Tetrahedron Letters,Vol.30,No.8,pp 1005-1008,1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
Pergamon Press plc

A WATER-SOLUBLE CYCLIC TETRAMER FROM REACTING CHROMOTROPIC ACID WITH FORMALDEHYDE

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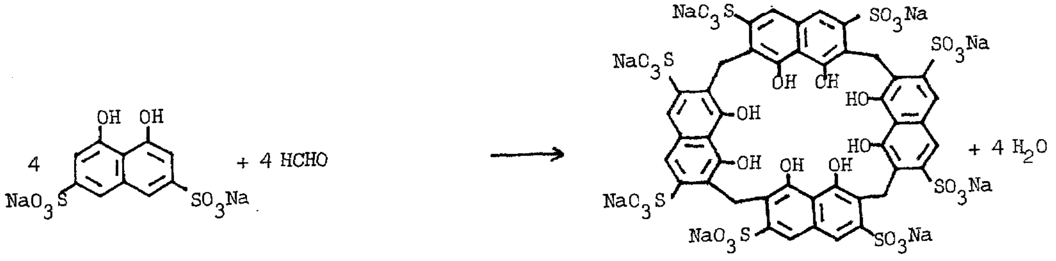
Chromotropic acid, disodium salt, reacts with an excess amount of formaldehyde in water to give a dark red plastic-like water-soluble cyclic tetrameric compound.

Water-soluble synthetic macrocyclic compounds have been the focus of interest of many chemists in recent years.[1-3] We report in this paper a water-soluble cyclic tetrameric compound prepared by reacting chromotropic acid, disodium salt, with an excess amount of formaldehyde.

An aqueous solution containing chromotropic acid, disodium salt, and an excess of formaldehyde (1:5), left standing in a stoppered flask for a week, gives a dark red solution. After evaporating the water, a quantitative yield of a dark red plastic-like product (decomposes above 400°C) which is soluble in water is obtained.[4] This product is assigned the cyclic tetrameric structure 1, based on the following data.



1

The mass spectra of 1 and the corresponding S-benzylthiuronium salt, 2, (mp 180°C (d), obtained by reacting 1 with S-benzylthiuronium chloride) are shown in Figs. 1 and 2 respectively. The spectra indicate sample decomposition. Nevertheless, the presence of peaks at m/e 1327 and 1312 indicates a tetrameric structure.

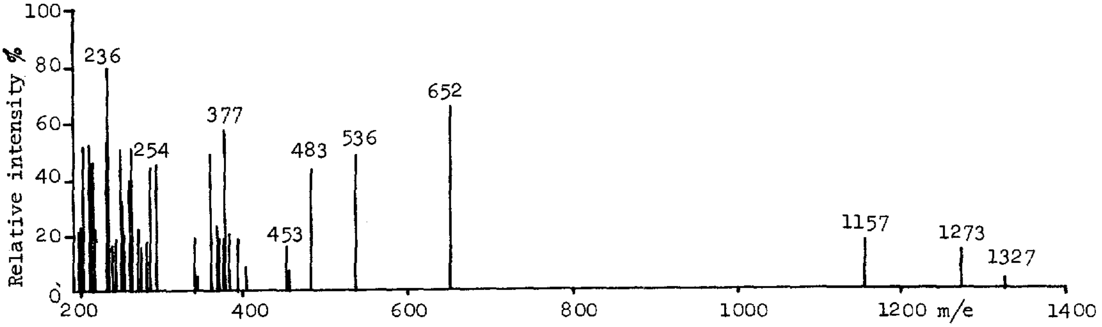


Fig. 1 Mass spectrum of compound 1 (m/e < 200 not shown)

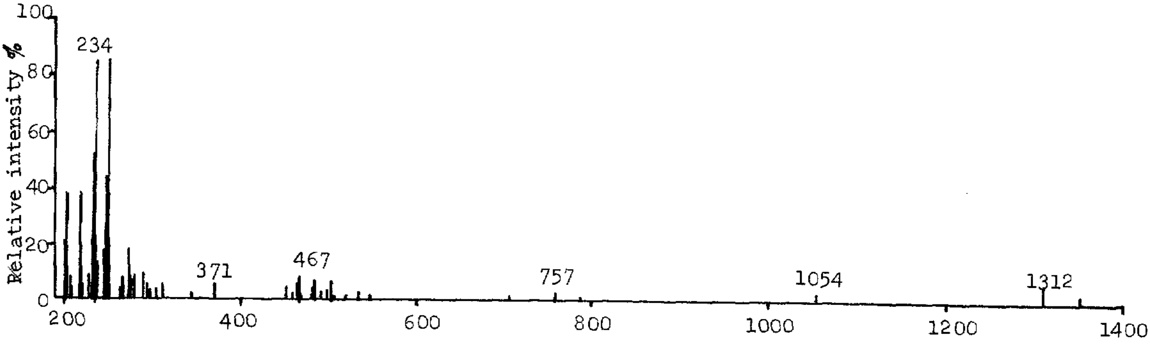


Fig. 2 Mass spectrum of compound 2 (m/e <200 not shown)

The ^{1}H nmr spectrum of 1 in CD_3OD (Fig. 3) shows a singlet for the aromatic protons (δ 8.05) and a singlet for the methylene protons (δ 4.68), consistent with a flexible cyclic tetrameric structure (analogoues to the case of cyclotetraveratrylene[5-7]).

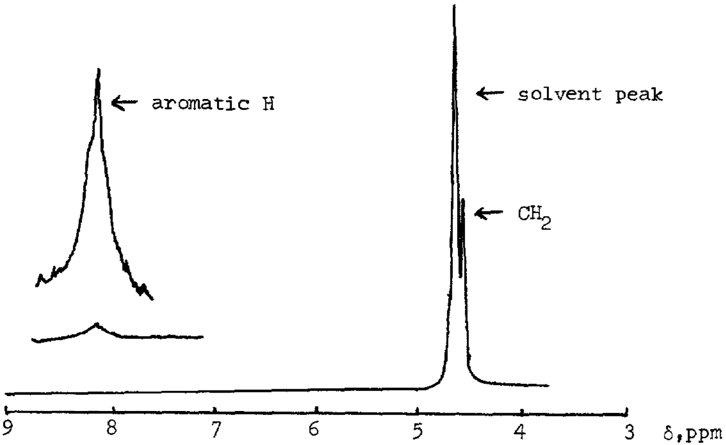


Fig. 3 ^{1}H nmr spectrum of compound 1 in CD_3OD
(TMS as external reference)

The ^{13}C nmr spectrum[8] of 1 in D_2O shows six aromatic carbons (δ 119-153) and one methylene carbon (δ 28.1) and is also consistent with 1.

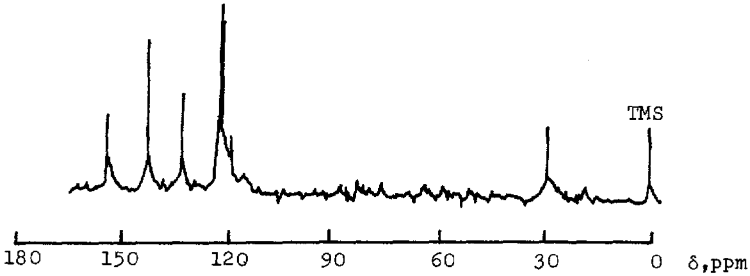


Fig. 4 ^{13}C nmr spectrum of compound 1 in D_2O
(TMS as external reference)

Karl-Fischer titrations for water content and C,H,N,S analyses on 2 are in good agreement with the formula of $(C_{11}H_6O_8S_2)_4\cdot(C_8H_{11}N_2S)_8\cdot 3H_2O$.[9]

1 shows an absorption band in the visible region (λ_{max} at 540 nm, ε 4,000 cm^2 mol^{-1} and a shoulder at 570 nm) whereas chromotropic acid, disodium salt, is transparent in this region. When the solution is made alkaline, it turns green and there is a bathochromic shift to λ_{max} at 640 nm. This change is due to the ionization of the hydroxyl groups since the original red colour is restored upon acidification of the green solution.

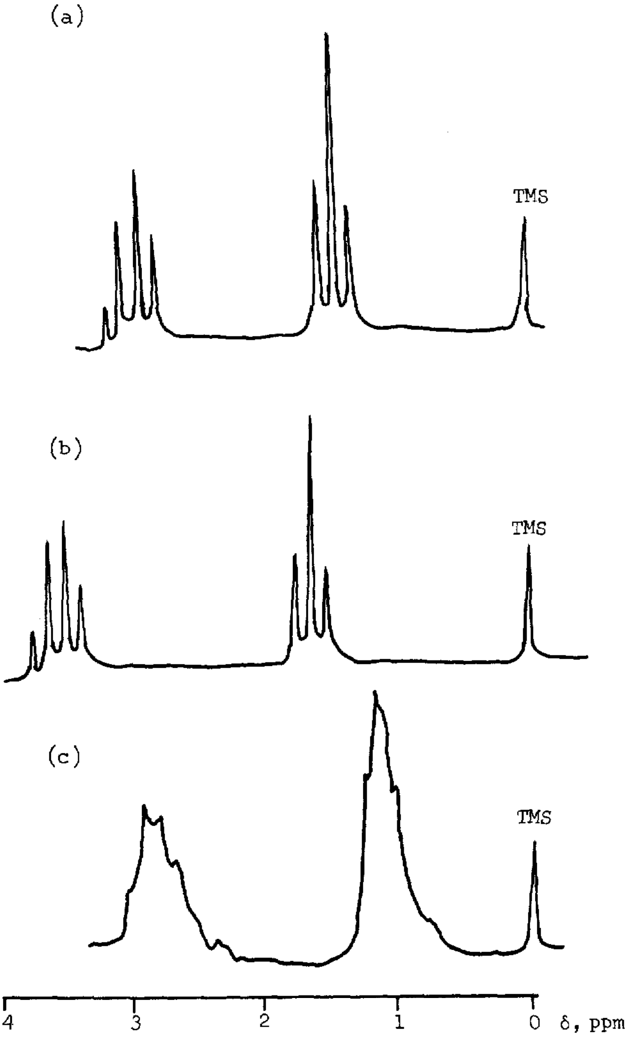


Fig. 5 ^{1}H nmr spectrum of triethylamine in D_2O(TMS as external reference): (a) no host, (b) in the presence of chromotropic acid, disodium salt (amine: chromotropic acid = 1:1); (c) in the presence of 1 (amine:1 = 1:2).

The cyclic structure of 1 is further supported by our preliminary finding of its ability to include amines and some metal cations into its cavity. Fig. 5 shows the effect of inclusion of triethylamine into 1 on the ^{1}H nmr spectrum of the former.

In the presence of an equal molar or an excess of 1 the triethylamine is expected to exist in the protonated form since the first pk_a value of the hydroxyl groups of 1 is 5.8 ± 0.2 (this work) and the pk_a value of the amine is 11.0. Chromotorpic acid, disodium salt with a similar pk_a value $(5.5)^{10}$ is shown to fully protonate triethylamine when an equal molar concentration is used (Fig. 5b), the methyl and methylene protons are deshielded. An analogous system has been reported for calixarenes.[11] That triethylamine is included into the cavity of 1 is indicated by (1) its broad nmr spectrum (Fig. 5c) and (2) the shielding of its methyl and methylene protons (0.50 and 0.65 ppm respectively, compared to the free protonated triethylamine). The restricted rotation of the ethyl groups within the cavity of 1 can explain the broadness of the nmr spectrum. The upfield proton chemical shifts are due to the shielding effects of the napthalene rings on the included ethyl groups. We are currently investigating the potential of 1 as a host molecule for various amines and metal cations in an aqueous system. The results will be submitted for publication shortly.

Veratrole reacts with formaldehyde in the presence of sulphuric acid to give cyclotetraveratrylene as well as cyclotriveratrylene.[5] In our case, only the tetramer 1 (we whall give it the trivial name of cyclotetrachromotropylene) is obtained. Both CPK and Dreiding models show that the trimer is sterically unfavourable.

The authors thank Dr. T.L. Ooi of Palm Oil Research Institute of Malaysia for recording the mass spectra.

1. F. Vögtle, H.-G. Löhr, J. Franke, and D. Worsch, Angew. Chem. Int. Ed. Engl., 24, 727 (1985).
2. I.O. Sutherland, Chem. Soc. Rev., 15, 63 (1986).
3. F. Diederich, Angew. Chem. Int. Ed. Engl., 27, 362 (1988).
4. The crude product is 99% pure, as checked against a pure sample of 1 at 540 nm. TLC on Merck precoated silica gel 60 F_{254} with MeOH: *n*-BuOH (2:3 v/v) as eluting solvent shows that only a trace of a fluorescent substance is present in the crude sample. Recrystallization from H_2O-EtOH mixed solvent removes the trace impurity.
5. J.D. White and B.D. Gesner, Tetrahedron Letters, 1591 (1968).
6. H. Erdtman, F. Haglid, and R. Ryhage, Acta Chem. Scand., 18, 1249 (1964).
7. A.G.S. Högberg, J. Org. Chem., 45, 4498 (1980).
8. It is difficult to obtain a good ^{13}C nmr spectrum of 1 with our Varian CFT-20 80 MHz spectrometer. The spectrum shown required three days and a high sample concentration.
9. Calculated for $(C_{11}H_6O_8S_2)_4 \cdot (C_8H_{11}N_2S)_8 \cdot 3H_2O$: C 47.82%; H 4.13%; N 8.27%; S 18.89%. Found: C 47.30%; H 4.18%; N 8.29; S 18.87%.
10. E.P. Serjeant and B. Dempsey, "Ionization Constants of Organic Acids in Aqueous Solution", Pergamon Press, Oxford, 1979, p. 549.
11. C.D. Gutsche, M. Iqbal, and I. Alam, J. Am. Chem. Soc., 109, 4314 (1987).

(Received in UK 9 January 1989)