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STRUCTURAL STUDIES ON THE ISOMERS OF TRIPLY BRIDGED RING SUBSTITUTED DIFLUOROTRITHIACYCLOPHANES USING ^{1}H AND ^{19}F NMR SPECTROSCOPY

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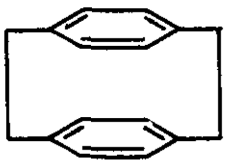
Abstract - The isomeric 5,16- and 7,16-difluoro-2,11,20-trithia[3.3.3]-(1,3,5)cyclophanes were obtained in good yields from a single coupling reaction. Their structures were readily characterized by ^{1}H nmr studies. Comparison of the ^{19}F nmr data helps to suggest a possible ring staggered conformation for the reported 9,18-difluoro-2,11-dithia[3.3]metacyclophane.

The unique properties of [2.2]paracyclophane 1 reported by Cram[1] have undoubtedly led to the studies of a series of cyclophanes with the two benzene rings held face-to-face rigidly by multiple bridges.[2] The ultimate climax was represented by the synthesis of superphane 2.[3] Crystallographic data have shown that the aromatic rings of superphane 2 are planar.[4] However, the benzene rings in [2.2]paracyclophane 1 are not flat with the C-1 and C-4 ring atoms tilted out of the C-2, C-3, C-5, C-6 plane.[5] On the other hand, [2.2.2](1,3,5)cyclophane 3 has the benzenoid rings distorted into boat shapes.[6] The synthetic precursor of 3 was the trithiacyclophane 4,[7] which was shown to have parallel benzenoid rings[8] presumably due to the longer bridges. We are however interested in studying the effect of polar ring substitution on the geometry of some of these cyclophanes and wish to report the synthesis and structural studies of the difluorotrithiacyclophanes 5 and 6 using nmr spectroscopy.



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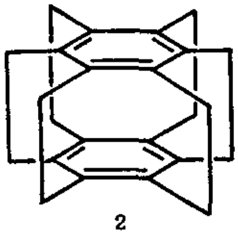

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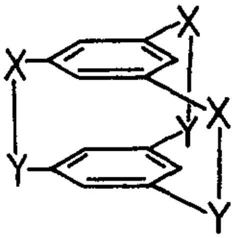
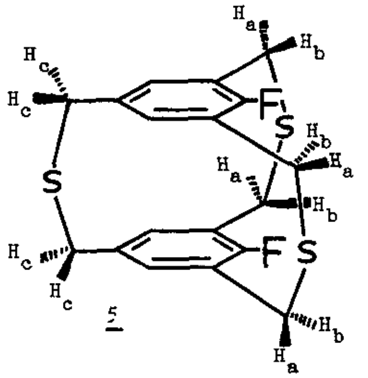


	X—Y
3	CH_2-CH_2
4	CH_2SCH_2

The coupling of 2,4,6-tris(bromomethyl)-1-fluorobenzene and 1-fluoro-2,4,6-tris(mercaptomethyl)benzene readily afforded the isomeric trithiacyclophanes 5 (25%) and 6 (36%). Separation of the two isomers proved to be difficult. Repeated chromatography yielded only a pure sample of 5. Both isomers could however be characterized by their respective nmr spectral data. The cyclophane 5 was expected to be the minor isomer considering only the unfavorable dipole-dipole interaction between the parallel polarized carbon-fluorine bonds. However, if couplings of two aryl rings have the same probabilities, 6 should be formed twice of 5, since two types of approach are possible for 6, while only one for 5. Our results (5:6 = 5:7) thus show that the ease of formation of the triply bridged trithiacyclophanes 5 and 6 was not governed solely by the resulting dipole-dipole interaction in the former.



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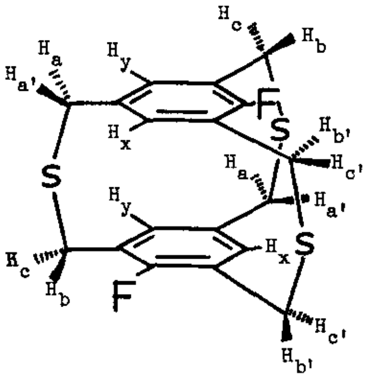

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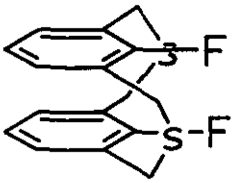
The ^{1}H nmr spectrum of 5 is simple (Figure 1a). The aromatic protons were observed as a broad doublet at δ 7.11 (J = 6.4 Hz) arising from the meta F-H coupling. The meta H-H coupling is presumably small and not resolved thus resulting in the broad signals. Three different types of methylene protons were clearly observed. We have assigned the singlet at δ 3.82 for the H_c protons. This is consistent with the chemical shift observed at δ 3.83 for the singlet corresponding to the methylene protons of 4.[7] The unsymmetrical AB quartet (δ_a = 4.31, δ_b = 3.40; J = 15.3 Hz) would correspond to the H_a and H_b protons respectively. The latter, which experience a small but unresolved long range coupling with the fluorine, appeared as a broader doublet. The reported[9] AB quartet of the methylene protons in 7 at δ_a 4.33 and δ_b 3.39 (J = 15 Hz) agree surprisingly well with the data obtained for 5 described above.

The ^{1}H nmr spectrum of the trithiacyclophane 6 is comparatively more complicated (Figure 1b). Although the sample of 6 still contained about 15% of 5, the signals due to the latter could be readily differentiated and would not interfere with the assignments of the spectrum of 6.

Transannular long range F-H coupling has been observed in some closely-stacked cyclophanes. The



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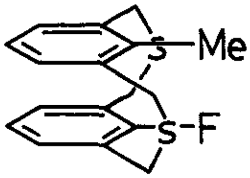

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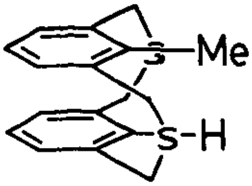

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methyl protons in 8, for example, were observed as a sharp doublet (J = 2.5 Hz) due to the coupling with the fluorine on the opposite ring.[10] In addition the close proximity of the methyl protons parallel to the electronegative fluorine has apparently caused a small down-field shift[10] of the methyl protons in 8 (δ 2.42) compared with those in 9 (δ 2.14).

The aromatic protons in 6 were observed as a broad doublet and a slightly more resolved double doublet. We have assigned the broad doublet (J = 7.1 Hz) to the H_y protons which experience a large meta F-H coupling but a small, unresolved meta H-H coupling. The meta H-H coupling for the H_x protons would also be expected to be unresolved. However, being held parallel to the fluorines on the opposite benzene rings, the H_x protons are shifted slightly to lower field as described for 8. The larger coupling (J = 7.0 Hz) is the H_x-F coupling on the same ring; the slightly resolved, small coupling (J = 2.4 Hz) might in fact be due to transannular H_x-F coupling similar to that mentioned earlier for 8. The assignments for the methylene protons seemed to be more complex. The rather broad singlet at δ 3.78 was assigned to the H_a, $H_{a'}$-protons which, although in principle should be magnetically slightly different, were not affected significantly in any way by the fluorines and were unresolved. Their chemical shift agrees well with that of the equivalent H_c protons of 5 (δ3.82). The other methylene protons of 6 are expected to appear as two sets of AB quartets. The two rather broad doublets (δ 3.54, 3.51; J = 15 Hz, 14 Hz) would correspond to the H_b, $H_{b'}$-protons which are adjacent to the fluorines and thus experience a small long-range coupling and result in the broadening of the peaks. The sharp 'triplet' observed is likely due to the overlap of the two corresponding doublets (δ 4.22, δ 4.06; J = 14 Hz, 15 Hz) assigned to the H_c,$H_{c'}$-protons.

We have also attempted to correlate the chemical shifts observed for 7, 5 and 6 at -125 ppm, -128 ppm and -122 ppm respectively (relative to $CFCl_3$). With the two benzene rings closely stacked in all three cyclophanes, the only difference is that the two fluorines in 7 and 5 are held in the syn-positions - an unfavorable orientation with strong dipole-dipole interaction - and the two fluorines in 6, although not entirely anti, are well staggered and would experience no significant dipole effect. The chemical shifts of the fluorines in 5 and 6 are 6 ppm apart and this difference is believed to be mainly due to the effect from the proximity of the two fluorines in the former. With the 4,4'-positions in 7 not locked, the two benzene rings could twist in the opposite directions slightly. This would to a certain extent stagger the two fluorines to reduce the dipole-dipole interaction and result in an intermediate effect between the locked arrangements in 5 and 6. An intermediate chemical shift for the fluorines in 7 would thus be expected, which agrees with the data observed.

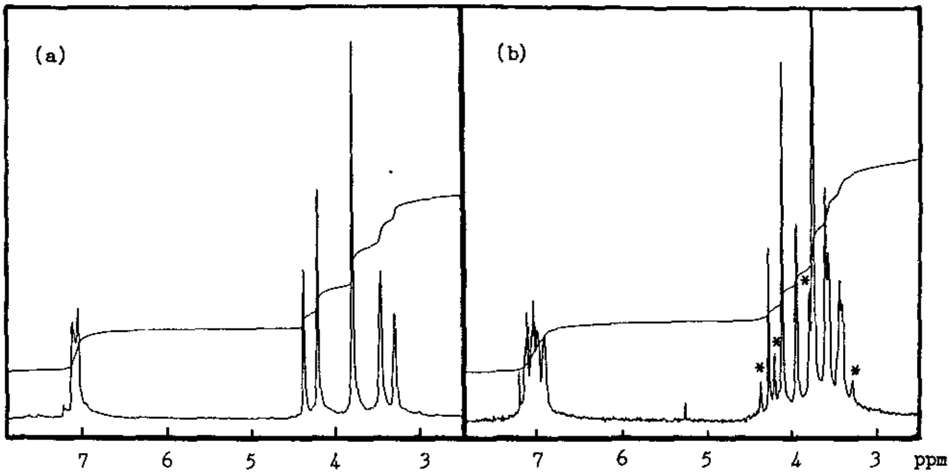

FIGURE 1. ^{1}H nmr spectra (90 MHz, $CDCl_3$) of (a) trithiacyclophane 5; (b) trithiacyclophane 6 (*signals due to trithiacyclophane 5)

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