

## NOTES

### CONVENIENT SYNTHESSES OF SOME $\alpha$ -DEUTERATED ALKYL MESITYL KETONES BY EXCHANGE REACTIONS

#### SUMMARY

Three alkyl mesityl ketones (methyl, ethyl, and isopropyl) deuterated in the  $\alpha$ -positions were prepared in good yields (82-89%) by exchange with deuterium oxide using dioxane solvent and various catalysts. Little or no exchange was obtained when reactions were attempted under conditions used in published procedures for other ketones. Infrared and  $^1\text{H}$  nmr spectral evidence in support of structural assignments of deuterated ketones is given.

Key words:  $\alpha$ -deutero-alkyl mesityl ketones; synthesis;  $^1\text{H}$  nmr, ir spectra.

#### INTRODUCTION

$\alpha$ -Deuteration with water-soluble ketones such as acetone (1,2) or 3-pentanone (1,3) can be readily effected by exchange with excess deuterium oxide (1,2) alone or with added potassium carbonate (1,3). Certain  $\alpha$ -deuterated ketones were needed for the evaluation of isotope effects in mechanistic studies (4) on the enolization reaction with Grignard reagents. However, it was found that essentially no exchange occurred when the ketone was stirred with deuterium oxide with or without sodium deuterioxide for a substantially longer period of time (ca. 2 days) than specified. We wish to report simple successful procedures for  $\alpha$ -deuteration of water-insoluble ketones developed by a modification of a recent method (5) used for deuteration of tin compounds. Evidence of complete deuteration in the  $\alpha$ -positions of the ketones was obtained from  $^1\text{H}$  nmr and ir spectra.

## EXPERIMENTAL

[<sup>2</sup>H<sub>3</sub>]-Methyl 2,4,6-Trimethylphenyl Ketone\*

Methyl mesityl ketone (20.0 g; 0.123 mol) was dissolved in 70 ml of 1,4-dioxane (Mallinckrodt) in a 100 ml round-bottomed flask equipped with a magnetic stirrer and a reflux condenser protected with a calcium chloride drying tube. Deuterium oxide (20.0 ml; 22.1 g; 1.10 mol) of 98.4% purity (Aldrich) and anhydrous sodium carbonate (15.0 g; 0.142 mol) were introduced into the flask. The mixture was stirred 20 hr at reflux. The solution was decanted from the solid carbonate into another flask and the solid was washed with small quantities of dioxane. The washings were combined with the original solution and solvent was removed with a rotary evaporator. During this process, H<sub>2</sub>O and unreacted deuterium oxide is also removed by evaporation along with the solvent. The residue was distilled under reduced pressure, bp 94.5-96°C/1 Torr; yield 18 g, 89%; D(23°C) 0.9869 g/ml. In a second preparation the exchange reaction was repeated with the deuterated ketone sample. The same infrared spectrum was obtained from this sample as that from the first exchange, indicating complete exchange; bp 93-94°C/3 Torr.

In the <sup>1</sup>H nmr spectrum, the singlet at 2.33 ppm corresponding to methyl protons α to the carbonyl group had disappeared showing complete deuteration. <sup>1</sup>H nmr data on hydrogen and deuterated analogs respectively are: o-CH<sub>3</sub> 2.16, 2.14; p-CH<sub>3</sub> 2.23, 2.23; m-Ar-H 6.78, 6.75. Relevant features of ir spectra pertaining to labeling position are discussed below.

1-[<sup>2</sup>H<sub>2</sub>]-Ethyl 2,4,6-Trimethylphenyl Ketone\*

The title compound was prepared by an analogous procedure from ethyl mesityl ketone in 86% yield; bp, 106-107°C/2 Torr; D(23°C) 0.9690 g/ml. Complete deuteration

\*Nomenclature according to: International Union of Pure and Applied Chemistry, Organic Chemistry Division, Commission on Nomenclature of Organic Chemistry, Nomenclature of Organic Chemistry. Section H: Isotopically Modified Compounds (First Ed.), Pure Appl. Chem., 51, 353-380 (1979).

was confirmed by the nmr spectrum. The quartet for the methylene protons  $\alpha$  to the carbonyl group present in the undeuterated ketone at 2.58 ppm had disappeared and the triplet for the methyl protons  $\beta$  to the carbonyl group at 1.13 ppm was replaced by a poorly resolved quintet also centered at 1.13 ppm. Other  $^1\text{H}$  nmr data on hydrogen and deuterated analogs respectively are: o- $\text{CH}_3$  2.11, 2.11; p- $\text{CH}_3$  2.23, 2.23; m-Ar-H 6.75, 6.73. Relevant features of ir spectral data are discussed below.

1-Methyl-1- $[\text{}^2\text{H}_1]$ -Ethyl 2,4,6-Trimethylphenyl Ketone\*

The deuteration of isopropyl mesityl ketone was carried out by a modification of the above procedure with aceto- and propio-mesitylenes since complete deuteration could not be achieved. The ketone (23.4 g; 0.123 mol) was dissolved in dioxane (70 ml) and the solution was refluxed with deuterium oxide (22 g; 1.1 mol) in the presence of 0.25 ml of sodium deuterioxide (Norell) (40% in  $\text{D}_2\text{O}$ ) and anhydrous sodium carbonate (15.1 g; 0.142 mol). The rest of the procedure was the same as with methyl mesityl ketone; yield 82%; bp 135-138°C/9 Torr; D(23°C), 0.9588 g/ml.

The  $^1\text{H}$  nmr spectral data of the compound confirm the expected position of deuteration. The septet of the  $\alpha$ -methine proton present in the spectrum of the undeuterated ketone at 2.87 ppm had disappeared and the doublet of the  $\beta$ -gem-dimethyl group at 1.10 ppm was replaced by a broad unresolved multiplet centered at 1.08 ppm. Other  $^1\text{H}$  nmr data on hydrogen and deuterated analogs respectively are: o- $\text{CH}_3$  2.11, 2.11; p- $\text{CH}_3$  2.23, 2.23; m-Ar-H 6.75, 6.73. The ir spectrum showed a weak C-D stretching band at  $2180\text{ cm}^{-1}$ . Relevant features of ir spectral data are discussed below as they relate to labeling position.

#### NMR and IR Spectra

$^1\text{H}$  nmr spectra were obtained with a Perkin-Elmer model R12B instrument at 60 MHz. Chemical shifts are in ppm ( $\delta$  scale) from tetramethylsilane internal standard. Concentrations were 10% W/V in spectral grade carbon tetrachloride.

Infrared spectra were obtained with a Perkin-Elmer model 521 spectrophotometer. The samples were neat liquids as films between sodium chloride plates. Frequencies were calibrated against closest bands of polystyrene film.

## DISCUSSION

Comparisons of the infrared spectra (6) of the three deuterated ketones with their hydrogen analogs serve to substantiate nmr evidence for position of labeling. For the three deuterated ketones, the C-D stretching modes appear in the spectra as weak bands at 2250, 2130, and 2180  $\text{cm}^{-1}$  for methyl, ethyl, and isopropyl mesityl ketones respectively. The C-H bending modes for methyl mesityl ketone at 1425 and 1350  $\text{cm}^{-1}$  are missing from the spectrum of the  $\alpha$ -deuterated analog; the corresponding modes appear in the spectrum of the latter at 1090 and 980  $\text{cm}^{-1}$ . For ethyl mesityl ketone the C-H bending vibrations ( $\delta_{\text{as}}$  and  $\delta_{\text{s}}$ ) which appear at 1420 and 1340  $\text{cm}^{-1}$  respectively do not appear in the spectrum of the  $\alpha$ -deuterated analog and are replaced by bands at 1262 and 1140  $\text{cm}^{-1}$  in the spectrum of the latter. The C-H twisting and rocking modes are evidently the bands at 1220 and 1010  $\text{cm}^{-1}$ . The C-D band corresponding to the 1220  $\text{cm}^{-1}$  mode evidently is the band at 1085  $\text{cm}^{-1}$ . (The latter bending assignments are tentative.) For isopropyl mesityl ketone, a strong C-H bending mode appears at 1220  $\text{cm}^{-1}$  which does not appear in the spectrum of the deuterated analog. A new strong band appears at 990  $\text{cm}^{-1}$  in the spectrum of the  $\alpha$ -deuterated isopropyl compound. The gem-dimethyl doublet for the isopropyl group which appears at 1380 and 1360  $\text{cm}^{-1}$  for both hydrogen and deuterium compounds shows that  $\alpha$ -substitution by deuterium has no effect on this vibrational mode.

It is interesting to note that although the differences in chemical shifts between some of the deuterated and non-deuterated analogs are small (0.02 to 0.03 ppm), they are slightly larger than the experimental error ( $\pm 0.01$  ppm) and reproducible; also the fact that they are consistently in the same direction would tend to make them valid. The observed values for deuterated compounds (where present) always appear at higher field strengths for the aromatic protons, isopropyl methyls, and ortho methyls for the methyl ketone. The ortho methyl protons show a shielding shift from methyl (2.16 ppm) to ethyl (2.11 ppm) mesityl ketone which levels off for the isopropyl ketone at 2.11 ppm.

ACKNOWLEDGMENTS

The authors express appreciation to The Robert A. Welch Foundation of Houston, Texas for support of this work under Research Grant AA-111 and to Prof. Malcolm Dole for use of the ir spectrophotometer.

REFERENCES

1. Murray, A., III, and Williams, D. L., Organic Syntheses with Isotopes. Part V. Organic Compounds with Isotopes of the Halogens, Hydrogen, Nitrogen, Phosphorus, and Sulfur, Interscience, N.Y., 1958, p 1511 ff.
2. Condon, F. E., J. Am. Chem. Soc., 73, 4675 (1951).
3. Wijnen, M. H. J., and Steacie, E. W. R., Can. J. Chem., 29, 1092 (1951); McNesby, J. R., Drew, C. M., and Gordon, A. S., J. Phys. Chem., 59, 988 (1955).
4. Pinkus, A. G. and Servoss, W. C., J. Chem. Soc., Perkin Trans. II, in press.
5. McWilliam, D. C., Balasubramanian, T. R., and Kuivila, H. G., J. Am. Chem. Soc., 100, 6407 (1978).
6. Assignments based on: Nakanishi, K., Infrared Absorption Spectroscopy, 2nd ed., Holden-Day, San Francisco, 1977; Bellamy, L. J., The Infra-red Spectra of Complex Molecules, 3rd ed., Wiley, N.Y., 1975; Silverstein, R. M., Bassler, G. C., and Morrill, T. C., Spectrometric Identification of Organic Compounds, 3rd ed., Wiley, N.Y., 1974.

A. G. Pinkus, A. Sabesan,<sup>†</sup> and Ravi Subramanyam<sup>‡</sup>

Department of Chemistry, Baylor University

Waco, Texas 76703, U.S.A.

---

<sup>†</sup>Robert A. Welch Foundation postdoctoral fellow on sabbatical leave from Presidency College, Madras, India.

<sup>‡</sup>Robert A. Welch Foundation predoctoral fellow.