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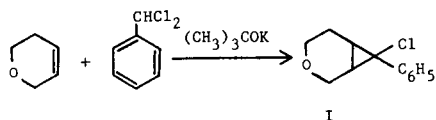
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A method for making stereochemical assignments based on nmr data for the 7-phenyl-3-oxabicyclo[4.1.0]heptanes is described.

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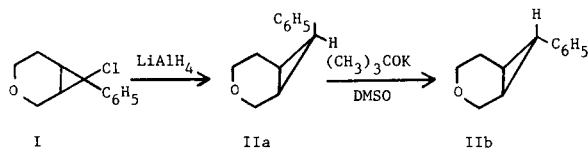
Recently we have reported on a method for making stereochemical assignments for the 7-phenyl-2-oxabicyclo[4.1.0]heptanes (1) based on nmr considerations. As a continuation of this study, we wish to report the synthesis and stereochemical assignments of the 7-phenyl-3-oxabicyclo[4.1.0]heptanes.

Synthesis of the title compounds was accomplished by the reduction of the epimeric 7-chloro-7-phenyl-3-oxabicyclo[4.1.0]heptanes I, which were prepared by reacting potassium *t*-butoxide, benzal chloride, and 3,6-dihydro-2*H*-pyran. This reaction furnished a 20% yield of the mixed chloro compounds in a 2:1 ratio. The structure of



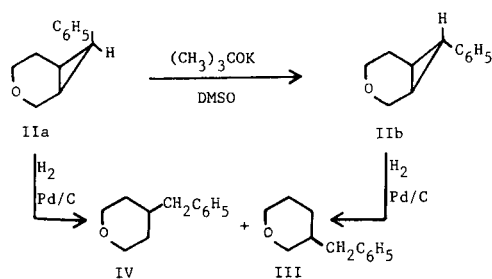
these compounds was substantiated from a correct elemental analysis for $C_{12}H_{13}ClO$, an ultraviolet absorption band at 219 nm (ϵ 9438), which has been shown to be characteristic of phenyl substituted cyclopropanes (1-4), molecular ions in their mass spectrum at m/e 208 and 210 (3:1 ratio), and nmr absorptions at δ 7.05-7.56 (m, 5H), 3.71-4.12 (m, 2H), 2.65-3.65 (m, 2H) and 1.20-2.12 (m, 4H). These data were consistent with the assigned structure for I.

Reduction of I with lithium aluminum hydride (5) produced a 92% yield of *endo*-7-phenyl-3-oxabicyclo[4.1.0]heptane IIa, which analyzed correctly for $C_{12}H_{14}O$,



furnished an ultraviolet absorption band at 221 nm (ϵ 9489), a molecular ion in its mass spectrum at m/e 174, and nmr absorptions at δ 7.32 (s, 5H), 3.98-4.15 (m, 2H), 2.91-3.20 (m, 2H) and 1.17-2.28 (m, 5H). IIa was then treated with a 10% solution of potassium *t*-butoxide in dimethyl sulfoxide (6) to give *exo*-7-phenyl-3-oxabicyclo[4.1.0]heptane IIb. The structure of IIb was established in the same manner as IIa.

Additional evidence supporting the gross structures of IIa and IIb was obtained from the hydrogenation of these compounds. Although the ir spectrum revealed no olefinic linkage, both IIa and IIb absorbed one equivalent of hydrogen upon catalytic hydrogenation, which is characteristic of cyclopropanes. Both IIa and IIb furnished a mixture of the expected hydrogenation products, 3-benzyltetrahydropyran III, and 4-benzyltetrahydropyran IV, which were identified based upon a comparison of



their nmr and ir spectra with that obtained from authentic samples of these compounds (7).

The stereochemical assignments of IIa and IIb were made based on spectral as well as chemical data. The nmr spectrum of IIa displayed a singlet for the absorption of the aromatic protons, while the same protons furnished a split signal for IIb. As has been shown previously for the *endo*- and *exo*-7-phenylnorcaranes (1,6), the *ortho* protons of the phenyl ring in the *exo* isomer are located directly below the cyclopropane ring and experience a diamagnetic shift resulting in a split nmr signal for the phenyl protons. For steric reasons, this conformation is not possible for the *endo* isomer and a singlet is observed for these protons. Additional nmr evidence supporting these structural assignments was derived from a comparison of spectra obtained at 25° with spectra obtained at 180°. A coalescence of the phenyl absorption was observed for IIb as the temperature was increased and the energy barrier for rotation of the phenyl ring overcome. A change of this nature was neither expected nor observed for IIa, since rotation of the phenyl ring is not possible with the *endo* configuration. These results agree with the data we have previously obtained for the *endo* and *exo* isomers of 7-phenylnorcarane (8) and 7-phenyl-2-oxabicyclo[4.1.0]heptane (1).

Chemical evidence supporting these stereochemical assignments was obtained from the base equilibration of IIa to the more thermodynamically stable *exo* isomer, IIb; this conversion is possible only if IIa has the *endo* configuration (6). Further, lithium aluminum hydride reductions of compounds structurally related to I have been shown to be stereoselective, producing only the *endo* isomer (5). On the basis of this data, IIa and IIb were assigned the *endo* and *exo* configuration, respectively.

The information obtained from this study of the 7-phenyl-3-oxabicyclo[4.1.0]heptanes supports this method of assigning stereochemistry for this type of compound based on nmr considerations.

EXPERIMENTAL

An F & M gas chromatograph, Model 810, equipped with a flame ionization detector, was employed for all gas chromatographic analyses. Infrared spectra were obtained using a Beckman Model 10 grating infrared spectrophotometer with potassium bromide cells. Nmr spectra were recorded in carbon tetrachloride with a Varian A-60 spectrometer employing tetramethylsilane as an internal reference. Ultraviolet spectra were recorded in cyclohexane with a Beckman Model DK-2A spectrophotometer. The elemental analyses were performed by M-H-W Laboratories, Garden City, Mich. Boiling points are uncorrected.

7-Chloro-7-phenyl-3-oxabicyclo[4.1.0]heptanes (I).

A solution of 90 g. (1.07 mole) of 3,6-dihydro-2H-pyran (9) and 90 ml. of dry diglyme was added to a four-necked 500 ml. round-bottomed flask containing 71.7 g. (0.64 mole) of potassium *t*-butoxide. The flask was equipped with a mechanical stirrer, a reflux condenser, a dropping funnel, and a thermometer. The mixture was heated with stirring in an oil bath to 55° as 34.5 g. (0.214 mole) of benzal chloride was added dropwise, making certain the reaction temperature did not exceed 70°. After the reaction mixture was stirred for 4.5 hours, it was cooled to room temperature and an equal amount of water was added. The resulting mixture was placed in a separatory funnel, extracted with ether, and the aqueous layer was extracted with ether two more times. All ether layers were combined, washed with water until neutral, and then dried over magnesium sulfate. The ether was removed *in vacuo*, and the residue distilled, yielding 9.14 g. (20% yield), b.p. 128-130°/1 mm, of I present in a 2:1 ratio as determined by gas chromatographic analysis; nmr (carbon tetrachloride): δ 7.05-7.56 (m, 5H), 3.71-4.12 (m, 2H), 2.65-3.65 (m, 2H), 1.20-2.12 (m, 4H); uv (cyclohexane): λ max 219 nm (ϵ 9438).

Anal. Calcd. for C₁₂H₁₃ClO: C, 69.09; H, 6.25; Cl, 17.01; O, 7.67. Found: C, 68.89; H, 6.06; Cl, 17.11; O, 7.80.

endo-7-Phenyl-3-oxabicyclo[4.1.0]heptane (IIa).

Lithium aluminum hydride (0.65 g., 17.04 mmoles) was added to 25 ml. of dry diglyme in a four-necked 100 ml. round-bottomed flask equipped with a mechanical stirrer, dropping funnel, thermometer, and a calcium chloride drying tube. A solution of 0.5 g. (2.39 mmoles) of I, and 5 ml. of diglyme was added to the reaction vessel at 60°. After 15 hours the reaction mixture was cooled, the excess lithium aluminum hydride was destroyed by the slow sequential dropwise addition of 0.7 ml. of water, 0.7 ml. of 15% sodium hydroxide and 2.4 ml. of water (10). The mixture was filtered, the filtrate taken up in ether, washed with water and dried over magnesium sulfate. The ether was removed *in vacuo*, and the residue distilled, furnishing 0.34 g. (82% yield) of IIa, b.p. 87-88°/1 mm, which analyzed by gas chromatography to be 99% pure; nmr (deuteriochloroform): δ 7.32 (s, 5H), 3.98-4.15 (m, 2H), 2.91-3.20 (m, 2H), 1.17-2.28 (m, 5H); uv (cyclohexane): λ max 221 nm (ϵ 9489). A molecular ion was observed in the mass spectrum at *m/e* 174.

Anal. Calcd. for C₁₂H₁₄O: C, 82.71; H, 8.09; O, 9.18. Found: C, 82.47; H, 8.30; O, 9.00.

exo-7-Phenyl-3-oxabicyclo[4.1.0]heptane (IIb).

To a stirred solution of 1.20 g. of potassium *t*-butoxide and 25 ml. of dry dimethyl sulfoxide was added 0.28 g. (1.6 mmoles) of IIa (99% pure), and the mixture was allowed to react at 100° under a dry nitrogen atmosphere for 24 hours. The reaction mixture was hydrolyzed, extracted with ether, washed with water, and dried over magnesium sulfate. Evaporation and subsequent distillation of the residue resulted in 0.21 g. (75% yield) of IIb (98% pure), b.p. 86.5-88.5°/1 mm; nmr (deuteriochloroform): δ 6.81-7.42 (m, 5H), 3.80-4.19 (m, 2H), 2.90-3.79 (m, 2H), 0.91-2.17 (m, 2H); uv (cyclohexane): λ max 220 nm (ϵ 9677). A molecular ion was observed in the mass spectrum at *m/e* 174.

Anal. Calcd. for C₁₂H₁₄O: C, 82.71; H, 8.09; O, 9.18. Found: C, 82.52; H, 8.02; O, 9.11.

Hydrogenation of *endo*-7-Phenyl-3-oxabicyclo[4.1.0]heptane (IIa).

Hydrogenation of 0.75 g. (4.3 mmoles) of IIa was carried out in 50 ml. of absolute ethanol with 0.058 g. of 5% Palladium on charcoal in a Parr reaction apparatus (50 psi) for 84 hours. The solution was filtered, the alcohol was evaporated, and the residue was distilled *in vacuo* furnishing 0.59 g. (78% yield) of a mixture of III and IV, b.p. 83-85°/1 mm; nmr (carbon tetrachloride): δ 6.95-7.40 (m, 5H), 3.80-4.08 (m, 2H), 2.75-3.72 (m, 2H), 0.85-2.20 (m, 5H).

Anal. Calcd. for C₁₂H₁₆O: C, 81.77; H, 9.15; O, 9.08. Found: C, 81.69; H, 9.25; O, 9.11.

Hydrogenation of *exo*-7-Phenyl-3-oxabicyclo[4.1.0]heptane (IIb).

A solution of 0.25 g. (1.4 mmoles) of IIb and 50 ml. of absolute ethanol containing 0.043 g. of 5% Palladium on charcoal was hydrogenated at 48 psi for 108 hours. The reaction mixture was worked up as before and distilled *in vacuo* to yield 0.16 g. (64% yield) of a mixture of III and IV, b.p. 84.5-85.5°/1 mm. The positions of nmr absorptions were the same as for the hydrogenation products from IIa.

Anal. Calcd. for C₁₂H₁₆O: C, 81.77; H, 9.15; O, 9.08. Found: C, 81.51; H, 9.02; O, 9.47.

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