1,3,5-Trineopentylbenzene

VI.* Long-Range Proton-Fluorine Spin-Spin Coupling in Some Fluorinated 1,3,5-Trineopentylbenzene Derivatives

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Five selected 2-fluoro-1,3,5-trineopentylbenzene derivatives and 3,5-di-*t*-butyl-2-fluoroneopentylbenzene have been prepared and studied by means of PMR spectroscopy. Proton-fluorine spin-spin coupling has been observed between ring fluorine atoms and neopentyl protons separated by six and four bonds.

The numerical value of the coupling constants has been found to increase with the van der Waals volumes of the substituents in the 4- and 6-positions, which is explained by a change in time-averaged conformation of the neopentyl groups.

The six-bond couplings between a fluorine and the *o*-neopentyl protons are discussed in terms of a "through-space" mechanism and the corresponding four-bond couplings in terms of a "through-bond" mechanism.

Continuing work on the conformational behaviour of neopentyl groups has included NMR investigations of hindered rotation [1-3] and measurements of steric hydrogen isotope effects in electrophilic aromatic substitution [4-6] in 1,3,5-trineopentylbenzene and its derivatives. In connection with this work it was considered of interest to study long-range proton-fluorine spin-spin coupling between a ring fluorine and the *t*-butyl protons in the *ortho* neopentyl groups in fluoro-substituted derivatives of 1,3,5-trineopentylbenzene.

Proton-fluorine spin-spin coupling has been observed between ring fluorine atoms and side-chain protons in *o*-fluoroalkylaromatics over four to six bonds. [7-13] It has been suggested that spin-spin interaction of this type involves both "through-space" and "through-bond" terms in differing proportions.***

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*** For leading references, see Ref. 12.

Proximity of the nuclei appears to be a necessary condition for the "through-space" interaction. The magnitude of the five-bond proton-fluorine coupling constants ($^5J_{HF}$) in some 2,4,6-trialkylhalobenzenes was shown to be extremely sensitive to the internuclear separation of the interacting nuclei.[10] The magnitude of the six-bond coupling constants ($^6J_{HF}$) in the fluoro derivatives of 1,3,5-trineopentylbenzene (1) should thus give a measure of the conformational dependence of a neopentyl group with respect to the buttressing effect of *ortho* substituents (X) with fluorine as the common reference.
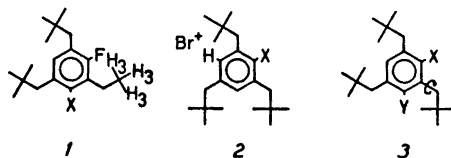
The van der Waals volume of fluorine (5.80 cm³/mol) is comparatively close to the volume of a proton (3.4 cm³/mol),* while other substituents have a volume of 10 − 20 cm³/mol.[14] This means that the picture of the conformational behaviour of a neopentyl group acquired from such spin-spin coupling measurements should be closely related to results obtained from other studies of conformationally dependent properties of the neopentyl groups in 1,3,5-trineopentylbenzene systems containing hydrogen instead of fluorine.

Among these studies, measurements of hydrogen isotope effects in the bromination of some 2-halo-1,3,5-trineopentylbenzenes (2, X=Cl, Br, I) have shown that their strength depends on the size of the halo substituent.[4] This steric repulsion effect probably has a large conformational contribution, involving torsion of a neopentyl group towards the site of reaction.

Additional results that are pertinent in the present context have been obtained from studies on hindered rotation of the 3-neopentyl group in some 2-X-4-Y-1,3,5-trineopentylbenzenes (3, X=Cl, Br, I; Y=Cl, Br).[3] The major part of the rotational barrier is considered to be due to the steric effect of the substituents X and Y.[1] The measured activation parameters therefore provide an estimate of the effective size of the substituents with respect to the passage of a neopentyl group.


DISCUSSION OF SYNTHESES

Initial efforts to prepare 2-fluoro-1,3,5-trineopentylbenzene (1, X = H) were unsuccessful. Attempted Schiemann decomposition of 2,4,6-trineopentyl-benzenediazonium tetrafluoroborate resulted in a ring-closure reaction yielding 2,2-dimethyl-4,6-dineopentylindane, as in the thermal decomposition of the corresponding hydrogen sulphate.[15] The idea of substituting fluoride nucleo-

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* Calculated as the difference in volume between aromatic − CH− and − C− units, Table 14.4 in Ref. 14.

philicly for bromide in 2-bromo-1,3,5-tripivaloylbenzene, followed by subsequent reduction to yield 2-fluoro-1,3,5-trineopentylbenzene, could never be carried out because all efforts to prepare the brominated 1,3,5-tripivaloylbenzene [16] were fruitless.

Recently a new method of fluorinating aromatics with xenon difluoride was published by Shaw *et al.*[17] Dr. Shaw kindly agreed to test the usefulness of xenon difluoride as a fluorinating agent on a small sample of 1,3,5-trineopentylbenzene. A very small amount (2 % yield) of 2-fluoro-1,3,5-trineopentylbenzene could be isolated in pure form after a complicated separation from the crude reaction product, which contained 41 % of the desired fluoro compound.[18]

Since the present study was intended to deal primarily with derivatives of 2-fluoro-1,3,5-trineopentylbenzene the problems of separation were solved in an indirect way. The crude product from a fluorination of 1,3,5-trineopentylbenzene, obtained from Dr. Shaw, was reacted with the appropriate reagent — "bromonium perchlorate" ($Br_2/AgClO_4$), *t*-butylhypochlorite or nitric acid. The resulting product mixtures could be separated more easily than the starting
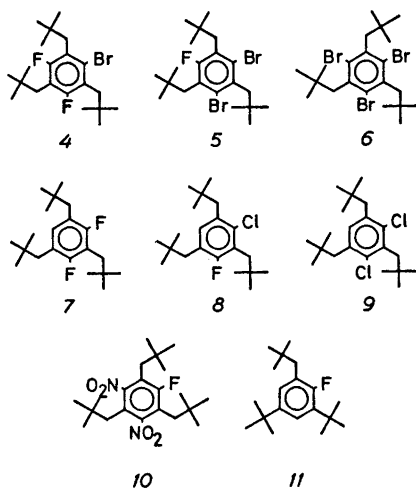
material by preparative GLC. In this way 2-bromo-4,6-difluoro-1,3,5-trineopentylbenzene (*4*), 2,4-dibromo-6-fluoro-1,3,5-trineopentylbenzene (*5*), and 2,4,6-tribromo-1,3,5-trineopentylbenzene (*6*) could be isolated from the brominated product. 2,4-Difluoro-1,3,5-trineopentylbenzene (*7*), 2-chloro-4-fluoro-1,3,5-trineopentylbenzene (*8*), and 2,4-dichloro-1,3,5-trineopentylbenzene (*9*) were isolated from the chlorinated product. Only one product, 2-fluoro-1,3,5-trineopentyl-4,6-dinitrobenzene (*10*) was isolated in pure form from the nitrated product.

Due to the difficulties in the preparation of 2-fluoro-1,3,5-trineopentylbenzene, parallel efforts to prepare 3,5-di-*t*-butyl-2-fluoroneopentylbenzene (*11*) from available 3,5-di-*t*-butyl-2-fluorotoluene were initiated according to a sug-

gestion by Professor Philip C. Myhre. This o-fluoroneopentylbenzene derivative was designed with the two t-butyl groups in order to direct further substitution into the 6-position. In this way molecules with the desired arrangement of a fluorine and another substituent *ortho* to the neopentyl group would be available. However, this project was not pursued further than to the preparation of 3,5-di-t-butyl-2-fluoroneopentylbenzene (11), which was used in place of 2-fluoro-1,3,5-trineopentylbenzene for the determination of the coupling constants in a neopentyl group surrounded by a proton and a fluorine. The latter compound was not available in the present investigation, but its PMR spectrum has been reported.[18] 3,5-Di-t-butyl-2-fluoroneopentylbenzene has the advantage over 2-fluoro-1,3,5-trineopentylbenzene of having only one neopentyl group. Thus there is no problem with partly overlapping neopentyl peaks in its PMR spectrum as in the trineopentylbenzene derivative.[18]

RESULTS AND DISCUSSION

The fluoro-substituted trineopentylbenzene derivatives have been studied by means of PMR. Observed PMR data are summarized in Table 1.

The 60 MHz PMR spectrum at 40°C of 2,4-dibromo-6-fluoro-1,3,5-trineopentylbenzene (5) in CCl_4 is shown in Fig. 1. There are three equally intense
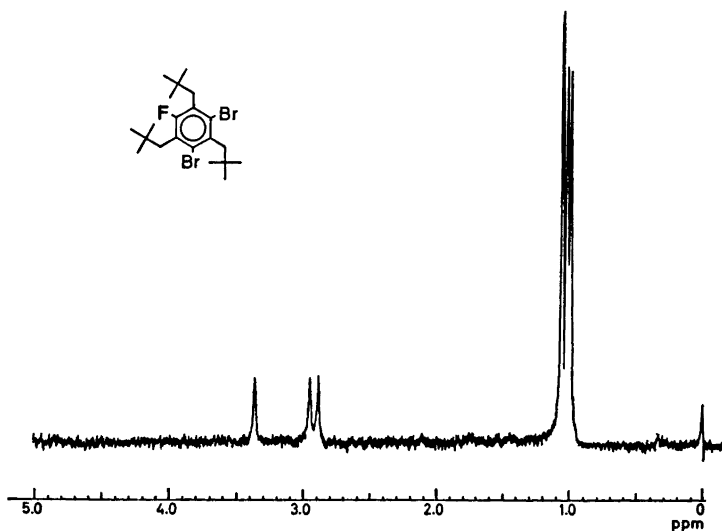

Fig. 1. 60 MHz PMR spectrum at 40°C of 2,4-dibromo-6-fluoro-1,3,5-trineopentylbenzene (5) in CCl_4.

t-butyl resonances and three equally intense methylene resonances. A fluorine decoupling experiment, carried out at 100 MHz with a decoupling frequency of 6205 Hz, caused the up-field pairs in each set of peaks to collapse to a singlet. This enabled the assignment of the t-butyl doublet ($|{}^6J_{HF}| = 1.7$ Hz)

Table 1. Characteristic PMR data of fluoroneopentylbenzene derivatives in CCl$_4$ at about 40°C.

Number	Compound	Chemical shift in ppm, multiplicity, numerical value of coupling constant in Hz and number of corresponding protons		
		Aromatic	Methylene	t-Butyl
4	2-Bromo-4,6-difluoro-1,3,5-trineopentylbenzene	—	2.87,m,4H 2.57,t,J_{HF}=2.0,2H	1.00,broad,$\Delta\nu_{1/2}$=2.7,18H 0.97,t,Jhf=1.2,9H
5	2,4-Dibromo-6-fluoro-1,3,5-trineopentylbenzene	—	3.34,s,2H 2.92,d,J_{HF}=3.6,4H	1.06,s,9H 1.02,d,J_{HF}=1.7,18H
7	2,4-Difluoro-1,3,5-trineopentylbenzene	6.72,t,J_{HF}=8.3,1H	2.57,t,J_{HF}=2.0,2H	0.94,t,J_{HF}=1.2,9H
8	2-Chloro-4-fluoro-1,3,5-trineopentylbenzene	6.82,d,J_{HF}=8.3,1H	2.47,broad,$\Delta\nu_{1/2}$=3.2,4H 2.84,d,J_{HF}=3.2,2H 2.73,s,2H	0.92,broad,$\Delta\nu_{1/2}$=2.0,18H 1.01,d,J_{HF}=1.7,9H 0.99,s,9H
10	2-Fluoro-1,3,5-trineopentyl-4,6-dinitrobenzene	—	2.52,d,J_{HF}=1.9,2H 2.79,s,2H 2.74,d,J_{HF}=3.0,4H	0.97,d,J_{HF}=0.9,9H 0.93,d,J_{HF}=1.6,18H 0.83,s,9H
11	3,5-Di-t-butyl-2-fluoro-neopentylbenzene	7.09,q,J_{HF}=8.0,J_{HH}=2.8,1H 6.88,q,J_{HF}=7.1,J_{HH}=2.8,1H	2.52,d,J_{HF}=2.1,2H	0.92,d,J_{HF}=0.9,9H
—	2-Fluoro-1,3,5-trineo-pentylbenzene [a]	6.65,d,J_{HF}=7.4,2H	2.48,d,J_{HF}=2,4H 2.38,s,2H	0.91,s,18H 0.89,s,9H

[a] Taken from Ref. 18.

at 1.02 ppm to the 1- and 5-neopentyl groups, while the singlet at 1.06 ppm was assigned to the t-butyl moiety of the 3-neopentyl group. Similarly, the methylene doublet ($|{}^4J_{HF}| = 3.6$ Hz) at 2.92 ppm was assigned to the 1- and 5-neopentyl groups and the methylene singlet at 3.34 ppm was assigned to the 3-neopentyl group. To summarize, the neopentyl group $para$ to the fluorine showed no multiplicity, but the t-butyl protons as well as the methylene protons in the neopentyl groups between the fluorine and a bromine showed coupling to the fluorine.

It is interesting to compare these coupling constants with those found for a neopentyl group surrounded by a proton and a fluorine. As mentioned above 3,5-di-t-butyl-2-fluoroneopentylbenzene (11) was studied for this purpose and the values found, $|{}^6J_{HF}| = 0.9$ Hz and $|{}^4J_{HF}| = 2.1$ Hz, showed that the substitution of a bromine for a proton caused an increase in the coupling constants. The published PMR data for 2-fluoro-1,3,5-trineopentylbenzene [18] did not contain any report of a six-bond coupling, possibly due to partly overlapping t-butyl resonances.

2-Fluoro-1,3,5-trineopentyl-4,6-dinitrobenzene (10) gave a PMR spectrum of the same type as that of 2,4-dibromo-6-fluoro-1,3,5-trineopentylbenzene (5). The 1- and 3-neopentyl groups gave rise to a t-butyl doublet ($|{}^6J_{HF}| = 1.6$ Hz) at 0.93 ppm and a methylene doublet ($|{}^4J_{HF}| = 3.0$ Hz) at 2.74 ppm, while the 5-neopentyl group was represented by singlets at 0.83 and 2.79 ppm. These assignments were made by running spectra at different field strengths and observing the field-independent spacings. The six-bond as well as the four-bond coupling constants were somewhat smaller in the dinitro than in the dibromo compound.
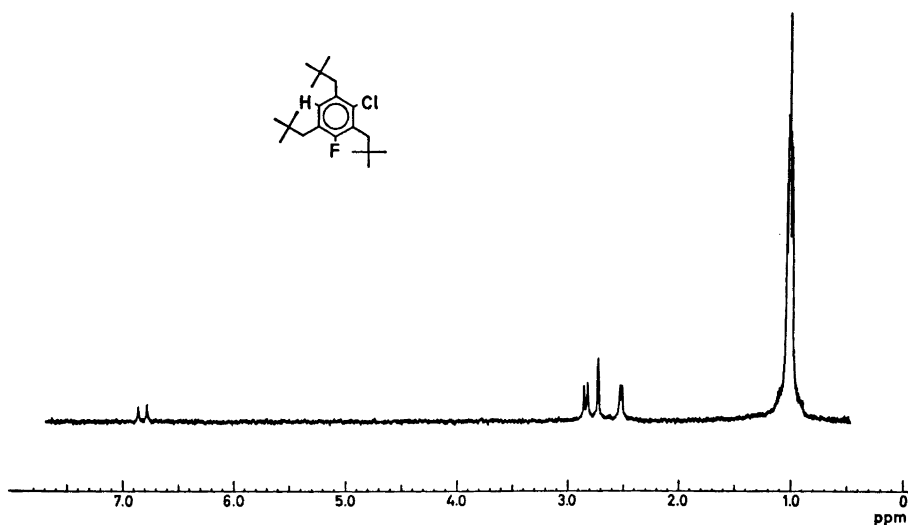

Fig. 2. 100 MHz PMR spectrum at 25°C of 2-chloro-4-fluoro-1,3,5-trineopentylbenzene (8) in CCl$_4$.

2-Chloro-4-fluoro-1,3,5-trineopentylbenzene (8) offered the opportunity to observe coupling constants in two neopentyl groups with dissimilar surroundings in the same molecule. The 100 MHz PMR spectrum at 25°C in CCl_4 is shown in Fig. 2. There are five t-butyl and five methylene resonances besides an aromatic doublet at 6.82 ppm ($|J_{HF}| = 8.3$ Hz). The t-butyl and methylene regions are expanded in Fig. 3. The t-butyl resonances were assigned from a
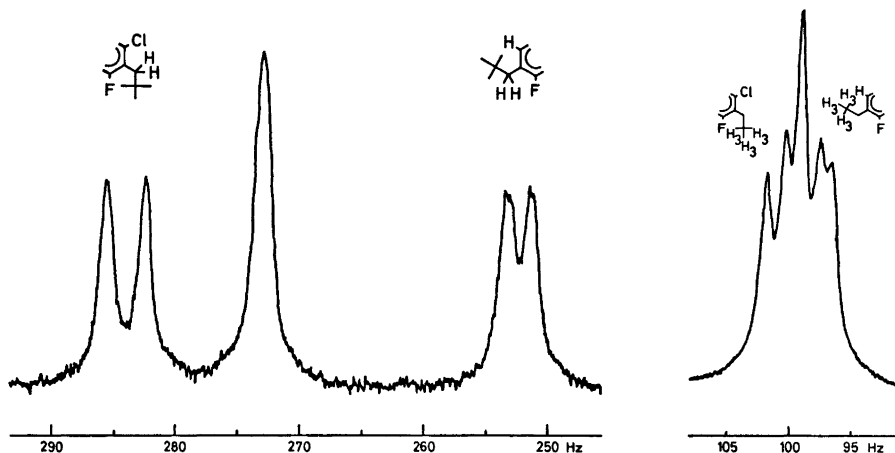

Fig. 3. Expanded (100 Hz sweep width) t-butyl and methylene regions of the 100 MHz PMR spectrum of 2-chloro-4-fluoro-1,3,5-trineopentylbenzene (Fig. 2).

comparison of the chemical shift of *ortho* neopentyl protons by fluorine [18] and by chlorine [19] in the following way: A doublet ($|^6J_{HF}| = 0.9$ Hz) at 0.97 ppm from the 5-neopentyl group, a singlet at 0.99 ppm from the 1-neopentyl group (*para* to the fluorine), and a doublet ($|^6J_{HF}| = 1.7$ Hz) at 1.01 ppm from the 3-neopentyl group. The methylene resonances were assigned analogously: a doublet ($|^4J_{HF}| = 1.9$ Hz) at 2.52 ppm, a singlet at 2.73 ppm, and a doublet ($|^4J_{HF}| = 3.2$ Hz) at 2.84 ppm from the 5-, 1-, and 3-methylene groups, respectively. Again it was observed that the coupling constants between fluorine and the protons of the 3-neopentyl group, which is buttressed by the chlorine, were larger than the coupling constants in the 5-neopentyl group, which is next to the proton.

The two difluoro derivatives investigated gave the following 100 MHz PMR patterns at 25°C. 2,4-Difluoro-1,3,5-trineopentylbenzene (7) exhibited a t-butyl triplet ($|^6J_{HF}| = 1.2$ Hz) at 0.94 ppm and a methylene triplet ($|^4J_{HF}| = 2.0$ Hz) at 2.57 ppm, by symmetry assigned to the 3-neopentyl group. This neopentyl group is thus spin-spin coupled to two o-fluorines. The 1- and 5-neopentyl groups gave a broad t-butyl resonance ($\Delta \nu_{1/2} = 2.0$ Hz) at 0.92 ppm and a broad methylene resonance ($\Delta \nu_{1/2} = 3.2$ Hz) at 2.47 ppm, which were not resolved. If the methylene resonance is assumed to be the A_2A_2' part of an $A_2XX'A_2'$ system, this would imply that the methylene protons are coupled to the *ortho* as well as to the *para* fluorine, although there was no detectable

para coupling in the *mono*fluorotrineopentylbenzenes. In analogy to this it has been reported that the methyl protons of pentafluorotoluene show a doublet ($J_{HF}^{para} = 1.5$ Hz) of triplets ($J_{HF}^{ortho} = 2.5$ Hz).[8] A similar value has also been reported for p-fluorotoluene, $J_{HF}^{para} = 0.9$ Hz.[8] It is unknown, however, what caused the broadening of the t-butyl resonance at 0.92 ppm. There was also an aromatic triplet ($|J_{HF}| = 8.3$ Hz) at 6.72 ppm. Interestingly, the 3-neopentyl group, which is situated between two fluorines, gave a $|^4J_{HF}|$ that was very similar to that measured for a neopentyl group between a fluorine and a proton. This was also true — to a somewhat smaller degree — of the $|^6J_{HF}|$ and is considered to reflect the similarity in spatial requirements of a proton and a fluorine.

2-Bromo-4,6-difluoro-1,3,5-trineopentylbenzene (*4*) also exhibited two t-butyl absorptions at 100 MHz and 25°C: A triplet ($|^6J_{HF}| = 1.2$ Hz) at 0.97 ppm from the 5-neopentyl group and a poorly resolved resonance ($\Delta v_{1/2} = 2.7$ Hz) at 1.00 ppm from the 1- and 3-neopentyl groups. There were also two methylene absorptions: A triplet ($|^4J_{HF}| = 2.0$ Hz) at 2.57 ppm from the 5-methylenes and a multiplet at 2.87 ppm from the 1- and 3-methylenes. This multiplet may be the A_2A_2' part of an $A_2XX'A_2'$ system, in analogy with the unbrominated difluoro compound *7*. It is again unknown what caused the t-butyl resonance to be unresolved. The exact agreement between the coupling constants measured in the two difluoro compounds is worthy of note.

A comparison of all measured coupling constants and the van der Waals volumes of the buttressing substituents is made in Table 2. The last entry in

Table 2. Heteronuclear coupling constants in fluoroneopentylbenzene derivatives and van der Waals volumes of the buttressing substituents.

Environment of neopentyl group		$|^6J_{HF}|$	$|^4J_{HF}|$	van der Waals volume $(cm^3/mol)^a$
H	F	0.9	1.9 − 2.1	3.4^b
F	F	1.2	2.0	5.80
Cl	F	1.7	3.2	12.00
Br	F	1.7	3.6	15.12
NO_2	F	1.6	3.0	—
max ^{c}	F	2.2	—	—

^{a} Taken from Ref. 14. ^{b} Calculated as the difference in volume between aromatic −CH− and −C− units, Table 14.4 in Ref. 14. ^{c} Taken from the bicyclic compound *12* with a locked neopentyl group (see text).

the table is an estimate of the maximum six-bond coupling constant for a neopentyl group locked in the ring-plane over the fluorine with the t-butyl group freely rotating. It is taken from the value reported by Heaney *et al.*[11] for the bicyclic compound *12*. The numerical value of the coupling constant was 2.2 Hz at temperature when the t-butyl group was freely rotating.

The correlation of the numerical value of the coupling constants and the van der Waals volumes of the substituents seen in Table 2 is most easily ex-
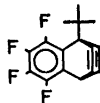
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plained in terms of a change in time-averaged conformation of the neopentyl group. Studies on hindered rotation in 1,3,5-trineopentylbenzene derivatives have shown that a neopentyl group readily passes a proton or a fluorine at temperatures around room temperature, whereas a substituent with greater spatial demands such as chlorine, bromine, or a nitro group interacts markedly and hinders the passage of the neopentyl group.[1] Application of this reasoning to a neopentyl group which is surrounded by a fluorine and a larger substituent indicates that the *t*-butyl protons come closer to fluorine when the size of the non-fluorine substituent increases.

This proximity condition together with the single-bond character of the bonds in the neopentyl group strongly suggest a "through-space" mechanism for the spin-spin coupling. The relatively small numerical value of the $^6J_{HF}$ measured in this study compared to those recently reported in derivatives of 4-fluoro-5-methylfluorene (up to 8.3 Hz) [12] and in derivatives of 4-fluoro-5-methylphenanthrene (up to 11.9 Hz) [13] can depend on many factors. To start with, the maximum coupling constant contribution of *one* of the methyl groups in the neopentyl group may be taken as three times the observed coupling constant, *cf.* Ref. 10. The resulting values of $2.7 - 5.1$ Hz should be used in a comparison with the values found in the fluorene and phenanthrene derivatives. Also, the fluorine and the methyl group may be forced into closer contact in the fluorene and phenanthrene derivatives, although the distance of closest approach between the fluorine and a proton (measured with Dreiding models) was reported to be about 1.44 Å in 4-fluoro-5-methylfluorene [12] and about 0.4 Å in 4-fluoro-1,5,8-trimethylphenanthrene,[13] while there is full contact between the fluorine and a methyl proton in corresponding models of 2-fluoro-1,3,5-trineopentylbenzene. Still, the much higher flexibility of the neopentyl group and the probable intermeshing of the *t*-butyl group with the fluorine will increase the effective distance of closest approach between the fluorine and a proton in the 2-fluoro-1,3,5-trineopentylbenzene derivatives.

There is a report of six-bond proton-fluorine couplings in *o*-fluoro-*N*,*N*-dimethylbenzamide ($|^6J_{HF}| = 1.2$ Hz) and *o*-fluoro-*N*-cyclohexyl-*N*-methyl-benzamide ($|^6J_{HF}| = 1.3$ Hz).[20] A comparison between these and the six-bond couplings found in the present study is considered somewhat uncertain due to the π-system in the dialkylamido groups. Although the flat dimethylamido group is reported to be slightly (about 25°) turned out of the plane of the benzene ring by the fluorine, there should be considerable overlap with the aromatic π-system, facilitating "through-bond" contributions to the coupling.

The relatively small $|^6J_{HF}|$ reported for a *t*-butyl group in intimate * contact

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* The *t*-butyl group in *12* was reported to be freely rotating only at temperatures near 200°C.[11] Dreiding models indicate that the distance of closest approach between the fluorine and a proton in *12* is very similar to the corresponding distance in 4-fluoro-1,5,8-trimethylphenanthrene, about 0.4 Å.

with a fluorine in *12*[11] may indicate that there is some "through-bond" contribution to the coupling in the fluorene and phenantrene derivatives. The methyl protons in these derivatives are benzylic, which should facilitate transmission of spin information through the bonds, *cf.* the benzylic *para* couplings to the fluorine discussed above.

The benzylic four-bond proton-fluorine couplings found in this study may be seen from Table 2 to increase with the size of the buttressing substituent. This must mean that there is an inverse dependence of these J_{HF}'s on the proximity of the fluorine to the benzylic protons, because this internuclear distance increases when a larger substituent turns the *t*-butyl moiety of the neopentyl group towards the fluorine.* Although proximity might not be the only important factor for large long-range coupling through space, the observed inverse dependence strongly suggests a different and most probably a "through-bond" mechanism for the benzylic couplings in contrast to the *t*-butyl couplings.

A comparison of the coupling constants over six bonds measured in this study with those over five bonds measured by Myhre *et al.*[10] in some fluorinated 1,3,5-triethyl-, 1,3,5-triisopropyl- and 1,3,5-tri-*t*-butylbenzenes is made in Table 3. It seems too early to draw any other conclusions from this comparison than to say that the marked sensitivity to internuclear separation previously found for the $^5J_{HF}$'s is paralleled among the $^6J_{HF}$'s.

Table 3. Long-range coupling constants ($|^5J_{HF}|$ and $|^6J_{HF}|$) in some 2-fluoro-1,3,5-trialkylbenzene derivatives.

Environment of alkyl group		Ethyl [a]	Isopropyl [a]	*t*-Butyl [a]	Neopentyl [b]
H	F	0.3	0.3	0.9	0.9
F	F	—	0.7	—	1.2
Cl	F	—	1.8	4.2 [c]	1.7
Br	F	—	1.9	4.2	1.7
NO$_2$	F	—	—	1.9	1.6

[a] Taken from Ref. 10. [b] This study. [c] Taken from Tilley, J. W., Senior Thesis, Harvey Mudd College 1968 (unpublished results).

A priori, there appeared to be an interesting possibility of observing the individual coupling constants J_{AX} and J_{BX} for the magnetically nonequivalent methylene protons A and B at low temperatures in 2,4-dibromo-6-fluoro-1,3,5-trineopentylbenzene (*5*).

It is known from studies of hindered rotation that the neopentyl group between two bromines in 2,4-dibromo-1,3,5-trineopentylbenzene (*3*, X = Y = Br) rotates slowly on the NMR time-scale, at some temperatures causing observable magnetic nonequivalence between the methylene protons in the other two neopentyl groups.[1] 2,4-Dibromo-6-fluoro-1,3,5-trineopentylbenzene (*5*)

* Similar observations have been made in some other 2-fluoro-1,3,5-trialkylbenzenes by Professor Philip C. Myhre (personal communication).

should show similar rotational behaviour and under the proper conditions the 1- and 5-methylene protons should be observable as the A_2B_2 part of an A_2B_2X system. (Under conditions when the 1- and 5-neopentyl groups would rotate slowly as well, low-energy rotamers (Fig. 4) should give rise to

Fig. 4. A low-energy rotamer of 2,4-di-bromo-6-fluoro-1,3,5-trineopentylbenzene (*5*) with all three neopentyl groups in frozen conformations, showing the magnetically nonequivalent methylene protons H_A, H_B, H_C and H_D.
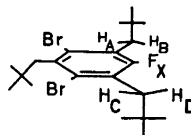
ABCDX systems as well.[1]) The signs of J_{AX} and J_{BX} might be determined by relating them to the known negative sign of J_{AB}. A complementary study of the X part of the A_2B_2X (or ABCDX) system by means of proton-decoupled ^{19}F NMR spectroscopy would also be helpful in this context.

When 2,4-dibromo-6-fluoro-1,3,5-trineopentylbenzene was studied at 60 or 100 MHz in a temperature region where the rotation of the 3-neopentyl group is frozen, however, there was no observable magnetic nonequivalence in the 1- and 5-methylene groups. Evidently the chemical shift difference between the geminal methylene protons was not large enough to permit their individual observation in the low-energy rotamer. Not even the use of a field strength of 220 MHz (17°C) enabled a complete resolution of the methylene spectrum, but a poorly resolved pattern of four closely spaced lines resulted.

To solve this problem one would have to study a 2-fluoro-1,3,5-trineopentyl-benzene derivative with 4- and 6-substituents, which differ still more from fluorine in shielding properties than bromine does. However, preliminary PMR studies of an additional compound, 2-fluoro-1,3,5-trineopentyl-4,6-dinitrobenzene (*10*), have been discouraging in this respect.

EXPERIMENTAL

The PMR spectra were recorded on Varian A-60, HA-100 or HR-220 spectrometers equipped with Varian variable temperature controllers. The 220 MHz spectrometer was located at the California Institute of Technology. TMS was used as internal standard for the shift measurements and for the purpose of signal-locking, when needed. Coupling constants are given as the average of the peak-to-peak separations measured in several spectra recorded with expanded sweep width. The effect of imperfect resolution on the apparent magnitude of splitting [21] has been taken into account.

Preparative GLC was carried out on an Aerograph A-700 Autoprep equipped with an SE-30 column, 10 ft. × 3/8 in. at 200 − 250°C and 180 ml min⁻¹ of helium. Generally the recovery of the 1,3,5-trineopentylbenzene derivatives from the gas phase was rather low, of the order of 40 %, due to aerosol formation. These aerosols could not be broken by methods that gave good results with 1,3,5-tri-*t*-butylbenzene derivatives under identical GLC conditions.

1,3,5-Trineopentylbenzene was prepared as previously described.[22]

2 - F l u o r o - 1,3,5 - t r i n e o p e n t y l b e n z e n e   d e r i v a t i v e s

The fluorination of 10.9 g (37.8 mmol) of 1,3,5-trineopentylbenzene with 8.5 g (50.2 mmol) of xenon difluoride in 50 ml of carbon tetrachloride (with 4.8 mmol of added hy-

drogen fluoride) was kindly performed by Dr. Shaw according to his published procedure.[18] The crude reaction product was sublimed *in vacuo*, and 4.8 g of a white semi-solid was collected. The three major components, identified by their further substitution products (see below) as unreacted 1,3,5-trineopentylbenzene, 2-fluoro-1,3,5-trineopentylbenzene and 2,4-difluoro-1,3,5-trineopentylbenzene, were present in amounts of 15 %, 60 %, and 15 %, respectively, according to GLC. (The remainder was composed of a number of components, which were not characterized.) This mixture withstood all efforts at separation with reasonable recovery. It was used in its impure state in the following preparations and is referred to as "the fluorinated mixture".

   Perbromination of the fluorinated mixture with bromine and silver perchlorate in acetic acid-dioxane at room temperature yielded as the major products *2-bromo-4,6-difluoro-1,3,5-trineopentylbenzene* (4), *2,4-dibromo-6-fluoro-1,3,5-trineopentylbenzene* (5) and *2,4,6-tribromo-1,3,5-trineopentylbenzene* (6). This product composition supports the assumed composition of the starting material. Smaller amounts of other products, which were not fully characterized but indicated by PMR to contain acetoxy groups, were also present. Acetoxylation may have occurred by the addition-elimination mechanism, which has been suggested to govern the acetoxylation accompanying halogenation of 1,3,5-tri-*t*-butylbenzene.[23]

   A solution of 0.92 g (about 3 mmol) of the fluorinated mixture in 5 ml of dioxane was mixed with a solution of 1.39 g (6.8 mmol) of silver perchlorate in 25 ml of acetic acid. To the resulting solution 1.1 g (6.9 mmol) of bromine in 10 ml of acetic acid was added in one portion. The solution was stirred magnetically in the dark at room temperature for 5 h before it was filtered. The precipitate was triturated with 100 ml of cyclohexane, in small portions, on the filter, and the cyclohexane solution was combined with the filtrate. The combined organic solutions were washed with dilute sodium hydroxide (10 %) followed by water to neutral reaction. After drying over magnesium sulphate and evaporation, the crude product weighed about 1.4 g and was shown by GLC to contain essentially three components in roughly the same proportions as the three major components of the starting material. Enrichment of the two components with longer retention times could be achieved, at the expense of the component with shortest retention time, by recrystallization from ethanol, but preparative GLC had to be used to obtain pure materials. The PMR spectra of (4) and (5) are reported in Table 1. The PMR spectrum of 2,4,6-tribromo-1,3,5-trineopentylbenzene (6) in carbon tetrachloride contained a *t*-butyl singlet at 1.09 ppm and a methylene singlet at 3.43 ppm.

   Monochlorination of the fluorinated mixture was carried out with 1 mol of *t*-butyl hypochlorite in acetic acid at room temperature. The three major products, isolated by preparative GLC, were *2,4-difluoro-1,3,5-trineopentylbenzene* (7), *2-chloro-4-fluoro-1,3,5-trineopentylbenzene* (8), and *2,4-dichloro-1,3,5-trineopentylbenzene* (9). This composition of the product also contributes to the determination of the composition of the starting material.

   To a solution of 306 mg (about 1 mmol) of the fluorinated mixture in 10 ml of acetic acid 0.4 ml (3.5 mmol) of *t*-butylhypochlorite was added in one portion. The solution was stirred at room temperature for 5 h before it was diluted with 200 ml of water and extracted with cyclohexane. The organic phase was dried over magnesium sulphate and the solvent was evaporated. The remaining 370 mg was separated by preparative GLC. The PMR spectra of (7) and (8) are reported in Table 1. The PMR spectrum of (9) has been reported previously.[19]

   Dinitration of the fluorinated mixture was achieved with an excess of fuming (90 %) nitric acid. The only component of the crude reaction product that was isolated in pure form was *2-fluoro-1,3,5-trineopentyl-4,6-dinitrobenzene* (10). The other compounds could not be separated on the available preparative GLC columns.

   To 0.92 g (about 3 mmol) of the fluorinated mixture 25 ml of fuming (90 %) nitric acid was added dropwise at 0°C. The resulting mixture was stirred magnetically during the period of addition and for another 5 h, while the temperature was allowed to slowly reach room temperature. The mixture was poured into 200 ml of water and extracted with cyclohexane. The organic phase was dried over magnesium sulphate and evaporated to yield 1.1 g of crude product. Preparative GLC yielded pure (10). Its PMR spectrum is given in Table 1.

3,5 - D i - *t* - b u t y l - 2 - f l u o r o n e o p e n t y l b e n z e n e *(11)*

1-Bromomethyl-3,5-di-t-butyl-2-fluorobenzene was prepared by benzylic bromination of 3,5-di-*t*-butyl-2-fluorotoluene, kindly supplied by Professor Philip C. Myhre.

A mixture of 30.0 g (0.135 mol) of 3,5-di-*t*-butyl-2-fluorotoluene, 18.0 g (0.101 mol) of *N*-bromosuccinimide and 0.1 g of benzoylperoxide in 400 ml of freshly distilled carbon tetrachloride was refluxed until no more *N*-bromosuccinimide remained at the bottom of the flask (about 4 h). Filtration yielded about 13 g of succinimide and evaporation of the filtrate yielded about 41 g of an oil, which was distilled *in vacuo*. After a forerun of unreacted starting material the bromo compound was collected at 135 – 138°C (6 torr). The yield was 21.9 g (72 % calculated on *N*-bromosuccinimide).

3,5-Di-t-butyl-2-fluoroneopentylbenzene (11) was obtained from the reaction of the Grignard reagent of 1-bromomethyl-3,5-di-*t*-butyl-2-fluorobenzene with *t*-butyl chloride in low yield.

In a 50 ml round-bottomed two-necked flask 0.12 g (5 mmol) of magnesium was covered with 5 ml of anhydrous ether under nitrogen. A solution of 1.48 g (4.5 mmol) of 1-bromomethyl-3,5-di-*t*-butyl-2-fluorobenzene in 10 ml of anhydrous ether was added dropwise very slowly with stirring. The mixture was refluxed for 4 h before 0.46 g (0.55 ml, 5 mmol) of *t*-butyl chloride was added dropwise very slowly. A catalytic amount of cobalt(II) carbonate was added and the mixture was refluxed for 8 h. Saturated aqueous ammonium chloride solution was added and the phases were separated. The aqueous phase was extracted with ether and the combined ether phases were washed with water, dilute sodium hydrogen carbonate and water again. Drying over magnesium sulphate and evaporation left a brown oil, which slowly crystallized. The solid was filtered off and recrystallized from ethanol – benzene (1:1) to yield 1,2-bis(2-fluoro-3,5-di-*t*-butyl-phenyl)ethane. PMR (CCl$_4$): 1.25 (s, 18H, 5-*t*-butyl), 1.40 (d, $|J_{HF}|=1.0$ Hz, 18H, 3-*t*-butyl), 2.99 (broad, $\Delta v_{1/2}=2.9$ Hz, 4H, methylene), 7.01 (q, $|J_{HH}|=2.8$ Hz, $|J_{HF}|=7.0$ Hz, 2H, 4-H-aromatic), 7.23 (q, $|J_{HH}|=2.8$ Hz, $|J_{HF}|=8.1$ Hz, 2H, 4-H-aromatic).

The filtrate was chromatographed on a column of alumina. Elution with pentane yielded a mixture of compounds, which had as the major components 3,5-di-*t*-butyl-2-fluoroneopentylbenzene and 3,5-di-*t*-butyl-2-fluorotoluene. Distillation afforded a 90 % pure sample of the neopentyl derivative, which was used in the determination of its PMR spectrum (Table 1). The PMR spectrum of 3,5-di-*t*-butyl-2-fluorotoluene in carbon tetrachloride had the following characteristics: 1.28 (s, 9H, 5-*t*-butyl), 1.37 (d, $|J_{HF}|=0.9$ Hz, 9H, 3-*t*-butyl), 2.21 (d, $|J_{HF}|=2.6$ Hz, 3H, methyl), 6.93 (q, $|J_{HH}|=2.7$ Hz, $|J_{HF}|=7.2$ Hz, 1H, 6-H-aromatic), 7.06 (q, $|J_{HH}|=2.7$ Hz, $|J_{HF}|=7.9$ Hz, 1H, 4-H-aromatic).

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