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Steric Interaction between the 1-Methyl and 9-Hydrogen of 1,2,3,4-Tetramethyldibenzofuran[1)]

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Synopsis. 1,2,3,4-Tetramethyldibenzofuran was newly synthesized and the steric interaction between the hydrogen atom at the 9-position and the methyl group at the 1-position was examined from the nuclear Overhauser effects.

Recently, we have reported that the electrophilic substitution on the 1-position of dibenzofuran was hindered sterically by the hydrogen at the 9-position.[2)] This kind of the steric hindrance has never been pointed out in the heteroaromatic compounds such as dibenzofuran, dibenzothiophene, *etc.* In this paper, we wish to report the synthesis of 1,2,3,4-tetramethyldibenzofuran (**5**) and the measurements of the intramolecular nuclear Overhauser effects (NOE) in order to confirm the steric interaction between the hydrogen at the 9-position and the substituent at the 1-position. New compound **5** was synthesized in a 54.4% total yield according to the procedures described in the experimental section. The NMR chart of this compound and the results of the NOE are shown in Fig. 1 and Table 1, respectively. The assignments of the methyl signals were made by the comparison of the spectrum of **5** with those of mono- and polymethyldibenzofurans. The proton or methyl-protons at the 1- and 9-positions of dibenzofuran are most deshielded by the induced ring currents of the outer aromatic and furan rings, followed by those at 4- and 6-positions. For example, the methyl signals of 1-, 2-, 3-, and 4-methyldibenzofurans were observed at δ 2.72, 2.50, 2.48, and 2.58 respectively.[3)]

Saturation of 1-methyl signal resulted in an enhancement of 38% of the integrated area of the multiplet of 9-hydrogen, leaving the other parts of the spectrum unaltered, whereas saturations of [2-methyl+3-methyl] and 4-methyl frequencies had no effect on the signals of the aromatic protons. Irradiation at the [2-methyl+3-methyl] frequencies gave a small increase in the integrated area of the 1-methyl signals. It is clear, from these results, that the methyl group at the 1-position of dibenzofuran affects significantly the hydrogen at the 9-position in the NOE. Martin and Nouls have reported[4)] in the studies on the NOE of overcrowded aromatic hydrocarbons that the proton signals at the 5-position of phenanthrene increased in intensity by 33.5% on saturation of the methyl signal at the 4-position. The steric interaction between the 1- and 9-positions of dibenzofuran is comparable to that between the 4- and 5-positions of phenanthrene. Consequently, we should consider that not only the increase in the electronegativity of the 1-carbon by a strain effect[5)] of the fused ring and the steric hindrance by the hydrogen at the 9-position are responsible for the low reactivity[6)] of the 1-position in electrophilic substitutions of dibenzofuran derivatives.

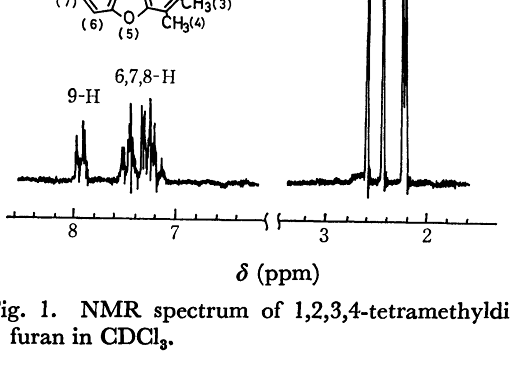

Fig. 1. NMR spectrum of 1,2,3,4-tetramethyldibenzofuran in $CDCl_3$.

Table 1. The results of the NOE measurements

Irradiation protons (δ in $CDCl_3$)	Enhancements of the observed protons[a)] (%) 9-H	1-CH_3	6,7,8-H
1-CH_3 (2.63)	+38		—
[2-CH_3+3-CH_3] (2.26) (2.24)	+ 3	+12	—
4-CH_3 (2.46)	—	—	—

a) Average of 3 runs.

Experimental

Measurements. NMR spectra were measured at 100 MHz on JEOL Co. Model PS-100 spectrometer using TMS as an internal standard. IR and UV spectra were measured with Hitachi EPI-S2 and EPS-2U spectrophotometers, respectively. For NOE measurements, 13% $CDCl_3$ solutions of freshly sublimed **5** were thoroughly degassed under high vacuum. These solutions were studied at 100 MHz by a frequency sweep method. The enhancements of the quotient of the integrated intensities of the observing protons with and without irradiation of the another proton signals.

Synthesis of 5. *2-(2,3,5-Trimethylphenoxy)cyclohexanone (1)*: A solution of α-bromocyclohexanone (prepared from 20 g of cyclohexanone and 36.4 g of *N*-bromosuccinimide in carbon tetrachloride) and sodium 2,3,5-trimethylphenoxide (prepared from 28 g of 2,3,5-trimethylphenol and 4.7 g of sodium) in benzene (200 ml) was shaken for 5 hr at room temperature. The reaction mixture was washed with water, dilute alkali, and water and the solvent was removed. Recrystallization of the residue from methanol gave 31.5 g (66.9%) of **1**. Mp 75—76 °C. IR (cm^{-1}, KBr): 1728, 1157, and

838. Found: C, 77.82; H, 8.52%. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68%.

1,3,4-Trimethyl-6,7,8,9-tetrahydrodibenzofuran (2): A mixture of **1** (20 g), polyphosphoric acid (200 ml), and phosphorus pentaoxide (100 g) was shaken at 100 °C for 3 hr, poured into ice-water, and filtered out. Recrystallization of the product from methanol gave 19.5 g (quantitatively) of **2**. Mp 95—96 °C. IR (cm^{-1}, KBr): 1450, 1215, 1100, and 860. NMR (CCl_4, δ): 6.52 (2-H, s, 1H), 2.60—2.80 (m, 4H), 2.39 (1-CH_3, s, 3H), 2.26 (4-CH_3, s, 3H), 2.22 (3-CH_3, s, 3H), and 1.70—1.90 (m, 4H). Found: C, 84.03; H, 8.54%. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47%.

1,3,4-Trimethyl-2-chloromethyl-6,7,8,9-tetrahydrodibenzofuran (3): **2** (5.0 g) was added to a solution of zinc chloride (0.3 g), formaldehyde (3.0 g, 37%), and concd hydrochloric acid (20 ml) with vigorous stirring. The mixture was kept at 75—80 °C for 10 hr under an introduction of hydrogen chloride, and then, it was filtered out. Recrystallization of the product from ethanol gave 5.8 g (94.8%) of **3**. Mp 131—131.5 °C. IR (cm^{-1}, KBr): 1448, 1322, 1096, and 713. NMR (CCl_4, δ): 4.68 (CH_2Cl, s, 2H), 2.60—2.88 (m, 4H), 2.56 (1-CH_3, s, 3H), 2.37 (4-CH_3, s, 3H), 2.36 (3-CH_3, s, 3H), and 1.80—2.00 (m, 4H). Found: C, 73.25; H, 7.44%. Calcd for $C_{16}H_{19}OCl$: C, 73.13; H, 7.29%.

1,2,3,4-Tetramethyl-6,7,8,9-tetrahydrodibenzofuran (4): A solution of **3** (2.0 g) in dry ether was added to a suspension of lithium aluminum hydride (0.4 g) in dry ether (20 ml) with stirring. The mixture was refluxed for 2 hr, poured into dilute hydrochloric acid, and the ether solution was evaporated to dryness. Recrystallization of the residue from ethanol gave 1.6 g (92%) of **4**. Mp 94—95 °C. IR (cm^{-1}, KBr): 1194 and 1094. NMR (CCl_4, δ): 2.60—2.90 (m, 4H), 2.40 (1-CH_3, s, 3H), 2.33 (4-CH_3, s, 3H), 2.22 (2-CH_3, s, 3H), 2.18 (3-CH_3, s, 3H), and 1.70—2.00 (m, 4H). Found: C, 84.12; H, 8.96%. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83%.

1,2,3,4-Tetramethyldibenzofuran (5): A mixture of **4** (5.0 g) and 5% palladium–charcoal (2.5 g) was heated at 220—230 °C for 3 hr under a slow stream of dry nitrogen, extracted with ether, and the solvent was removed. Recrystallization of the residue from ethanol gave 4.5 g (91%) of **5**. Mp 111—112 °C. IR (cm^{-1}, KBr): 1452, 1223, 1084, and 744. NMR (CCl_4, δ): 7.94 (9-H, m, 1H), 7.00—7.60 (6,7,8-H, m, 3H), 2.63 (1-CH_3, s, 3H), 2.46 (4-CH_3, s, 3H), 2.26 (2-CH_3, s, 3H), and 2.24 (3-CH_3, s, 3H). UV (cyclohexane, nm ($\log \varepsilon$)): 311.8 (3.53), 287 (4.32), 257.6 (4.24), 228.5 (4.59), and 214.6 (4.53). Found: C, 85.52; H, 7.20%. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19%.

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