SYNTHESIS OF 2,5,8-TRIMETHYL-3,4-DIHYDRO-1(2H)-NAPHTHALENONE-2-d AND 3,5,8-TRIMETHYL-3,4-DIHYDRO-1(2H)-NAPHTHALENONE-2,2-d_2

E. J. Eisenbraun, B. Dewprashad, and P. W. Geno
Department of Chemistry, Oklahoma State University
Stillwater, Oklahoma 74078

A. R. Taylor
Research and Engineering
CONOCO, Inc.
Ponca City, Oklahoma 74603

SUMMARY

The synthesis of specifically labeled 2,5,8-trimethyl-3,4-dihydro-1(2H)-naphthalenone-2-d and 3,5,8-trimethyl-3,4-dihydro-1(2H)-naphthalenone-2,2-d_2 through α-proton exchange using neat trifluoroacetic acid-d is described.

Key words: 2,5,8-Trimethyl-3,4-dihydro-1(2H)-naphthalenone-2-d, 3,5,8-Trimethyl-3,4-dihydro-1(2H)-naphthalenone-2,2-d_2, Trifluoroacetic acid-d, α-Exchange.

INTRODUCTION

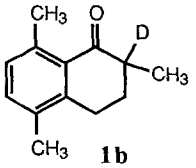
The two isomeric, α-deuterium labeled ketones 2,5,8-trimethyl-3,4-dihydro-1(2H)-naphthalenone-2-d (**Ib**) and 3,5,8-trimethyl-3,4-dihydro-1(2H)-naphthalenone-2,2-d_2 (**2b**) were needed as model compounds for instrumental studies (^1H and ^{13}C NMR and MS). Exchange, at the position alpha to the carbonyl group, via acid-catalyzed enolization using neat trifluoroacetic acid-d (TFA-d) at room temperature, as solvent and source of deuterium, was selected for the synthesis of **Ib** and **2b** from the unlabeled parent ketones **Ia** and **2a** (1). The ^1H and ^{13}C NMR data and the mass spectroscopic studies of the starting materials and the products show there was extensive exchange of protons at the position alpha to the carbonyl group and that exchange at all other positions did not take place to any significant extent.

Prior reports of the use of TFA-d, as a neat reagent, in alpha exchange are meager. An NMR study of the kinetic exchange of six ketones has been reported (2). In addition, alpha exchange of camphor to its d_1 and d_2 derivatives in 5% and 95% yields has been reported (3a). This procedure

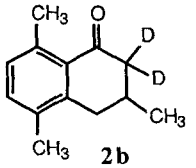
0362–4803/90/010025–04$05.00

Received May 16, 1989
Revised July 17, 1989

involves heating a 1:10:50 molar mixture of ketone, TFA-d and D_2O at 130°, in a sealed tube, for nine days (3a,b). Other alpha-exchange procedures, using acidic and basic catalysts, have been described (4a,b).



1b



2b

The ease with which the alpha-deuterium exchange was carried out, to provide **Ib** and **2b**, suggests that the described procedure and the attendant analyses can readily be extended to produce gram quantities of other alpha-deuterated ketones.

EXPERIMENTAL SECTION

^1H and ^{13}C NMR spectra were obtained from a Varian XL-300 spectrometer operating at 300 MHz and 75 MHz respectively. Chemical shifts are reported in ppm (δ) using tetramethylsilane as the internal standard.

2,5,8-Trimethyl-3,4-dihydro-l(2H)naphthalenone-2-d (lb). A previously baked (165 °C , 3 days) 50 mL, long-necked flask, teflon-coated magnetic stirring bar and condenser were assembled while hot. A 7.62 g (40 mmol) sample of **la** (l): ^1H NMR ($CDCl_3$) δ 1.19 (d, 3), 1.68 (m, l), 2.10-2.20 (m, l), 2.20 (s, 3), 2,45-2.60 (m, 4) (5), 2.69-2.92 (m, 2), 6.94 (d, l), 7.12 (d, l); ^1H NMR (TFA-d) δ 1.25 (d, 3), 1.72-1.88 (m, l), 2.11-2.25 (m, 4), 2.52 (s, 3), 2.60-2.80 (m, 2) (5), 2.85-2.98 (m, l), 6.98 (d, l), 7.20 (d, l); ^{13}C NMR ($CDCl_3$) δ 15.4 (113), 19.5 (92), 23.1 (115), 26.8 (124), 30.5 (125), 43.1 (126), 129.8 (137), 131.4 (28), 133.3 (144), 133.8 (42), 138.3 (43), 143.0 (41), 203.2 (30). m/e (rel. intensity) 188 (48), 146 (100), 118 (34), 117 (39), 115 (20), 91 (15), 39 (15) and 12 mL of TFA-d [prepared by dropwise addn. of 2.0 g of D_2O to 21.0 g (0.10 mol) of TFA anhydride] were added. The apparatus was connected, through the condenser, to a series of traps (two Dry Ice and three filled with 4-8 mesh soda-lime) to a vacuum pump. The reaction mixture was magnetically stirred for 20 h and then aspirated to remove spent TFA-d. A new batch of TFA-d was added and the process was repeated (four total). After the final treatment, 0.5 mL of anhydrous pentane was added to assist removal of last traces of TFA and TFA-d. The product was then aspirated at 0.1 mm for 48 h, at which time the ^{13}C NMR signals for TFA-d had vanished, to give 7.17 g (94.1 %) of **lb**: ^1H NMR (TFA-d) δ 1.24 (s, 3), 1.78-1.80 (m, l), 2.15-2.26 (m, 4), 2.57 (s, 3), 2.72-2.87 (m, l), 2.90-3.00 (d,t, l); ^1H NMR ($CDCl_3$) δ 1.22 (s, 3), 1.73-1.85 (m, l), 2.12-2.20 (m, l), 2.23 (s, 3), 2.56 (s, 3),

2.72-2.85 (m, 1), 2.85-2.95 (d,t, 1), 6.98 (d, 1), 7.16 (d, 1); ^{13}C NMR ($CDCl_3$) δ 15.3 (144), 19.5 (139) 23.1 (153), 26.8 (153), 30.4 (149), 129.7 (200), 131.4 (32), 133.3 (200), 133.8 (61), 138.2 (60), 142.9 (60), 204.3 (30). m/e (rel. intensity) 189 (45), 146 (100), 118 (35), 117 (35), 115 (15), 91 (12), 39 (11); 4.36% d_0, 95.59% d_1, 0.00% d_2, 0.04% d_3, 0.00% d_4, 0.00% d_5.

3,5,8-Trimethyl-3,4-dihydro-1(2H)-naphthalenone-2,2-d_2 (2b). A 1.880 g (10 mmol) sample of (**2a**) (1) : mp 70-71 °C; ^1H NMR ($CDCl_3$) δ 1.10 (d, 3), 2.20-2.35 (m, 6), 2.55-2.65 (m, 4), 2.90 (d, 1), 6.90 (d, 1), 7.12 (d, 1). ^1H NMR (TFA-d) δ 1.19 (d 3), 2.2-2.3 (m, 4), 2.45 (dd, 2), 2.60 (s, 3), 2.85 (d, 1), 3.05 (d or d,d 1) 7.06 (d, 1), 7.30 (d, 1); ^{13}C NMR ($CDCl_3$) δ 19.6 (112), 21.6 (130.0), 23.1 (126), 29.3 (138.3), 35.8 (139.2), 48.5 (147), 129.7, 130.8 (37), 133.7 (198.6), 138.4 (57), 142.8 (57); m/e (rel. intensity) 188 (64), 173 (32), 146 (100), 128 (10), 118 (41), 117 (36), 103 (12), 91 (14), 77 (9) in 6 mL of TFA-d was processed (four exchanges) as described above to give 1.84 g (97.0%) of **2b**: mp 70-71 °C; 1H NMR ($CDCl_3$) δ 1.15 (d, 3), 2.24-2.28 (m, 4), 2.37-2.46 (m, 1), 2.60 (s, 3), 2.92-3.00 (dd 1), 6.98 (d, 1), 7.19 (d, 1); ^1H NMR (TFA-d) δ 1.22 (d, 3), 2.20-2.35 (m, 4) 2.45-2.55 (m, 1), 2.65 (s, 3), 3.05-3.15 (d,d, 1), 7.08 (d, 1), 7.35 (d, 1); ^{13}C NMR ($CDCl_3$) δ 19.7 (110), 21.6 (126), 23.2 (1224), 29.3 (105, 229.4 (17), 35.9 (111), 129.8 (159), 131.0 (17), 133.8 (196), 138.6 (37), 143.0 (37), 201.0 (11); m/e (rel. intensity) 190 (58), 175 (18), 146 (100), 130 (7), 118 (42), 117 (38), 103 (12), 91 (11), 77 (7); 0.00% d_0, 5.53% d_1, 94.47% d_2, 0.00% d_3, 0.00% d_4, 0.005 d_5.

ACKNOWLEDGEMENTS

We thank N. Perreira and S. Sigle for mass spectroscopic and NMR data. We gratefully acknowledge funds from the National Science Foundation which contributed to the purchase of this instrumentation through grants BSS-8704089 and BMB-8603864.

REFERENCES AND NOTES

1. Eisenbraun, E. J. , Hinman, C. W. , Springer, J. M. , Burnham, J. W. , Chou, T.S. -J. Org. Chem. 36: 2480 (1971).
2. Leshina, T.V. , Kim, A.M. , Mamaev, V.P. ,Molin, Yu. N.-Reakts. Aposobnost Org. Soedin. Tartu. 4: 814 (1967). C.A. 69: 76147Y (1068).
3. (a) Weinberg, D.S. , Djerassi, C.-J. Org. Chem. 31: 115 (1966).
   (b) Thomas, A.F. , Schneider, R.A. , Meinwald, J.-J. Am. Chem. Soc. 89: 68 (1967).
4. (a) Thomas, A. F. "Deuterium Labeling in Organic Chemistry," Appelton-Century-Crofts Educational Division/Meredith Corp., NY, 1971.

(b) Lamathyl, G. "Deuterium Exchange in Carbonyl Compounds," in "Isotopes in Organic Chemistry-Isotopes in Hydrogen Transfer Processes," Buncel, E. , Lee, C.C. (Eds.), Elsevier, The Netherlands, Vol. 2: 33-88 (1976).

5. Significant chemical shifts were observed in comparing the NMR data in these two solvents.