lar rate constant, k_{esr}, is $(1.2 \pm 0.2) \times 10^4\ M^{-1}\ sec^{-1}$.[9] At $-135°$, k_{esr} is $(3 \pm 1) \times 10^3\ M^{-1}\ sec^{-1}$. The results over the entire temperature range give $k_{esr} = 10^{(5\pm1)} \exp[(-1000 \pm 500)/RT]\ M^{-1}\ sec^{-1}$.

Tertiary peroxy radicals exist in a reversible equilibrium with dimeric tetroxide below ~−90°. Dialkylnitroxides have never been reported to form dimers[10] and, in fact, we have used 2,2,6,6-tetramethylpiperidonenitroxide to calibrate radical concentrations at temperatures as low as −160° without seeing any evidence for dimer formation. However, perhaps because of decreased steric hindrance, diethylnitroxide does form a dimer in CF_2Cl_2 (and also in isopentane). The dimer was identified by the fact that the nitroxide concentration could be increased and decreased by raising and lowering the temperature in the range −100 to −145°. Because the irreversible decomposition of the nitroxide is quite rapid even at these low temperatures it is not possible to form very much of the dimer–nitroxide equilibrium mixture. That is, high concentrations of nitroxide decrease by irreversible decay up to the point where this rate is small compared with the length of an experiment. It is this "residual" nitroxide concentration, maximum $\sim 2 \times 10^{-6}\ M$, which is in equilibrium with a "residual" concentration of dimer (eq 1). The

$$2(CH_3CH_2)_2NO\cdot \rightleftharpoons \{(CH_3CH_2)_2NO\}_2 \qquad (1)$$

equilibrium constant is given by

$$K_1 = \frac{k_{-1}}{k_1} = \frac{[(CH_3CH_2)_2NO\cdot]^2}{[\{(CH_3CH_2)_2NO\}_2]} = \frac{2[(CH_3CH_2)_2NO\cdot]^2}{[(CH_3CH_2)_2NO\cdot]_{max} - [(CH_3CH_2)_2NO\cdot]}$$

where $[(CH_3CH_2)_2NO\cdot]_{max}$ is the radical concentration at complete dissociation. The variation in the equilibrium constant with temperature can be represented by the van't Hoff relation

$$K_1 = e^{\Delta S_1/R} e^{-\Delta H_1/RT}$$

where ΔS is the change in entropy and ΔH the change in enthalpy. The variation in the nitroxide concentration with temperature gave $\Delta H = 8.5 \pm 0.5$ kcal/mol and $\Delta S = 32 \pm 4$ gibbs/mol at 1 mol/l. standard state. These values are remarkably similar to those we found previously for the tertiary peroxy radical–tetroxide equilibria, *viz.*,[5] $\Delta H = 9.0$ kcal/mol, $\Delta S = 33$ gibbs/mol.[13]

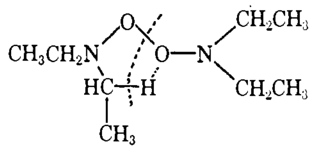
Although our data could be interpreted by a reaction scheme in which the dimer has no direct bearing on the overall reaction, *i.e.*

$$\{(CH_3CH_2)_2NO\}_2 \underset{-1}{\overset{1}{\rightleftharpoons}} 2(CH_3CH_2)_2NO\cdot \xrightarrow{2} (CH_3CH_2)_2NOH + CH_3CH{=}N(O)CH_2CH_3$$

it is difficult to believe that reaction 2, a hydrogen atom abstraction, could occur almost without activation energy and with a preexponential factor as low as 10^5 (*cf.* ref 14). We therefore prefer to represent the reaction as

$$2(CH_3CH_2)_2NO\cdot \underset{-1}{\overset{1}{\rightleftharpoons}} \{(CH_3CH_2)_2NO\}_2 \xrightarrow{3} (CH_3CH_2)_2NOH + CH_3CH{=}N(O)CH_2CH_3$$

with the measured decay rate constant $k_{esr} = k_3/K_1$, from which we obtain $k_3 = 10^{12} \exp(-9500/RT)\ sec^{-1}$. The preexponential factor for reaction 3 is within the range generally found for unimolecular decompositions proceeding by five- or six-center cyclic transition states.[14] Assuming the dimer is formed by head-to-head coupling of the nitroxide radicals[15] the transition state might be represented as



The measured entropy change accompanying step 1 is 32 gibbs/mol. The entropy loss accompanying the formation of the cyclic transition state will be that due to the loss from three hindered internal rotors at −3.6 gibbs/mol per rotor[14,16] plus a symmetry contribution of $R \ln 8$ since any of eight equivalent hydrogens may be transferred. That is, $\Delta S_3^{\ddagger} = 3(-3.6) + R \ln 8 = -10.8 + 4.2 = -6.6$ gibbs/mol. The preexponential factor for the overall decay can be estimated as $A_{esr} = (ekT/h)(10^{-6.6/2.3R}/10^{32/2.3R}) = 10^{4.6}\ M^{-1}\ sec^{-1}$ at the mean temperature of the experiments (220°K). This value is in gratifying agreement with the value found by direct measurement.

In conclusion, the present results indicate that diethylnitroxide radicals react reversibly with one another to form a dimer which can decompose *via* a cyclic transition state. The overall process is closely analogous to that proposed by Russell for secondary peroxy radicals.[17]

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[9] The room-temperature rate constant decreases by almost two orders of magnitude with increasing solvent polarity along the series isopentane > benzene > CF_2Cl_2 > methanol > H_2O. The N and H splittings increase along this series.

[10] Potassium nitrosodisulfonate ($(KSO_3)_2NO$, Fremy salt) is diamagnetic in the solid state[11] and bis(trifluoromethyl)nitroxide ($(CF_3)_2NO\cdot$) gives a diamagnetic solid at −160°.[12]

[11] A. R. Forrester, J. M. Hay, and R. H. Thomson, "Organic Chemistry of Stable Free Radicals," Academic Press, New York, N. Y., 1968, p 192.

[12] Reference 11, p 199.

[13] The calculated entropy change for this equilibria at 150°K is 30.4 gibbs/mol at 1 mol/l. standard state (S. W. Benson, private communication).

[14] S. W. Benson, "Thermochemical Kinetics," John Wiley & Sons, Inc., New York, N. Y., 1968.

[15] An analogous five-center structure can be drawn for $Et_2N(O)\cdot N(O)Et_2$ and either a four- or six-center structure for $Et_2NON(O)Et_2$.

[16] H. E. O'Neal and S. W. Benson, private communication.

[17] G. A. Russell, *J. Amer. Chem. Soc.*, 79, 3871 (1957).

Free Radical Epimerization at Unactivated Tertiary Carbon Atoms in Cyclohexane Derivatives

Sir:

We have recently reported[1] a new method for epimerization at unactivated tertiary carbon atoms in saturated cyclopentane derivatives by irradiation in the presence of mercuric bromide or N-bromosuccinimide in hydrocarbon solution. We have now extended this method to unactivated teritary carbon atoms in saturated cyclohexane systems.

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[1] M. Gorodetsky and Y. Mazur, *J. Amer. Chem. Soc.*, **90**, 6540 (1968).

The experimental procedure involves irradiation with an external uv source (Phillips germicidal lamps, emitting mainly at 254 nm) of a *ca.* 0.05 *M* cyclohexane solution[2] of the compound to which 1 equiv of mercuric bromide (only partly soluble) has been added, in evacuated and sealed quartz vessels at *ca.* 40°. The products were isolated by glpc or by other conventional methods.

It was found that saturated steroids in which hydrogen atoms are present at both *trans*-hydrindan and *cis*-decalin ring junctions such as **1a**[1] or **2a** epimerize preferentially at the former junction under the above specified conditions to give, after 12 hr, an equilibrium mixture consisting in each case of *ca.* 95% of the 5β,14β derivative (**1b**[1] or **2b**), and *ca.* 5% of the unchanged 5β,14α steroid (**1a** or **2a**). We could also observe the formation of small amounts of another epimer, the 5α,14β isomer (**1c** or **2c**, respectively). Irradiation for longer periods led to increasing amounts of the latter compounds possessing the *trans*-decalin ring junction; after 96 hr **1a** resulted in the formation of 10% of **1c** and in the case of **2a** 70% of **2c** was formed after the same period.

The 5β-*D*-homosteroid **3a**[3] was similarly observed to invert partially at the *cis*-decalin junction, yielding 25% of its 5α-isomer **3b** after irradiation for 90 hr. On the other hand, the axial 4β-methyl group in **4a** isomerized quantitatively to the equatorial 4α-position, concurrently with the expected epimerization at C-14, to give the thermodynamically more stable 4α-methyl-14β-steroid **4b**, after 12 hr.

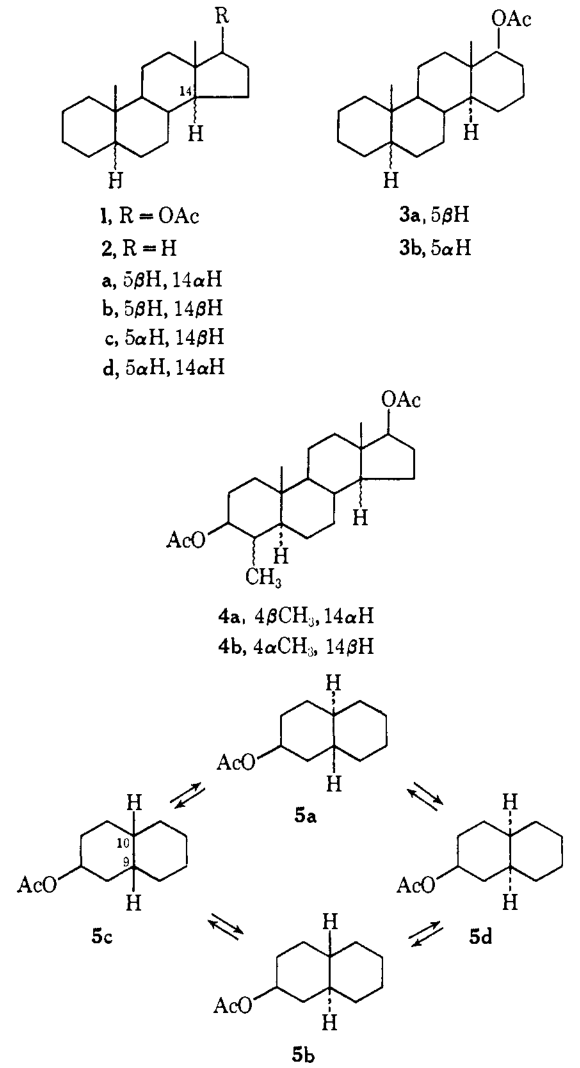
This method of epimerization at ambient temperature proved to be a general one through its application, among others, to mono- and bicyclic six-membered ring systems. Thus, *cis*- and *trans*-1,2-dimethylcyclohexanes gave, after irradiation at 42° for 12 hr, an identical mixture of both isomers in a ratio of 10.1:89.9, respectively. This equilibrium ratio corresponds to a free-energy difference of $\Delta G_{42}° = 1.38 \pm 0.05$ kcal/mol, which is in accord with the reported values.[4]

Under the same conditions, the *cis* and *trans* isomers of both 1,3- and 1,4-dimethylcyclohexane were converted to equilibrium mixtures consisting, in the former case, of 90.6:9.4 and, in the latter, of 9.9:90.1 *cis*:*trans* ratios, corresponding to $\Delta G_{42}° = -1.43$ and 1.39 ± 0.05 kcal/mol, respectively. For *cis*- and *trans*-decalin longer irradiation periods (90 hr) were necessary in order to reach equilibrium; the ratio of *cis*:*trans* epimers was found to be 1:99 corresponding to a $\Delta G_{42}°$ value of 2.9 ± 0.5 kcal/mol.[4]

Participation of the solvent in these reactions was proved by irradiation of the 14α-derivative **1d** in perdeuterated cyclohexane which resulted in the incorporation of one and two deuterium atoms, in 55 and 12%, respectively, into the isolated 14β-epimer **1c**.

The fact that hydrogen atoms α to the acetoxy groups do not participate in the epimerization reactions was shown by the full retention of the deuterium labeling in the irradiation product **1c** (**17**α-*D*) of the 14α-derivative **1d** (**17**α-*D*). Analogously, irradiation of each of the four isomers of 2-acetoxydecalin (**5**), in the presence of mercuric bromide, induced epimerization at the tertiary positions C-9 and C-10 only, as shown in Scheme I; each of the *cis*-isomers **5c** and **5d** was converted into a mixture of the *trans*-isomers **5a** and **5b**, while *trans*-compounds **5a** and **5b** interconverted only partly even after prolonged irradiation time.

Scheme I



However, acetoxy derivatives of methylcyclohexanes undergo equilibration under the same conditions. Thus both *cis*- and *trans*-1,4-acetoxymethylcyclohexane, when irradiated for 90 hr, gave the same 30:70 *cis*–*trans* mixture, corresponding to a $\Delta G_{42}° = 0.53 \pm 0.1$ kcal mol.[5]

Comparison of the initial rates of epimerization of the compounds studied reveals that the epimerization at a tertiary methyl group attached to a cyclohexane ring is much faster than at the ring junction in a decalin system and also that substitution by an acetoxy group in cyclohexanes, decalins, and steroids decreases the rates of epimerization.

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(2) Cyclohexane, BDH special for spectroscopy, was purified by spinning band column distillation in the presence of *ca.* 5% trimethyl borate. The fraction boiling at 81° was washed with water, dried over calcium chloride, and redistilled.

(3) Satisfactory analyses and ir, nmr, and mass spectra were obtained for all new compounds reported.

(4) For results of other methods of equilibrations *cf.* E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," John Wiley & Sons, Inc., New York, N. Y., 1965, pp 58–62, 231.

(5) The value of 0.7 kcal/mol was calculated from nmr measurements at room temperature by E. L. Eliel and M. H. Gianni, *Tetrahedron Lett.*, 97 (1962).

Acknowledgment. This work was supported by a grant of the Ministry of Commerce and Industry of Israel.

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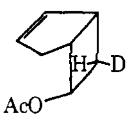
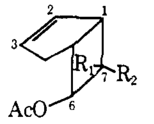
Steric Prohibition of the Inversion Pathway. A Test of the Orbital Symmetry Prediction of the Sense of Rotation in Thermal Suprafacial 1,3-Sigmatropic Rearrangements[1]

Sir:

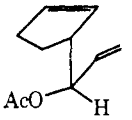
Inversion of configuration of the migrating group occurs in thermal suprafacial 1,3-sigmatropic rearrangements of bicyclo[3.2.0]hept-2-enes when the *exo* substituent is deuterium (**1**)[2,3] or methyl (**2**).[4] If this is a consequence of special stabilization of the transition state in an "allowed" concerted process,[2-5] the interchange of the C-7 methyl and hydrogen of reactant **2** (Scheme I) logically should produce drastic changes in behavior.



1



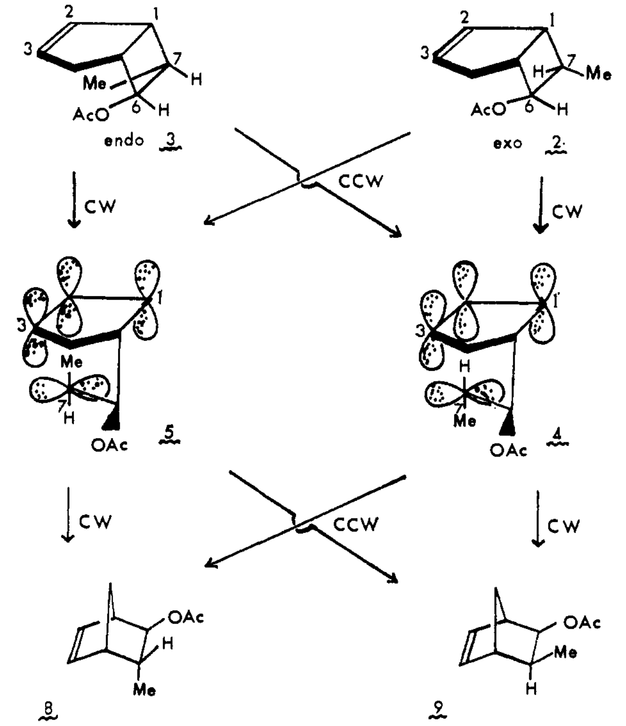
2, $R_1 = H$, $R_2 = Me$
3, $R_1 = Me$, $R_2 = H$



6

In the transition states (or intermediates) for inversion (**4** and **5**), the migrating group and its substituents would lie in a plane (or approximately so) that is perpendicular to the plane of the five-membered ring containing the allyl system. This would produce severe steric repulsion, especially in the array **5**, where the larger group (Me) is *inside*. Moreover, since it is the *back lobe* of the migrating carbon (C-7) of the reactant that must bond to C-3,[2,3,5] the approach to the transition state and the path from it to product would be by way of a *clockwise* (CW) rotation of C-7 about the C-6–C-7 axis. In reactions proceeding by this rotational mode, the increment of strain energy between the reactant and the transition state caused by methyl–ring repulsions would be larger for the case *endo*-methyl reactant (**3**) → *inside* methyl transition state (**5**) than for the case *exo*-methyl (**2**) → *outside* methyl (**4**). Conversely, if the rotations were for some reason contra orbital symmetry (counterclockwise, CCW), the situation would be reversed, since such rotations would relieve methyl–ring repulsive strain in the *endo*-methyl reactant and increase it in the *exo*.[6]

Scheme I



It follows that the rate of rearrangement with configurational inversion in the CW mode should be substantially greater from *exo*-methyl reactant (**2**) than that from *endo*- (**3**) ($k_{inv}(exo) > k_{inv}(endo)$), whereas inversion by the CCW path should lead to $k_{inv}(endo) > k_{inv}(exo)$. We now report experiments that show $k_{inv}(exo) > k_{inv}(endo)$.

Since rearrangement products **8** and **9** suffer retro-Diels–Alder reaction at different rates (**9** > **8**) under the pyrolysis conditions (decalin solution at 290°), pyrolysis of each reactant **2** and **3** is carried only to a few per cent conversion so as to minimize fractionation.[7] The **9**:**8** ratios observed are therefore lower limits for the ratios of rearrangement rates. The pyrolysis of *exo*-methyl compound **2** at 290° gives predominant inversion (**9**:**8** $\geqslant$ 9.3), in sharp contrast to that of *endo*-methyl epimer **3**, which gives predominant retention (**9**:**8** $\geqslant$ 7.2).[8,9] Moreover, no observable trace of

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(1) This work was supported in part by grants from the National Science Foundation (Grant No. GP-6212X) and the National Institutes of Health (Grant No. AM-07515).

(2) J. A. Berson and G. L. Nelson, *J. Am. Chem. Soc.*, **89**, 5503 (1967).

(3) *Cf.* J. A. Berson, *Accounts Chem. Res.*, **1**, 152 (1968).

(4) (a) J. A. Berson and G. L. Nelson, unpublished; (b) G. L. Nelson, Ph.D. Dissertation, University of Wisconsin, 1969.

(5) R. B. Woodward and R. Hoffmann, *ibid.*, **87**, 2511 (1965); *Angew. Chem. Int. Ed. Engl.*, **11**, 781 (1969).

(6) The hypothetical CCW mode involves severe uncoupling of orbitals, so that the transition state might well have a geometry quite different from that in the CW mode. This does not materially affect the argument.

(7) A side reaction consumes most of **3**, 82% of the 7% total product from a low-conversion run being the monocyclic diene **6**, derived by shift of a methyl hydrogen. At longer reaction times, **6** undergoes further change, perhaps by Cope rearrangement, although we have not established this.

(8) All four products are identified by isolation (vpc) and spectroscopic comparison with samples synthesized independently.[4b] Synthesis and identification of reactants **2** and **3**[4b] will be described in a full paper.

(9) We have considered the possibility that the rearrangement passes over a stereochemically indeterminate diradical in the case of both *exo*- and *endo*-methyl-labeled reactants **2** and **3**, and that the observed predominance of *cis*-product **9** from each merely results from a preference for closure of the diradical to *cis-exo* (**9**) rather than *trans* (**8**) product. This possibility seems remote. It would require that the predominant inversion, very similar to that in **2**, observed in the deuterium-labeled system (**1**),[2] be ascribed to an entirely different cause, since no such preference can exist there. Moreover, one can make a reasonable guess that the ratio of rates of formation of **9** *vs.* **8** from the alleged diradical should be similar to this ratio determined from competition experiments on the Diels–Alder reaction of cyclopentadiene with the propenyl acetates. The transition states of the latter processes (regardless of whether one or two bonds are being formed) bear a close *geometric* resemblance to those for closure of the diradical. At 300°, the observed Diels–Alder ratio **9**:**8** is 0.25, but the rearrangement ratio **9**:**8** is about 7–10. The alleged diradical in question as the sole intermediate in the rearrangement provides no obvious explanation for the 40-fold discrepancy.