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THE EPIMERIC 7-PHENYL-7-CHLORO-2-OXABICYCLO [4.1.0] HEPTANES

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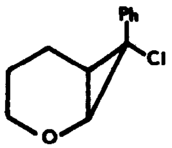
We have recently prepared and characterized the two epimeric 7-phenyl-7-chloro-2-oxabicyclo-[4.1.0] heptanes (**1** and **2**) and wish to comment on their relative reactivities in both thermal and solvolytic processes.



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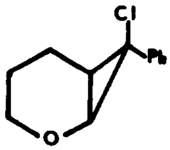

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The compounds in question were readily prepared according to the method of Moss (2). Chromatography of the crude reaction mixture on silica gel eluted first with petroleum ether and then with benzene afforded two isomeric compounds. Both analyzed correctly for $C_{12}H_{13}ClO$ and exhibited molecular ions in their mass spectrum at m/e 208 and 210 (3:1 ratio).

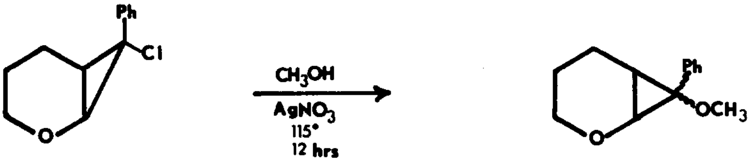
An nmr spectrum of the faster eluting epimer (mp. 34.5-35.5°) to which we have assigned structure **1** exhibits absorption at 0-1.34 ppm (2 protons, multiplet), 1.34-2.40 ppm (3 protons, multiplet), 2.86-3.14 ppm (2 protons, multiplet), 3.98 ppm (1 proton, doublet, J=8.0 Hz), 7.12-7.70 ppm (5 protons, multiplet).

The slower eluting isomer, **2** (mp 58.5-59°), exhibits nmr absorption at 0.88-2.32 ppm (5 protons, multiplet), 2.90-3.94 ppm (3 protons, multiplet) with a doublet (J=8.0 Hz) centered at 3.58 ppm, 6.84-7.42 ppm (5 protons, multiplet).

On the basis of our nmr data and the chemical behavior of the two isomers, we feel reasonably sure of the assignments of stereochemistry to **1** and **2**.

The high field absorption in the nmr spectrum of **1** (above 0.88 ppm) which is lacking in isomer **2** is characteristic of compounds of this type in which the phenyl group is _syn_ to the carbocyclic ring. Closs has studied a number of bicyclo [n.1.0] systems and found this to be the case (3). He attributes this to the shielding effect of the phenyl group on the γ protons in the carbocyclic ring. Nmr studies on the *syn* and *anti*-7-halo-2-oxabicyclo[4.1.0]heptanes by Ando and co-workers have demonstrated that the β proton bound to the carbon bearing oxygen is deshielded considerably by the halogen in the *anti* isomer (4). This is consistent with our assignments. The corresponding proton appears at 3.98 ppm in 1 while in 2 it occurs at 3.58 ppm.

When compound 1 is allowed to react with methanolic silver nitrate in a sealed tube at 115°, compound 3 is obtained in a 70% yield (eqn. 1). No other volatile products were detected by gas chromatography. The obtainment of 3 rather than the expected ring opened product lends further credence to our stereochemical assignments and is consistent with previous studies (3,5,6).



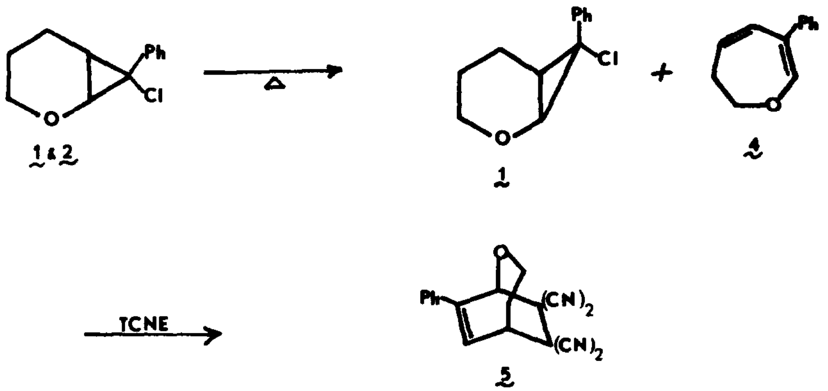
1 3 (1)

The nmr spectrum of 3 exhibits absorption at 0.5-2.10 ppm (5 protons, multiplet), 2.70-3.80 ppm (6 protons, multiplet) 7.00-7.65 (5 protons, multiplet), with a singlet at 3.00 ppm and a doublet at 3.65 ppm (J=8.5 Hz); analyzes correctly for $C_{13}H_{16}O_2$; and has a molecular ion at m/e=204 in the mass spectrum (7).

Compound 2 is completely consumed under identical conditions; however, no volatile products are obtained. We are presently investigating the nature of a plethora of non-volatile materials afforded by this reaction.

In comparing the relative reactivities of these two epimers toward methanolic silver nitrate, it was found that 2 is more reactive than 1. Both isomers were allowed to react with methanolic silver nitrate (1 equiv.) at 95° for 9.5 hours. Whereas 2 had completely reacted, starting material was recovered in the case of 1. This result is in direct contrast to the behavior observed in the solvolysis of the epimeric 7-phenyl-7-chloronorcaranes. In this system the *syn*-phenyl epimer is the more reactive of the two (3,5,6).

Attempted distillation of a mixture of 1 and 2 afforded a mixture of 1 and a diene to which we have assigned structure 4 (8). We did not characterize the diene due to its propensity to polymerize. Rather, it was converted directly to the Diels-Alder adduct 5 (eqn. 2).



(2)

Compound 5 (mp 228-229°) analyzed correctly for $C_{16}H_{12}N_4O$. Its infrared spectrum (KBr) shows a band at 2256 cm^{-1} while its nmr spectrum (acetone-d_6) has absorption at 3.30-5.00 ppm (3 protons, multiplet), 5.94 ppm (1 proton, doublet, J=2 Hz) and 7.10-7.90 ppm (5 protons, multiplet). The remainder of the spectrum was obscured by the acetone-d_6.

Distillation of pure 1 proceeds without formation of 4. Thus in both thermal and solvolytic processes 2 is the more reactive isomer.

We attribute the reversal of reactivity <u>in this system</u> (as compared to the 7-phenyl-7-chloronorcaranes) under solvolytic conditions to two factors: a) the inductive effect of the β oxygen retards the ionzation of the carbon chlorine bond in 1 while in 2 resonance participation of the oxygen's electrons can facilitate a concerted process; and b) substitution of oxygen for methylene lowers the relative difference in ground state energies of the two reactants (9). The two factors combine to increase the activation energy of 1 to a point where its rate of solvolysis is greater than that of 2.

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4) T. Ando, H. Yamanaka, and W. Funasaka, Tetrahedron Letters, 2587 (1967).

5) D. B. Ledlie and E. A. Nelson, Tetrahedron Letters, 1175 (1969).

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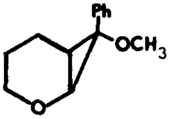
7) On examination of the nmr spectrum of 3 it appears that only one epimer is present. We therefore tentively assign the sterochemistry of 3 as depicted below based on nmr considerations similar to those employed in assigning the sterochemistry of 1 and 2.



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8) An nmr spectrum of the diene 4 (contaminated with approximately 20% of 1) has absorption at 2.54 ppm (2 protons, quartet, J=4.5 Hz), 4.17 ppm (2 protons, triplet, J=4.5 Hz), 5.58-6.20 ppm (3 protons, four-line pattern, J=6 Hz, overlapping a two-line pattern, J=12 Hz), 6.66 ppm (5 protons, singlet).

9) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, Conformational Analysis, John Wiley & Sons, New York (1967).