SYNTHESIS AND PROPERTIES OF DODECANE-1,12-$^{13}C_2$ and DODECANE-1,1,1,12,12,12-$^{2}H_6$

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SUMMARY

Normal dodecane labeled with either carbon-13 or deuterium at both the terminal methyl groups has been synthesized. The mass spectra and PNMR and CNMR spectra of these compounds have been measured and are reported.

Key Words: Dodecane, Carbon-13, Deuterium, Synthesis, Spectra

INTRODUCTION

The reactions occurring in the gas phase following collisional activation of ions derived from hydrocarbon molecules are fairly complex because rearrangement of the carbon skeleton appears to occur quite readily[1]. This, coupled with the fact that hydrogen rearrangement in such ions has been demonstrated to be a particularly facile process[2], places a limitation on the potential of deuterium as a label with which these reactions can be clarified. Accordingly, we undertook a synthesis of dodecane-1,12-$^{13}C_2$ and dodecane-1,1,1,12,12,12-$^{2}H_6$ in the hope that their collisional activation mass spectra, as compared to those of the unlabeled materials, would shed some light upon these rearrangements. The synthesis and characterization by NMR spectroscopy and electron ionization and chemical ionization mass spectrometry of these two compounds is described here.

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RESULTS AND DISCUSSION

The reduction of a 1,6-dicarboxylic acid dimethyl ester to the corresponding hydrocarbon has been described[3] and we decided to use this route for the preparation of the hexadeuterododecane. Treatment of dodecanedioic acid with methanolic hydrogen chloride led to the formation of the corresponding dimethyl ester which was readily reduced with commercial lithium aluminum deuteride[4] (99 atom % excess D), giving 1,12-dodecanediol-1,1,12,12-$^{2}H_4$. This was converted to its bis p-toluenesulfonate ester which was reduced, also with lithium aluminum deuteride, to form dodecane-1,1,1,12,12,12-$^{2}H_6$.

A modified synthetic procedure was employed for the synthesis of dodecane-1,12-$^{13}C_2$. The starting point was 1,10-dibromodecane, which was treated with sodium cyanide-^{13}C in aqueous ethanol[5]. The dinitrile formed was not isolated, but was hydrolyzed *in situ* and the product, dodecanedioic-1, 12-$^{13}C_2$ acid was isolated from the reaction mixture. Reduction of this dicarboxylic acid with borane-methyl sulfide[6] led to the appropriate 1,12-dodecanediol in 90% yield.

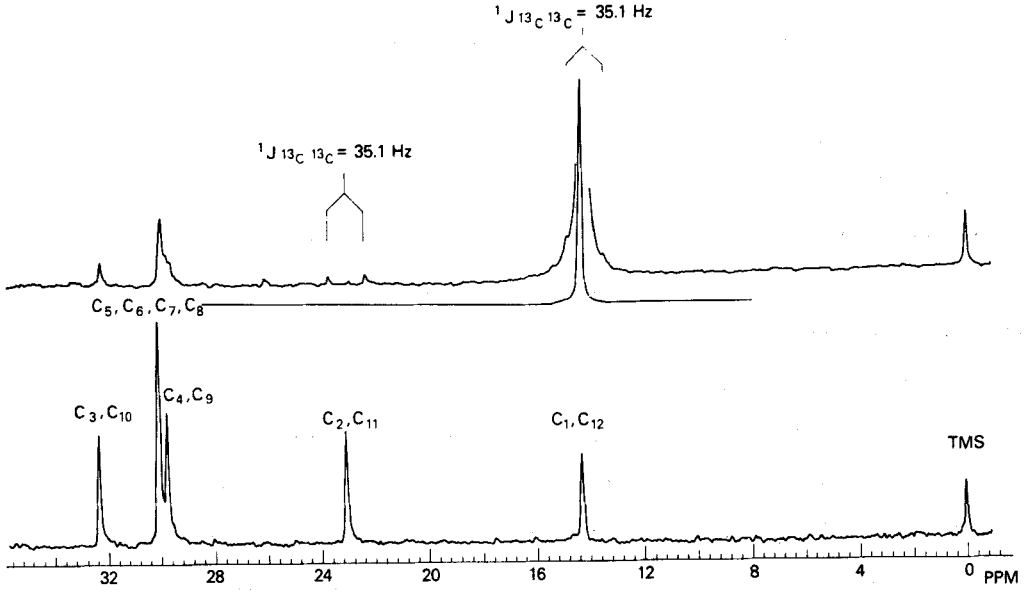

Figure 1. CNMR spectra of dodecane-1,12-$^{13}C_2$ (upper trace) and dodecane (lower trace).

The bis p-toluenesulfonate ester of 1,12-dodecanediol-1,12-$^{13}C_2$ was formed by reaction of the diol in pyridine at 0°C with p-toluenesulfonyl chloride and finally, reduction of this bis-tosylate with excess lithium aluminum hydride in refluxing ether for 48 hr gave dodecane-1,12-$^{13}C_2$ in 30% yield.

The CNMR spectrum (Figure 1) of dodecane-1,12-$^{13}C_2$ shows the most intense peak at 14.13 ppm downfield from internal TMS due to carbons C-1 and C-12. This signal agrees with shifts reported for terminal carbons of n-alkanes[7] and with our own measurement (14.4 ppm) on unlabeled dodecane. The shoulders on the side of this main peak are due to ^{13}C-^{13}C coupling (J = 35.1 Hz) between C-1 and C-2, C-11 and C-12. Evidence of the same coupling is seen in the signal from C-2 and C-11 at 22.9 ppm. The other signals at 29.5, 29.9 and 32.1 ppm are unaffected by the isotope and are assigned as shown in Figure 1.

The electron ionization mass spectra of dodecane-1,1,1,12,12,12-$^{6}H_2$, dodecane-1,12-$^{13}C_2$ and dodecane are shown in Figure 2. In the mass spectrum of the dodecane-1,12-$^{13}C_2$, the molecular ion at m/e 172 is the only peak that contains both C-1 and C-12 of the original molecule: all the fragment ions are displaced by 1 amu to higher mass compared with the unlabeled compound. This permits the reasonable conclusion that the molecule fragments from one end or the other rather than by loss of some portion of the center of the chain and linking up the terminal residues. Inspection of the mass spectrum of dodecane-1,1,1,12,12,12-$^{2}H_6$ supports this conclusion.

The methane chemical ionization mass spectrum of dodecane-1,12-$^{13}C_2$ shows a quasi-molecular ion at m/e 171 (MW-1). The same ion is found at m/e 169 in the spectrum of the unlabeled compound. The same fragment ions are produced by both compounds, displaced by 1 amu to higher mass in the case of the labeled compound.

EXPERIMENTAL SECTION

All melting points were determined on a Kofler hot stage and are uncorrected. Proton NMR spectra were recorded on a Varian-60 spectrometer in continuous wave mode. A Varian XL-100 spectrometer, operating in the Fourier transform mode was used to measure CNMR spectra. The chemical shifts were measured relative to TMS as an internal standard. Electron ionization mass spectra were measured using an LKB-9000 mass spectrometer and chemical ionization mass spectra with a Finni-

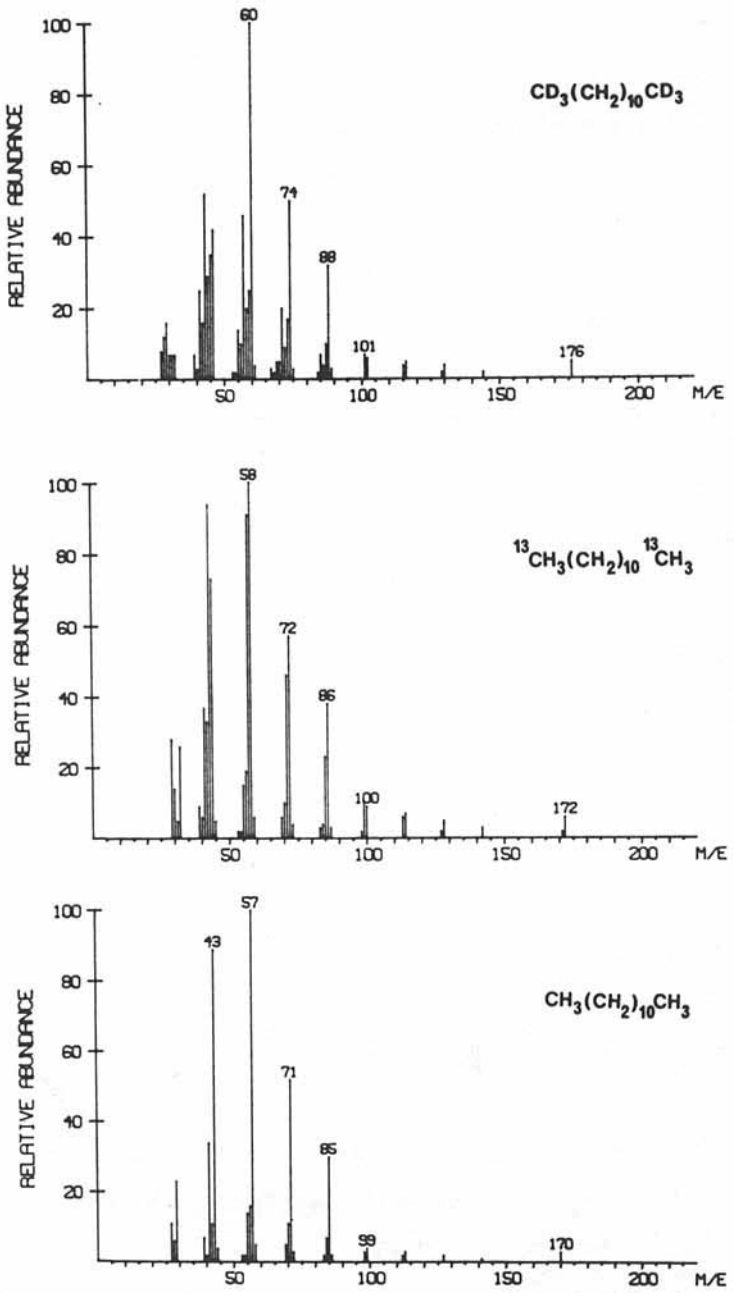

Figure 2. Electron impact mass spectra of dodecane-1,1,1,12,12,12-$^{2}H_6$ (upper trace), dodecane-1,12-$^{13}C_2$ (middle trace) and dodecane (lower trace).

gan 3200 quadrupole mass spectrometer. Precise isotopic enrichments were calculated from the electron ionization mass spectra using a computer program developed by C. F. Hammer and A. J. Vlietstra.*

Dodecanedioic-1,12-$^{13}C_2$ Acid -- To a solution of sodium cyanide-^{13}C (1.0 g, 0.02 mole, 90 atom %[4]) in water (1.5 ml) and ethanol (7.0 ml) was added over a period of 10 mins, 1,10-dibromodecane (3.62 g, 0.012 mole). After the mixture had been gently refluxed for 5 hrs. concentrated hydrochloric acid (5.0 ml) was added and the mixture was then refluxed for a further 12 hrs. At this point the solution was cooled and extracted with ether. The ethereal extract was dried over sodium sulfate and then evaporated to dryness to give the crude dicarboxylic acid as a white solid, which was recrystallized from hot water as needles (mp 127-128°, lit.[8] 129°, 3.3 g, yield = 86%. Mass spectrum (relative abundance): 113(22), 99(100), 98(24), 85(66), 69(27), 61(20), 55(20).

1,12-Dodecanediol-1,12-$^{13}C_2$ -- A solution of borane-dimethyl sulfide in tetrahydrofuran[6] (40 ml, 1M) was added dropwise, under nitrogen at 25°, to a stirred solution of dodecanedioic-1,12-$^{13}C_2$ acid (3.2 g, 0.014 mole) in dry tetrahydrofuran (30 ml) during a 15 min. period. The mixture was stirred for a further 8 hrs at room temperature and then anhydrous methanol (200 ml) was added slowly and the resulting solution was evaporated to dryness to give the diol as a solid which was recrystallized from ethanol as needles (mp 81-83°, lit.[9] 80-81°, 2.53 g, yield = 90%). Mass spectrum: 168(31), 112(32), 111(40), 110(40), 98(40), 97(80), 96(56), 84(64), 83(100), 82(64), 81(40), 70(72), 69(88), 68(64), 67(48), 57(41), 56(80), 55(96), 54(31), 44(64), 43(55), 42(41), 40(71).

1,12-Dodecanediol-1,12-$^{13}C_2$ bis p-Toluenesulfonate -- To a solution of 1,12-dodecanediol-1,12-$^{13}C_2$ (2.5 g, 0.012 mole) in pyridine (40 ml) at 0° was added 8.0 g, (0.042 moles) of p-toluenesulfonyl chloride. After solution was complete, the reaction mixture was allowed to stand for 24 hrs at 0°. Ice (ca. 100 g) was added, the mixture was stirred for 15 mins and the precipitate was filtered and washed with water. The product was recrystallized from ethanol as plates (mp 90-

*This program, LABDET, is a component of the NIH/EPA computer-based Chemical Information System. For further details of this, contact GWAM.

91°, 3.15 g, yield = 80%). Mass spectrum: 512(1)(M+), 173(100), 98(42), 97(44), 91(96), 84(57), 83(59), 71(42), 70(58), 69(53), 68(43), 42(42), 40(52).

Dodecane-1,12-$^{13}C_2$ -- The bis p-toluenesulfonate of 1,12-dodecanediol-1,12-$^{13}C_2$ (3.0 g, 5.8 mmole) was added at room temperature to a stirred suspension of lithium aluminum hydride (1.0 g) in dry ether (50 ml). The mixture was stirred and refluxed for two days and then cooled for the addition of dilute hydrochloric acid. The ether layer was removed and dried over sodium sulfate. After filtering, the ether was evaporated in vacuo to give the product as an oil (0.7 g). This material was distilled (212-216°, 760 mm) and the distillate finally purified by chromatography on silica gel. Elution with petroleum ether gave pure dodecane-1,12-$^{13}C_2$ as a colorless oil (0.3 g, yield = 30%, isotopic enrichment = 88.9%, mole fractions: $^{13}C_0$ = 2.2%, $^{13}C_1$ = 19.4%, $^{13}C_2$ = 78.4%). Mass spectrum: given in Figure 2.

1,12-Dodecanediol-1,1,12,12-$^{2}H_4$ -- Dimethyl dodecanedioate was prepared from dodecanedioic acid by reaction with methanolic hydrogen chloride. This ester (2.0 g, 0.01 mole) in ether (20 ml) was added at room temperature to a stirred solution of lithium aluminum deuteride (0.5 g, 0.012 mole) in ether (20 ml). After 30 min excess dilute hydrochloric acid was added, the ether layer was removed and the residue extracted with ether. The ethereal extracts were combined, dried and the solvent was removed to afford 1,12-dodecanediol-1,1,12,12-$^{2}H_4$ as white needles from benzene (mp 80-82°, lit.[9] 80-81°, 1.1 g, yield = 70%). Mass Spectrum: 112(22), 99(23), 98(51), 83(85), 82(49), 81(34), 71(58), 70(85), 69(86), 68(70), 67(52), 59(28), 58(34), 57(92), 56(72), 55(100), 54(54), 44(40), 43(65), 42(60), 41(92), 33(49).

Dodecane-1,1,1,12,12,12-$^{2}H_6$ -- The bis p-toluenesulfonate of 1,12-dodecanediol-1,1,12,12-$^{2}H_4$ (1.0 g, 2.6 mmoles), prepared in an analogous manner to the ^{13}C-labeled compound, was refluxed in the presence of lithium aluminum deuteride (0.1 g, 2.6 mmoles) and 60 ml of dry ether. After refluxing, with stirring, for 48 hrs the excess reducing agent was destroyed by the addition of dilute hydrochloric acid. The ether layer was removed, dried, and evaporated under vacuum and the product worked up as before (0.12 g, yield = 37%, isotopic enrichment = 98%, mole fractions: $^{2}H_o$ = 0%, $^{2}H_1$ = 0%, $^{2}H_2$ = 0.9%, $^{2}H_3$ = 0.9%, $^{2}H_4$ 0.9%, $^{2}H_5$ =

6.3%, $^{2}H_6$ = 90.7%). Mass spectrum: given in Figure 2.

REFERENCES

1. (a) J. H. Beynon and R. G. Cooks. "Advances in Mass Spectrometry VI", A. R. West (ed.), Applied Science, Barking, Essex, 1974, p. 835.
(b) D. H. Williams, and I. Howe. "Principles of Organic Mass Spectrometry", McGraw-Hill, London (1974).
2. K. Levsen, Org. Mass Spectrometry 10, 43 (1975).
3. A. Streitwieser. "Organic Syntheses with Isotopes, Part II", A. Murray, III, and D. L. Williams (ed.), Interscience Publishers, Inc., New York, 1958, p. 1416.
4. Merck, Sharp and Dohme, Canada Ltd, Isotope Division, Pointe Claire, Quebec, Canada.
5. (a) C. S. Marvel and E. M. McColm, Org. Syntheses 5, 102(1925).
(b) F. B. LaForge, N. Breen, and W. A. Gersdoff, J. Amer. Chem. Soc. 70, 3709(1948).
6. (a), C. F. Lane, J. Org. Chem., 39, 1437(1974).
(b), C. F. Lane and H. Myatt, Technical Report of Aldrich-Boranes, Inc.(1975).
7. J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York and London, 1972, p. 56.
8. R. Bhattacharya, S. R. Saletore, and J. L. Simonsen, J. Chem. Soc. 2678(1928).
9. P. Chuit, Helv. Chim. Acta, 9, 268(1926).