

James D. Woodyard, Paul R. Morris, and Gregory D. Hobbs

Department of Chemistry and Killgore Research Center, West Texas State University, Canyon, Texas 79016

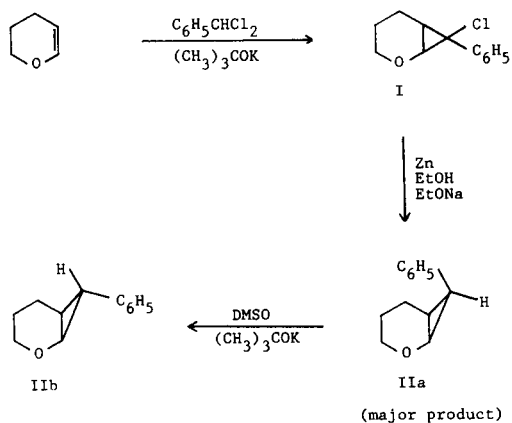
Received February 5, 1980

A rapid method for making stereochemical assignments based on variant temperature nmr data for the 7-phenyl-2-oxabicyclo[4.1.0]heptanes is described.

J. Heterocyclic Chem., 17, 1097 (1980).

Absorptions observed for the aromatic protons in the nmr spectra of the *endo*- and *exo*-7-phenylnorcaranes have been interpreted in different manners, leading to conflicting stereochemical assignments for these compounds (1-3). We have presented conclusive chemical evidence establishing the stereochemistry of these compounds by degrading each of them to a compound of known configuration (4). Those results supported the nmr interpretation of Closs (2) and Jensen (3) who had found that the isomer displaying a sharp singlet for the phenyl protons had the *endo* configuration, while the isomer furnishing a broad multiplet for the phenyl protons had the *exo* configuration. We wish to extend these nmr studies to include heterocyclic members of this family of compounds to determine if this rapid method of assigning stereochemistry is generally applicable to other structurally related compounds. The compounds chosen for this study were the *endo*- and *exo*-7-phenyl-2-oxabicyclo[4.1.0]heptanes, IIa and IIb, respectively.

The synthesis of the 7-chloro-7-phenyl-2-oxabicyclo[4.1.0]heptanes (I), from which IIa and IIb could be obtained, was accomplished by the method of Hodgkins (1) by reacting benzal chloride with potassium *t*-butoxide in the presence of 3,4-dihydro-2*H*-pyran. A 54% yield of a mixture of the *endo* and *exo* chloro isomers (olefin free)



was obtained. The structures of these compounds were substantiated from their elemental analysis, mass spectrum, and an nmr spectrum identical to that described by Ledlie (5) for these compounds. Additionally, the ultraviolet

spectrum exhibited absorption bands at 210.5 (ϵ 8510) and 218 nm (ϵ 8510). Rogers (6) has demonstrated that phenyl substituted cyclopropanes give a characteristic absorption at approximately 220 nm (ϵ 8400).

The 7-chloro-7-phenyl-2-oxabicyclo[4.1.0]heptanes were then reduced with zinc dust (1) in a 5% solution of sodium ethoxide furnishing IIa (55%) and IIb (45%) in 69% yield. The major product of this reaction, IIa, was a solid, m.p. 43-44°, which analyzed correctly for $\text{C}_{12}\text{H}_{14}\text{O}$. Its nmr spectrum displayed absorptions at 7.0-7.5 (5 protons, multiplet), 2.9-3.9 (3 protons, multiplet), 1.6-2.05 (3 protons, multiplet), and 0.5-1.4 (3 protons, multiplet). The infrared spectrum displayed a band in the 1000-1050 cm^{-1} region which is characteristic for most cyclopropyl rings (7), although this is not always reliable in cases where the compound contains an oxygen atom (8). The ultraviolet spectrum furnished absorption bands at 207.5 (ϵ 6390) and 217 nm (ϵ 5630). These data are in agreement with the assigned structure for IIa.

The *exo* isomer, IIb, was prepared in pure form by treating IIa with a 16% solution of potassium *t*-butoxide in dimethyl sulfoxide (2). The structure of IIb was confirmed in the same manner as IIa.

Additional evidence supporting the structure of IIa and IIb was derived from their mass spectra which exhibited molecular ions at m/e 174. Further, catalytic hydrogenation of IIa produced a product furnishing an nmr and ir spectrum identical with that obtained from authentic 2-benzyltetrahydropyran (III) prepared by the method of Shuikin (9). Unlike IIa, IIb furnished two products in the ratio of 1.3:1 when hydrogenated: 2-benzyltetrahydropyran (III) and a second product tentatively identified from its nmr spectrum as 3-benzyltetrahydropyran (IV). These compounds are expected products from this reaction.

The nmr spectra of both IIa and IIb displayed a considerable amount of splitting for the aromatic protons which prevented stereochemical assignments from being made based upon previous arguments. However, a decrease in the splitting of the phenyl absorption of IIb was observed when its ambient temperature spectrum was compared with its spectrum obtained at 200°. This was

the expected result for the *exo* isomer, since the same temperature dependence could be observed for *exo*-7-phenylnorcarane (10). The coalescence of the phenyl absorption occurs as the temperature is increased and the barrier for rotation of the phenyl ring is overcome. An examination of models demonstrated that this rotation of the phenyl ring could occur only in the *exo* isomer. No change of this nature was expected or observed for the *endo* isomer. We are presently investigating the variant temperature nmr spectra of other bicyclo[n.1.0] systems in order to determine the applicability of this rapid method of making stereochemical assignments to compounds structurally related to the 7-phenyl-2-oxabicyclo[4.1.0]heptanes.

EXPERIMENTAL

An F & M gas chromatograph, Model 810, equipped with a flame ionization detector, was employed for all gas chromatographic analyses and a thermal conductivity detector for all preparative gas chromatography. 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 Bausch and Lomb Model 505 spectrophotometer. The elemental analyses were performed by M-H-W Laboratories, Garden City, Mich. Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are corrected. Boiling points are uncorrected.

7-Chloro-7-phenyl-2-oxabicyclo[4.1.0]heptanes (I).

Benzal chloride (61.75 g, 0.384 mole) was added dropwise over a period of 30 minutes to a refluxing solution of 800 ml. of dry 3,4-dihydro-2H-pyran and 172 g. of potassium *t*-butoxide in a three-necked 1-l. flask equipped with a mechanical stirrer, condenser with calcium chloride drying tube, and thermometer (1). The reaction mixture was refluxed for an additional 6 hours, cooled, and 400 ml. water added. The organic phase was separated, washed with water, then with a saturated solution of sodium chloride, and dried over calcium chloride. The aqueous layer was extracted with ether, the extract washed with water followed by a saturated solution of sodium chloride, and then dried over calcium chloride. After evaporation of the solvents both residues were combined for distillation *in vacuo* yielding 43.3 g. (54% yield) of I, b.p. 108-112° at 1 mm. The ultraviolet spectrum exhibited bands at 210.5 (ϵ 8510) and 218 nm (ϵ 8510).

Anal. Calcd. for C₁₂H₁₃ClO: C, 69.06; H, 6.29; Cl, 16.99. Found: C, 69.30; H, 6.22; Cl, 17.19.

Reduction of the 7-Chloro-7-phenyl-2-oxabicyclo[4.1.0]heptanes (I).

To a vigorously stirred solution of sodium ethoxide (11) prepared from 600 ml. of ethanol and 24 g. of sodium were added 35 g. of activated zinc dust (12) and 20 g. (0.096 mole) of I. The mixture was then refluxed for 40 hours, cooled, decanted, and filtered. The filtrate was taken up in ether, washed with water, and then a saturated solution of sodium chloride before drying over calcium chloride. The ether was evaporated and the residue distilled *in vacuo* to give 11.48 g. (69%) of the 7-phenyl-2-oxabicyclo[4.1.0]heptanes, b.p. 124-132° at 10 mm.

The *endo* isomer was separated (13) by distillation through a Nester/Faust Auto Annular spinning band column to give 6.55 g.

of *endo*-7-phenyl-2-oxabicyclo[4.1.0]heptane, b.p. 113-114° at 11 mm; m.p. 43-44°; nmr: δ 7.0-7.5 (5 protons, multiplet), 2.9-3.9 (3 protons, multiplet), 1.6-2.05 (3 protons, multiplet), and 0.5-1.4 (3 protons, multiplet). The ultraviolet spectrum exhibited bands at 207.5 (ϵ 6390) and 217 nm (ϵ 5630).

Anal. Calcd. for C₁₂H₁₄O: C, 82.72; H, 8.10. Found: C, 82.62; H, 8.15.

Hydrogenation of *endo*-7-Phenyl-2-oxabicyclo[4.1.0]heptane (IIa).

Hydrogenation of 2.2 g. (0.0126 mole) of IIa was carried out in 50 ml. of absolute ethanol with 0.17 g. of 5% palladium on charcoal in a Paar pressure reaction vessel (50 psi) for 24 hours. The solution was filtered, the alcohol evaporated, and the residue distilled *in vacuo* to yield 2.03 g. (91%) of 2-benzyltetrahydropyran, b.p. 124° at 12 mm [lit. (9) b.p. 130-135° at 10 mm]; nmr: δ 7.03-7.25 (5 protons, singlet), 2.3-4.05 (5 protons, multiplet), and 0.95-1.9 (6 protons, multiplet); N_D²⁰ 1.5208; mass spectrum exhibited its molecular ion at m/e 176.

Anal. Calcd. for C₁₂H₁₆O: C, 81.77; H, 9.15. Found: C, 81.98; H, 9.22.

exo-7-Phenyl-2-oxabicyclo[4.1.0]heptane (IIb).

To a stirred solution of 20.4 g. of potassium *t*-butoxide and 114 ml. of dry dimethyl sulfoxide was added 4.75 g. of IIa (99% pure) after which the mixture was heated to 100° under a nitrogen atmosphere for 24 hours (2). The reaction mixture was hydrolyzed, extracted with ether, the extract washed with water and then dried over calcium chloride. Evaporation of the solvent and distillation of the residue *in vacuo* resulted in 3.78 g. (80% yield) of IIb (98% pure), b.p. 136-138° at 20 mm; N_D²⁰ 1.5555; nmr: δ 6.7-7.45 (5 protons, multiplet), 2.95-3.75 (3 protons, multiplet), and 1.0-2.15 (6 protons, multiplet). The ultraviolet spectrum exhibited bands at 204 (ϵ 7670) and 221.5 (ϵ 6480).

Anal. Calcd. for C₁₂H₁₄O: C, 82.72; H, 8.10. Found: C, 82.58; H, 8.23.

Hydrogenation of *exo*-7-Phenyl-2-oxabicyclo[4.1.0]heptane (IIb).

Hydrogenation of 1 g. of IIb was carried out in exactly the same manner described for the *endo* isomer. The yield was 0.9 g. (90%) of a mixture of two compounds. These products were separated by preparative gas chromatography utilizing a 6 ft. by 0.25 in. 10% Ucon 50HB 2000 (polar) column operated at 165°. The faster eluting compound, III, exhibited nmr absorptions at δ 7.03-7.25 (5 protons, singlet), 2.3-4.05 (5 protons, multiplet), and 0.95-1.9 (6 protons, multiplet) and infrared absorptions identical to an authentic sample of 2-benzyltetrahydropyran. The slower eluting compound, IV, was tentatively identified as 3-benzyltetrahydropyran on the basis of nmr absorptions at δ 6.72-7.35 (5 protons, narrow multiplet), 3.5-3.95 (2 protons, multiplet), 2.7-3.5 (2 protons, multiplet), 2.3-2.7 (2 protons, multiplet), and 0.7-2.2 (5 protons, multiplet). Compounds III and IV were produced in a ratio of 1.3:1, respectively.

Anal. Calcd. for C₁₂H₁₆O (III): C, 81.77; H, 9.15. Found: C, 81.88; H, 9.10.

Anal. Calcd. for C₁₂H₁₆O (IV): C, 81.77; H, 9.15. Found: C, 81.95; H, 9.12.

Acknowledgement.

The mass spectral analysis was kindly supplied by Clifford G. Venier and William H. Watson. The authors wish to acknowledge the financial support (Grant AE-361) of The Robert A. Welch Foundation.

REFERENCES AND NOTES

- (1) J. E. Hodgkins, J. D. Woodyard and D. L. Stephenson, *J. Am. Chem. Soc.*, **86**, 4080 (1964).
- (2) G. L. Closs and J. J. Coyle, *J. Org. Chem.*, **31**, 2759 (1966).
- (3) F. R. Jensen and D. B. Patterson, *Tetrahedron Letters*, 3837 (1966).
- (4) J. D. Woodyard, P. R. Morris, and R. G. Brown, *J. Org. Chem.*, **37**, 4473 (1972).
- (5) D. B. Ledlie and W. H. Hearne, *Tetrahedron Letters*, 4473 (1969).
- (6) M. T. Rogers, *J. Am. Chem. Soc.*, **69**, 2544 (1947).
- (7) N. B. Colthup, L. H. Daly and S. E. Wiberley, "Introduction to Infrared and Raman Spectroscopy", Academic Press, New York, N. Y., 1969, p. 198.
- (8) A. R. H. Cole, *J. Chem. Soc.*, 3807 and 3810 (1954).
- (9) N. I. Shuikin, I. F. Belskii, R. A. Karakhanov, B. Kozma, and M. Bartók, *Acta Phys. Chem.*, **9**, 37 (1963).
- (10) Unpublished results.
- (11) L. F. Fieser, "Experiments in Organic Chemistry", D. C. Heath and Company, Boston, Mass., 1957, p. 342.
- (12) R. L. Shriner and F. W. Neumann, "Organic Syntheses", Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 74.
- (13) Analysis by vpc was accomplished on a 6 ft. by 0.25 in. 10% Ucon 50 HB 2000 (polar) column operated at 165°.