**. Table III gives results for the isomerization of pure **8** under similar reaction conditions, showing that the above reactions are

(1) J. R. Anderson and C. Kemball, *Proc. Roy. Soc., Ser. A*, 223, 361 (1954).
(2) R. L. Burwell, Jr., B. K. S. Shim, and H. C. Rowlinson, *J. Amer. Chem. Soc.*, 79, 5142 (1957).
(3) F. G. Gault, J. J. Rooney, and C. Kemball, *J. Catal.*, 1, 255 (1962).
(4) K. Schrage and R. L. Burwell, Jr., *J. Amer. Chem. Soc.*, 88, 4555 (1966).
(5) J. J. Rooney, *J. Catal.*, 2, 53 (1963).
(6) Silica (Whatman chromatographic silica, 60–80 mesh) alone did not catalyze isomerization. Separate experiments employing palladium films in a static system showed the metal was responsible for reaction.

Table II. Isomerization of **6** and **7**

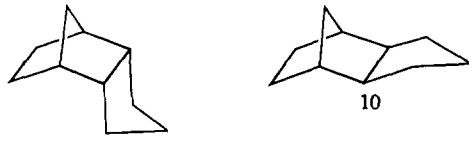
Temp, °C	6, %	7, %	8, %	Other products, %
222	47	53		
274	34	41	11	14
306	20	22	17	41

Table III. Isomerization of **8**

Temp, °C	6, %	7, %	8, %	Other products, %
278	1	2	97	
306	2	4	96	
324	5	8	71	16

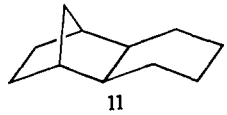
reversible. Again fragmentation predominates at higher temperatures.

Isomerization of di-*endo*-trimethylenenorbornane (**9**) into the di-*exo* isomer **10** was detected at 100° and was entirely selective at high conversions (≥90%) between 200 and 350°.[7] Isomerization of di-*exo*-tetramethylenenorbornane (**11**) to its *endo* isomer occurred at lower temperatures, but at 250° dehydrogenation became significant, and virtually complete conversion into benznorbornene (**12**) was recorded at 360°. Catalysts which had been deliberately contaminated with carbonaceous residues largely retained their activity for the dehydrogenation of **11** but showed greatly reduced isomerization activity, *e.g.*, of **9**. Normal isomerization activity was restored by heating the poisoned catalyst in oxygen at 430°, followed by hydrogen at 300°. Dehydrogenation of **11** must involve alkene- and alkenyl-type intermediates so the clear dichotomy of activity described above indicates that such species cannot account for the isomerization reactions.

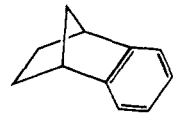


9

10



11



12

A further example of a reaction which can readily be explained by a cyclopropane intermediate, but not by any of the existing mechanisms, is the interconversion of bicyclo[3.2.2]nonane (**13**) and bicyclo[3.3.1]nonane (**14**) which we find to occur over palladium at 200° or above.

In summary, some of the above rearrangements can be explained by a combination of the previously proposed mechanisms A and B. However, all the rearrangements can be explained in terms of cyclopropyl intermediates analogous to **4**. Previous mechanisms cannot explain the interconversions of **6**, **7**, and **8**; of **13** and **14**; or the simultaneous formation of **2** and **3** from **1** in equal amounts. Our proposed mechanism for this latter result parallels the formation of equal amounts of *cis*- and *trans*-9-methyldecalins when tricyclo[4.4.1.0]undecane is hydrogenolyzed over a platinum catalyst.[8]

(7) This isomerization constitutes a very convenient method for the preparation of **10**. We have also found that **10** when treated with aluminum chloride gives adamantane in yields superior to those obtained from the *endo* isomer **9**: H. Hamill, unpublished observations; *cf.* R. C. Fort, Jr., and P. v. R. Schleyer, *Chem. Rev.*, **64**, 277 (1964).

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(8) Z. Majerski and P. v. R. Schleyer, *Tetrahedron Lett.*, 6195 (1968).

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Kinetic Analysis of the Action of Pancreatic Lipase on Lipid Monolayers[1]

Sir:

Pancreatic lipase catalyzes the hydrolysis of fatty acid esters of glycerol and of other simple alcohols.[2] While the enzyme acts readily on emulsions of lipids (the state of dispersion of lipase substrates under physiological conditions), it is by no means clear whether phase heterogeneity is a necessary requirement for enzymatic catalysis.[3] Even if the action of the enzyme were limited to interphase layers, the use of emulsions for mechanistic studies would present several theoretical and experimental difficulties: emulsions contain extraneous material of often ill-defined composition (*e.g.*, gum arabic), and cannot be prepared in reproducible fashion with homogeneous particle size. Furthermore, different substrates yield emulsions of different particle size and composition and the presence of a large lipid phase renders the substrate concentration available to the enzyme at any given time difficult to evaluate. Finally, the possible mechanistic role of the emulsifier, its interaction with the enzyme and the substrate, and its possible effect on transport across the phase boundaries are rather difficult to assess.

In contrast to emulsions, insoluble surface monolayers of substrate molecules would provide a system more amenable to quantitative experimentation. Stable homogeneous monolayers can be prepared with exceedingly small amounts of substrate esters, without the addition of any extraneous material. The surface concentration of the substrate and its change during the reaction can be evaluated accurately and with high sensitivity by monitoring changes in surface pressure. Finally, use of insoluble substrate monolayers automatically defines the site of the reaction at the interface. For nonenzymatic reactions at monolayers, detailed kinetic analyses have been carried out,[4] and semiquantitative studies indicate the feasibility of such an approach for phospholipase catalyzed reactions.[5] We

(1) This research was supported by grants from the U.S. Public Health Service, Medical Research Grants No. GM 13863 and GM 13885.

(2) P. Desnuelle, *Advan. Enzymol. Relat. Subj. Biochem.*, **23**, 129 (1961).

(3) (a) R. G. H. Morgan, J. Barrowman, H. Filipek-Wender, and B. Borgstrom, *Biochem. Biophys. Acta*, **167**, 355 (1968); (b) B. Entressangles and P. Desnuelle, *ibid.*, **159**, 285 (1968).

(4) G. L. Gaines, Jr., "Insoluble Monolayers at Liquid-Gas Interfaces," Interscience Publishers, New York, N. Y., 1966.

(5) (a) D. O. Shah and J. H. Schulman, *J. Colloid Interface Sci.*, **25**, 107 (1967); (b) R. H. Quarles and R. M. C. Dawson, *Biochem. J.*, **113**, 697 (1969); (c) G. Colacicco and M. M. Rapport, *J. Lipid Res.*, **7**, 258 (1966); R. M. C. Dawson, *Methods Enzymol.*, **14**, 633 (1969).