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CONFORMATIONS OF HIGHLY HINDERED ARYL ETHERS—XIX

SYNTHESIS AND NMR STUDY OF SOME CYCLIC ARYL POLYETHERS[1,2]

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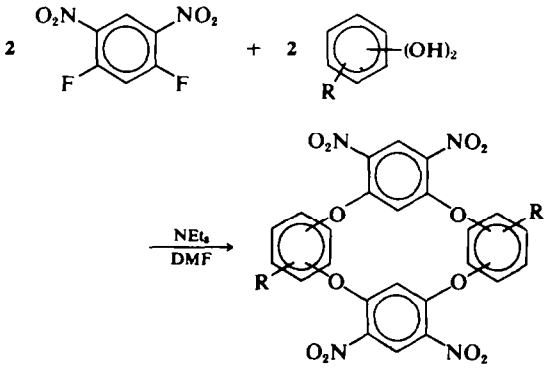
Abstract—Reaction of 1,3-difluoro-4,6-dinitrobenzene with some dihydroxybenzenes and naphthalenes or aminiphenols resulted in the formation of tetrameric macrocyclic aromatic ethers. In spite of their very low general solubility, PMR studies permitted partial conformational analyses. Whereas the *m,o,m,o*-tetraphenylenes exist exclusively in one preferred saddle-shaped conformation (as judged from the appearance of an aromatic proton at $\delta = 5{\cdot}67$), the *m,m,m,m*- and *m,p,m,p*-tetraphenylenes show surprisingly large conformational mobility. Comparison with analogous linear poly-(2,4-dinitrophenoxy)benzenes and other appropriate reference compounds afforded further evidence for the adoption of twist conformations in diaryl ethers and the additivity of aromatic ring magnetic anisotropy effects.

INTRODUCTION

The facile synthesis of diaryl ethers with 1-fluoro-2,4-dinitrobenzene[3] suggested the use of the corresponding bifunctional reagent 1,3-difluoro-4,6-dinitrobenzene† in conjunction with bis-phenols to prepare aryl cyclic ethers:



A literature search revealed that although quite a number of similar oligomeric macrocycles containing aromatic systems have been described,[5] only a few aromatic polyethers have been synthesized.[6] After the completion of this work two related thioethers were reported.[7] In spite of their obvious theoretical and practical importance, conformational studies on them have been quite limited.[6-8]

In such compounds (Fig 1) conformational freedom is greatly reduced in comparison to the corresponding linear poly-ethers[2] and they could be expected to be of use in the study of conformational preferences of diaryl compounds in general.

SYNTHESIS AND STRUCTURE PROOF

The previously described conditions for the prepatation of 2,4-dinitrophenyl aryl ethers[3] also worked well for the cyclic ethers **1–8** of Table 1.‡ In general good yields were obtained of highly pure

†This reagent has been employed in the past to prepare derivatives of phenols.[4]

‡Naming this type of macrocycle according to the cyclophane system[5a] is awkward because: (a) the benzene-ring building blocks are not all explicitly designated; (b) annelation is limited to *o*-disubstituted benzenes, and (c) the resulting numbering is cumbersome and not always unequivocal. As an alternative we suggest the following system: (a) *o*-, *m*-, or *p*-phenylene denotes the disubstituted-benzene repeating unit, (b) the prefix cyclotri-, cyclotetra-, etc., indicates its cyclic nature and the number of units composing it; (c) the bridging elements (O, S, NH, CH_2, etc.) are placed in square brackets before the name, their order and number being clearly indicated; (d) rings and their substituents are denoted by sequential priming, starting with the most highly substituted one as unprimed; (e) the parent macrocycle is not numbered, but the positions on each ring are numbered individually in such a way as to give the bridging positions the lowest numbers; (f) for macrocycles incorporating aromatic units other than benzene (e.g. naphthalene, pyridine or biphenyl), appropriate endings, additions or substitutions are used.

According to this system **1** is numbered as shown in Fig 1 and named 4,6,4″,6″-tetranitro [0.0.0.0] cyclotetra [*m,o,m,o*] phenylene, **6** is 4,6,4″,6″-tetranitro [*d′,d‴*] dibenzo [0.0.0.0]-cyclotetra [*m,m,m,m*] phenylene, and **8a** is 4,6,4″,6″-tetranitro-[NH.O.NH.O] cyclotetra [*m,p,m,p*] phenylene.

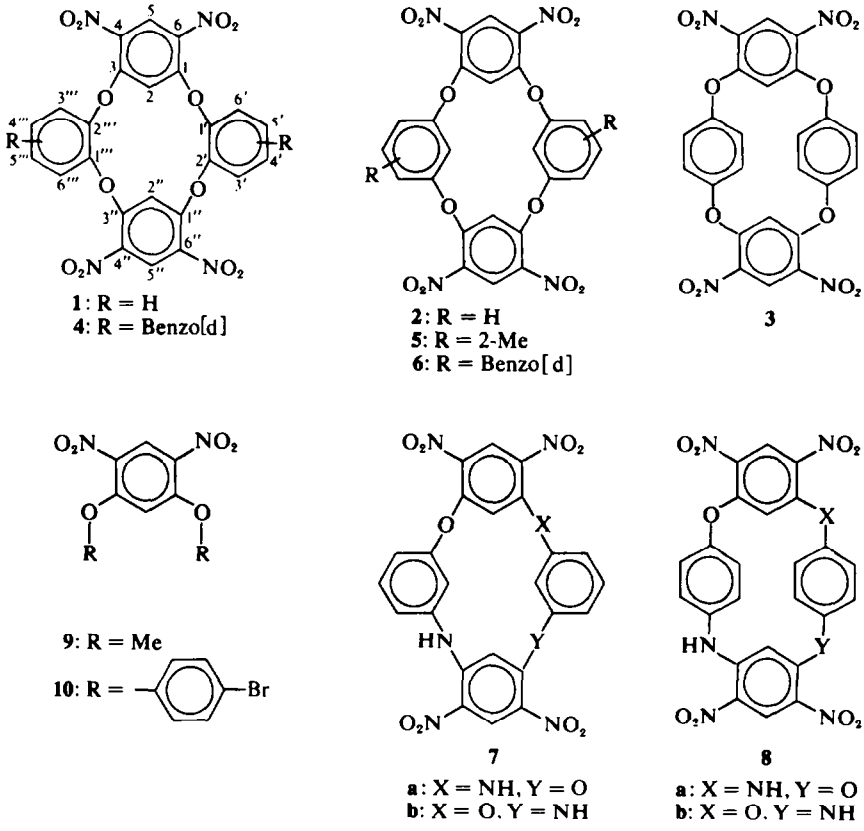


Fig 1. Structures of the compounds studied.

products due in part to their extreme insolubility.* Further purification by recrystallization was impossible because of their very slight solubility in a wide variety of solvents (DMSO, DMF, DMA, nitrobenzene, hexamethyl phosphoramide, etc), but thorough washing generally sufficed to obtain material giving good analyses.

All the cyclic ethers showed indistinct m.ps near or above 350°, precluding purity estimates from m.p. behavior. Since this suggested the possibility of polymer formation, the determination of molecular weights was indicated. Cryoscopic methods were impossible, but mass spectrometry on a few examples (Table 1) confirmed their tetrameric composition and clearly excluded lower or higher oligomers, which could not be differentiated by NMR.

The lower and broader m.p. range observed for ethers **6–8** reflects their isomeric composition (Discussion).

*This insolubility must be due in great part to strong crystal-state forces between compact molecules, since corresponding linear ethers[2] with the same number of nitro groups and equal or higher molecular weight, were considerably more soluble.

Further structure proof was afforded by their NMR spectra which, where obtainable, showed appropriate integrals and, with minor but conformationally important differences, the expected shifts for all protons.

NMR assignments

Solubility limitations resulted in useful spectra only for compounds **1**, **2**, **7** and **9–10** shown in Fig 2 together with the observed proton shifts assigned as follows:

Compound **1**. At very low signal-to-noise ratios a very dilute solution (*ca* 5 mg/ml) in DMSO showed two sharp singlets at low and high fields, and a broad peak at intermediate fields, estimated to represent four times the area of each of the other peaks. Comparison with **13**[2] permitted assignment of the two lower field peaks. Thus the singlet at 5·67 (estimated *ca* 5·3 in $CDCl_3$) must belong to the "inside" protons 2 and 2″, and represents one of the highest shifts ever observed for aromatic protons.[9]

Compound **2**. The spectrum was interpreted as shown in Fig 3. The peaks at middle fields were analyzed[10] as an AB_2X system, giving results in accord with the corresponding open chain analog **14**[2] and the parent tetraphenylene ether.[6] The shift

Table 1. Synthesis and analysis of new compounds

No.	M.p., °C	Yield,%	Formula	MW	Calcd. %C	Calcd. %H	Calcd. %N	Found MW	Found %C	Found %H	Found %N
1	> 350	23	$C_{24}H_{12}N_4O_{12}$	548				548[a]			
2[b]	350 dec	46	$C_{24}H_{12}N_4O_{12}$	548				548[a]			
3	> 350	45	$C_{24}H_{12}N_4O_{12}$	548	52·57	2·20	10·22	548[a]	52·45	2·19	10·06
4	350 dec	100 imp.	$C_{32}H_{16}N_4O_{12}$	648	59·26	2·49	8·64	648[a]	57·56	2·59	8·19
5	> 350	26	$C_{26}H_{16}N_4O_{12}$	576	54·18	2·80	9·72	—	53·98	2·78	9·68
6	215–305	77	$C_{32}H_{16}N_4O_{12}$	648							
7	210–255 dec	37	$C_{24}H_{14}N_6O_{10}$	546	52·76	2·58	15·38	546[a]	52·77	2·50	14·98
8	245–269 dec	73	$C_{24}H_{14}N_6O_{10}$	546				546[a]			
9	152–155	43	$C_8H_8N_2O_6$	228	42·12	3·53	12·28	—	42·21	3·45	12·39
10	163–165	95	$C_{18}H_{10}N_2O_6Br_2$[c]	510	42·37	1·97	5·49	—	42·16	1·90	5·50

[a] By mass spectrometry.
[b] Described previously[6] as melting with dec. at 370°; no further details seem to have been published.
[c] %Bromine: calcd. 31·32; found 31·22.

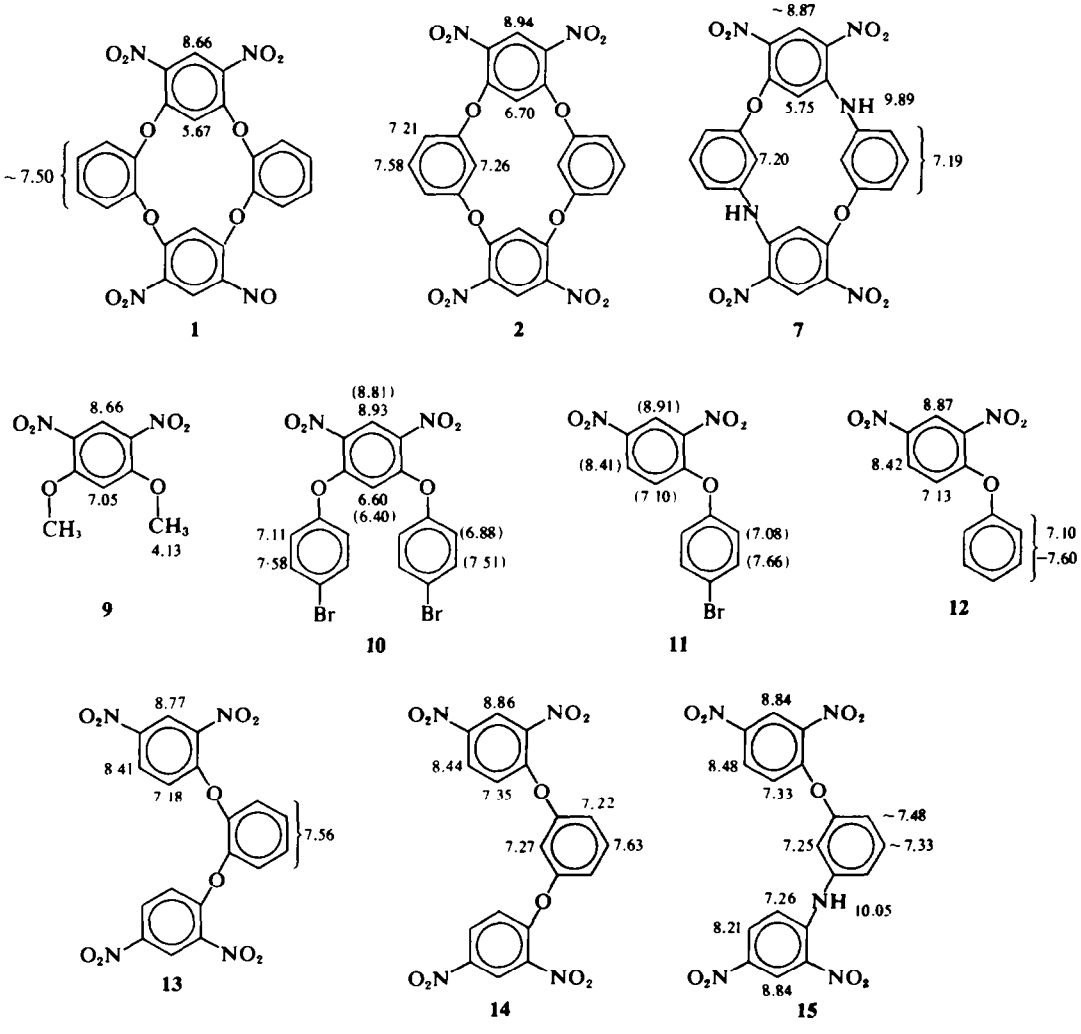


Fig 2. PMR shifts (ppm in DMSO); figures in parentheses are for $CDCl_3$ solutions.

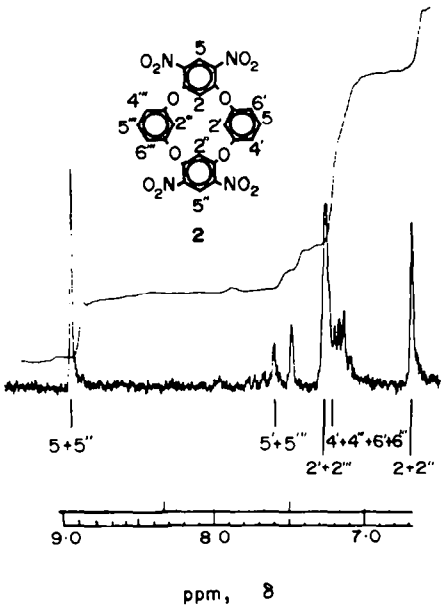


Fig 3. Partial NMR spectrum of **2**.

found for the "inside" protons 2 and 2″ (6·70) is identical to that reported for the analogous thio-ether.[7]

Compound **7**. Although more soluble than its tetraoxa analog, this compound gave a similar but unresolved spectrum due to the presence of two isomers **7a** and **7b**, The conformationally important peaks of the "inside" protons (2+2″ and 2′+2‴) could, however, be assigned unequivocally.

Compounds **9** *and* **10**. Assignments here were straightforward, and in agreement with the corresponding thio-ethers of **10**.[7]

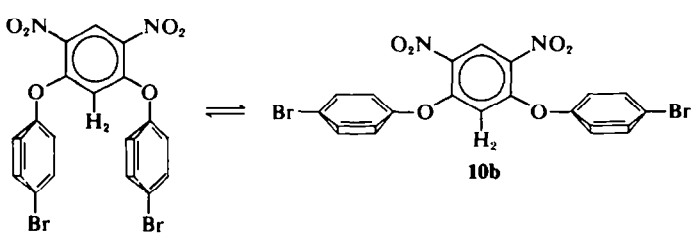
DISCUSSION

A. Conformation of **1** *and* **4**. Space-filling molecular models (Fisher-Taylor-Hirschfelder) of **1** (Fig 4a) show that a single saddle-shaped arrangement is possible for it. Although there are close approaches between certain atoms (e.g. H2, C1′, C2″ and H2, H2″), they are greater than van der Waals' radii as judged from the models. The unsubstituted rings are rigidly held in congruent positions on parallel planes with a separation of 3·82 Å, still somewhat larger than the estimated van der Waals' distance of 3·4 Å for unconstrained approach.[11] On the other hand, the dinitro rings are deployed with a dihedral angle of 60° between them. These can oscillate slightly, reducing this angle somewhat, but enlarging it is not possible due to interference between H2 and H2″. In effect this results in a skew conformation[12] in which each dinitro ring is positioned in a plane perpendicular to and bisecting the plane of both adjacent unsubstituted rings.

In this atropisomer the "inside" protons (2 and 2″) of each ring are held in a fixed position relative to the three other rings. The opposite dinitro ring exerts a deshielding effect, but the two other (unsubstituted) rings shield these inner protons very strongly (by −1·00 ppm each in the skew conformation[2]). The calculated net shift (geometric analysis and shielding tables[13]) is (−1·00)+(−1·00)+(+0·37)=−1·63 ppm. Compared to the appropriate reference compound **9**, the observed shift is −1·38 which is 85% of the calculated value. Although the quantitative agreement may be spurious due to inherent limitations in the calculation of the expected shieldings, qualitatively it may be interpreted as (1) a confirmation of the proposed preferred conformation (Fig 4); (2) supporting an earlier suggestion[2] that magnetic anisotropic effects of several benzene rings are equal and independent of each other; and (3) confirming our propasal[14] that 2,4-dinitrodiphenyl ethers in particular, and diaryl ethers in general, in the absence of other restraints, adopt preferentially a twist conformation since in them an equivalent positioned proton is never shielded as extensively.

A confirmation of the above is obtained from a comparison of analogous protons of **1** with those of **10** and **14**, both of which have a similar substitution pattern (two flanking ether oxygens) about these. In **10** extensive shielding is still present (−0·55 relative to **9**), but in **14**, this proton is deshielded relative to the dimethyl analog (resorcinol dimethyl ether = 6·28 in CCl_4).[15]

This can be explained as follows. Due to conjugative demand,[14] only the dinitro ring is positioned[12] (i.e. the dinitro ring is coplanar with both ether oxygen bonds) relative to the other ring; in **10** this results in conformers **10a** and **10b**:



10a **10b**

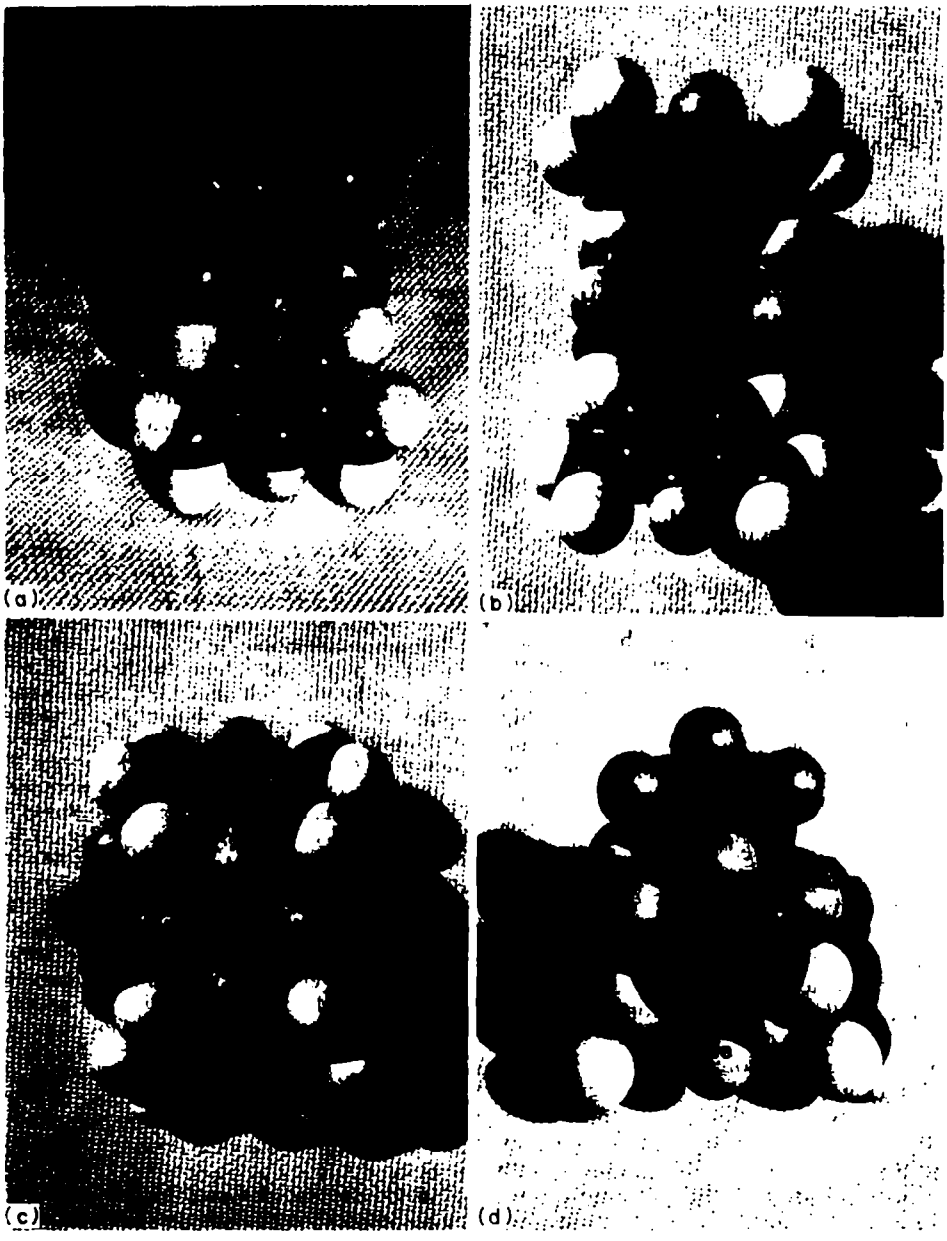


Fig 4. Fisher-Taylor-Hirschfelder models of: (a) "Saddle" conformation for **1**; (b) "Saddle" conformation for **2**; (c) "Basket" conformation for **2**; (d) "Saddle" conformation for **5**.

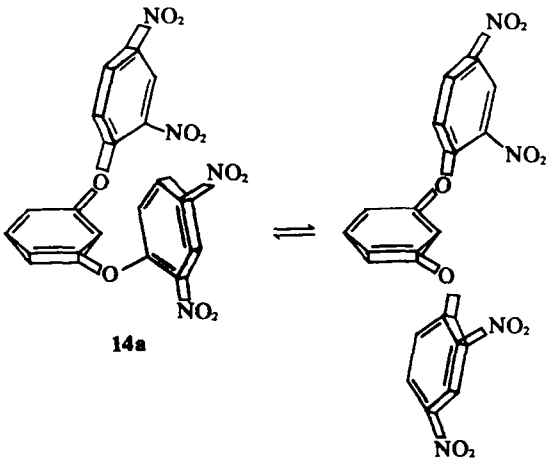
The shielding observed is due principally to **10a**.* On the other hand in **14** this consideration leads to conformers **14a** and **14b**[2].

In neither of these is the pertinent proton within the shielding cones of the adjacent rings and a net deshielding is observed.[2]

Further comparison of **10** with **11** and of **14** with **12** (Fig 2) supports this interpretation since removal of one of the two rings lessens the shielding in the first case and increases it in the second. The shifts observed in **13** also fall into place when all the above considerations are taken into account.

In ether **4**, the annellated rings introduce additional *cis, trans* and *syn, anti* isomerisms, but no

*With skew arrangements and assuming equal populations of **10a** and **10b**, a net shielding of $-2{\cdot}00+0{\cdot}36/2=-0{\cdot}82$ ppm is calculated for **10**; better agreement with the observed value of $-0{\cdot}55$ is achieved if twisted arrangements obtain.



14a 14b

further discussion is warranted in the absence of spectroscopic evidence.

B. Conformation of **2**, **5** *and* **6**. In the all-*meta* linked tetraether **2** a similar conformation (Fig 4b) can also be built with ease, possibly because any two alternate rings can rotate slightly in opposite directions leading to an all-twist arrangement.[14] In it the unsubstituted rings have the same relationship as in **1**, but the dihedral angle between the two dinitro rings has opened to 120°. The net shielding in the skew conformation calculated for the "inside" protons 2 and 2″ is − 1·92 (relative to **9**) whereas only − 0·35 ppm are observed. The explanation[6] for this resides in the surprisingly large conformational mobility possible in this macrocycle: relatively free concerted rotation[16] about the four ether links and freer passage of the "inside" protons past each other within the macrocyclic cavity, permit not only extensive oscillations, but also complete inversion of the rings relative to the molecular plane. Thus in addition to the afforementioned "saddle" conformation (Fig 4b) also "basket" (Fig 4c) and "stepladder" forms are possible. In consequence the four "inside" protons are exposed to a complex mixture of shielding and deshielding effects, with the former predominating slightly. The present results on the tetranitro analog (**1**) confirm quantitatively the qualitative results obtained earlier by Sommer and Staab[6] on the parent macrocycle and by Montaudo *et al.*[7] on the tetranitro-tetrathia analog.

The dimethyl analog **5** was prepared since models (Fig 4d) showed that in it the two methyl groups are positioned very near to the rings, and that they partially restrict inversion through the "cavity". Although our data (Table 1) indicate that the desired compound was in fact obtained, its extreme insolubility precluded NMR studies of the shieldings of the putative invertomers.

The same was also unfortunately true for the dibenzo analog **6**.

In the corresponding diaza ether **7** entirely similar shifts were observed as in **1**, except that the presence of two isomers (**7a** and **7b**) precluded a detailed interpretation of the NMR spectrum. Nevertheless, it would seem that substitution of oxygen by nitrogen bridges takes place with no significant change in conformational preference. Comparison of **7** with **15**[2] leads to analogous interpretations as given above.

Likewise the insolubility of the *m,p,m,p*-tetraphenylene **3** and its diaza analog **8**, precluded their conformational analysis.*

EXPERIMENTAL

General. M.ps were obtained with a Kofler hot-stage. PMR spectra were determined in DMSO or DMSO-d_6 using a Varian A-60 spectrometer. Mass spectra were obtained with a double focus Hitachi-Perkin Elmer RMU-7H spectrometer under the following conditions: E = 75 eV, entry port 4×10^{-7} Torr, 160–290°C, chamber temp 350°, accellerating voltage 1,820 V, total ionic current $12\text{–}18\times10^{-12}$ amp, total emission 80 μA, target current 70 μA with a 10 μA spread. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

Synthesis. (Table 1) Compounds **1–8** were prepared as follows: To 2 mmoles of the appropriate phenol dissolved in 20 ml DMF are added 2 mmoles (408 mg) 1,3-difluoro-4,6-dinitrobenzene and 4·4 mmoles (440 mg) triethylamine. The mixture is heated under reflux for 20 min, and after cooling, a few drops of water added. The resulting white or yellow ppt was often crystalline and could be purified adequately just by washing with DMSO and/or EtOH. The extreme insolubility of these compounds in all solvents tried forbade recrystallization, except for the aminoethers **7** and **8** where purification was achieved by precipitation from dioxane with water. All their m.ps were indistinct and accompanied by decomposition.

Compounds **9** and **10** were prepared the same way using two equivalents of MeOH or *p*-bromophenol to one of the difluoro-reagent. These were purified by recrystallization from aq. EtOH.

All the ethers gave typical blue or blue-violet colors under Janovsky conditions,[17] whereas the amino-ethers gave red-brown colors.

PMR spectra. Compounds **1**, **2**, **7** and **8** were slightly soluble in DMSO, and provided usable spectra under forcing conditions. Compounds **9** and **10** were readily soluble, whereas **3–6** were soluble to less than 5 mg/ml even in hot DMSO, and no spectra could be obtained. In view of this, assignments should be considered tentative until confirmed under more favorable operating conditions. Chemical shifts were determined accurately with reference to the DMSO signal ($\delta = 2{\cdot}50$), but are given relative to TMS at $\delta = 0{\cdot}00$ to permit comparison with related linear poly-(2,4-dinitrophenoxy)benzenes.[2]

Acknowledgement—It is a pleasure to acknowledge here the able technical assistance of Q.F.B. Arturo Ramírez M.

*The relationship of these compounds to the "crown" ethers (Ref 5*a*) has not escaped us, but all attempts at solubilizing them by association with metal ions were unfruitful.

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