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SYNTHESIS AND CONFORMATIONAL PROPERTIES OF 5,7-DISUBSTITUTED [3.3]METACYCLO(2,5)THIOPHENOPHANE-1,12-DIONES

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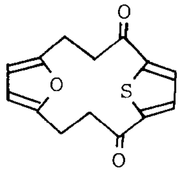
Summary: The title compounds showed unique conformational equilibria which were dependent upon the substituents in the 5,7-positions, the predominant conformers being in a syn O,S,O-cis,cis conformation with a highly deformed thiophene-2,5-dicarbonyl moiety.



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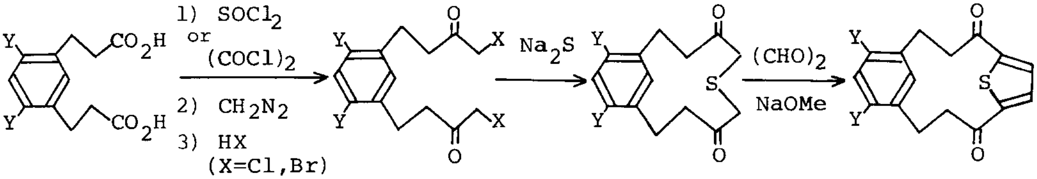
As reported previously, [3.3](2,5)furano(2,5)thiophenophane-1,11-dione **1** shows a yellow band arising from the charge-transfer interaction between its electron-rich furan and electron-deficient 2,5-diacylthiophene moieties[1]. While **1** shows only a slight change in its NMR spectrum over a wide temperature range, [3.3]metacyclo(2,5)-thiophenophane-1,12-dione **2a** exhibited unexpected DNMR spectra. We wish to report here the synthesis of **2a** and its derivatives **2b-d** with substituents Y, to simplify the NMR spectra, at the 5,7-positions and their unique conformational properties as determined by the DNMR spectroscopy and the X-ray crystallography.



3 **4** **5** **2**

a: Y=H b: Y=Me c: Y=MeO d: Y=Br

1,3-benzenedipropionic acid and its derivatives **3** were either prepared by the malonic ester synthesis from appropriate 1,3-bis(bromomethyl)benzenes (Y=H, Me, Br)[2,3] or by condensation of 1,3-dimethoxybenzene with methyl acrylate (Y=MeO)[4]. The diacids **3** were converted into the corresponding chloride by treatment with thionyl chloride or, after conversion to its sodium salt, with oxalyl chloride. The acid chlorides were then reacted with diazomethane followed by concentrated hydrochloric or hydrobromic acid to give the corresponding bis(halomethyl) ketones **4** in good overall yields[2,5]. The solution of **4** in benzene or tetrahydrofuran and the solution of sodium sulfide in 70% ethanol were added to refluxing ethanol over a period of 8 h under high dilution conditions under nitrogen to give cyclic diketo sulfides **5**[2,6]. When **5** were condensed with glyoxal in methanol and a suitable cosolvent by adding dilute sodium methoxide over a 12 h period, the desired thiophenophanediones **2** were readily obtained[2,7].

As already reported, thiophene protons in open chain 2,5-diacylthiophenes with a wide variety of substituents give rise to a sharp singlet at 7.6-7.7 ppm[8]. In contrast, the thiophene protons in **2** appeared as a broad singlet at 6.4 ppm at room temperature, which was sharpened at higher temperatures and split into a large singlet at ca. 6.5 ppm and a very small peak at ca. 7.5 ppm by lowering the temperature. Whereas the NMR signal for the inner benzene proton revealed similar changes, little alteration was observed for the outer proton. These changes are clearly demonstrated by the DNMR spectra of **2b** and **2c** in Fig. 1. Table I lists the chemical shifts of the thiophene and the inner benzene protons at low temperatures and the coalescence temperature Tc for these peaks. The conformer ratios as indicated by the peak areas at low temperatures were dependent upon Y; the amount of the minor conformer was largest for Y=Me (~15%) and smallest for Y=Br. The Tc also depended upon Y but in a different way as shown in Table I.

Table I. Chemical shifts (δ, ppm) at low temperatures and the Tc, °C (90 MHz, $CDCl_3$).

compd	thiophene-H		Tc	benzene-H_i		Tc
2a (Y=H)	7.53	6.50	6	6.03	5.78	-10
2b (Y=Me)	7.56	6.45	24	5.84	5.60	5
2c (Y=MeO)	7.48	6.48	40	5.70	5.58	25
2d (Y=Br)	7.59	6.59	33	6.13	---	20

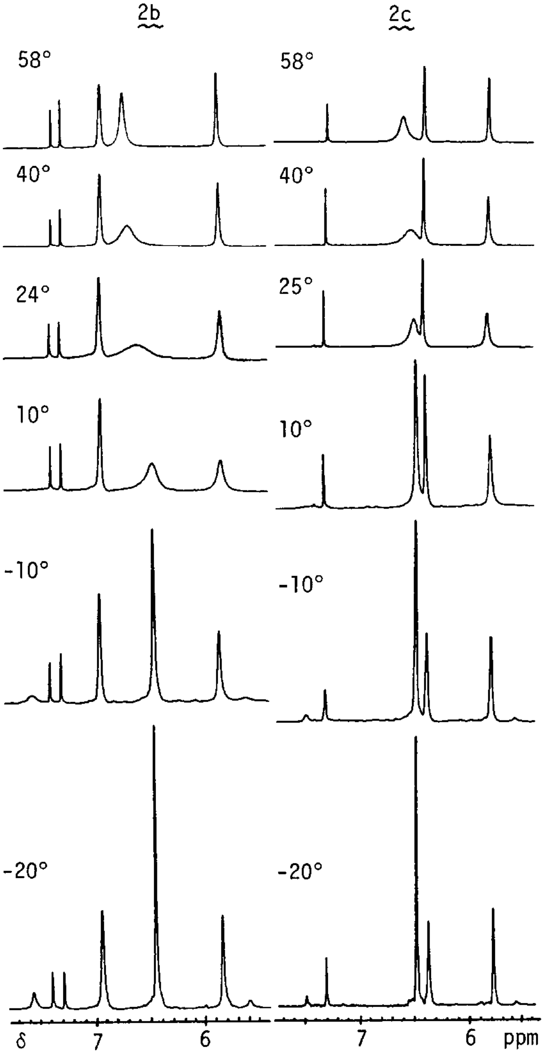


Fig. 1. The NMR spectra of **2b** and **2c** at different temperatures (90 MHz, $CDCl_3$).

Since none of the conformations suggested by molecular model examination seems to account for the observed NMR results, the structure of **2c** (Y=OMe) was determined by X-ray analysis. The crystal data for a yellow prism grown from acetone were as follows: monoclinic, space group $P2_1/n$, a=9.887(2), b=16.259(3), c=9.797(4) Å, β=91.75(2)°, V=1574.1(8) Å^3, Z=4, D_m= 1.39 (D_c=1.394) g.cm^{-3}. Intensity data were collected by ω-2θ scan method on a Rigaku AFC-5 diffractometer using Mo-Kα radiation (λ=0.7107 Å). A total of 3179 independent reflections were measured for $2.5° < 2\theta < 50.0°$, of which 2487 were considered to be observed [$I > 3.0\sigma(I)$]. The structure was solved by direct methods (MULTAN 78)[9] and refined by the block-diagonal least-squares method (UNICS III)[10]. The final R value applying anisotropic temperature factors to the non-hydrogen atoms and isotropic ones to hydrogen atoms was 0.047.

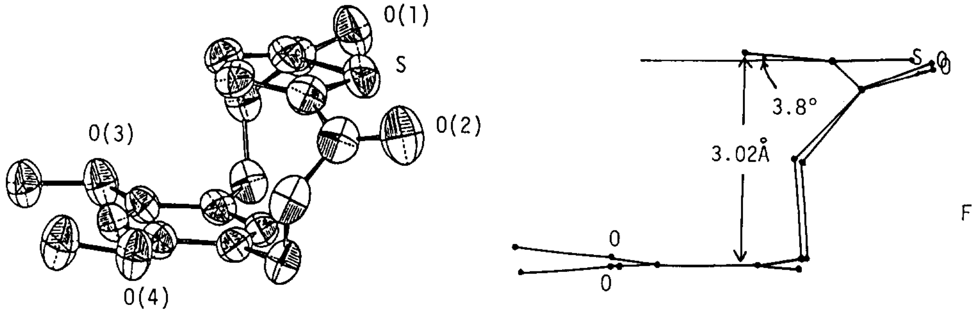
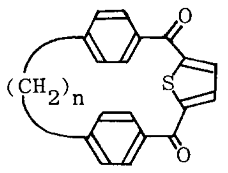


Fig. 2.

As depicted in Fig. 2 the molecular structure of 2c thus obtained is very remarkable, showing an extremely deformed thiophene-2,5-dicarbonyl moiety in an O,S,O-cis, cis conformation with respect to the thiophene S and the carbonyl O's. Whereas the O,S,O-cis, cis conformation has been demonstrated to be predominant in open chain 2,5-diacylthiophenes[11,12]. We have found that this moiety is O,S,O-trans, trans in unstrained [n.1.1]paracyclo(2,5)thiophenoparacyclophane-n+7, n+13-diones (6: n=7∿10)[12]. Therefore, in addition to the strong interactions between the thiophene S and the C=O groups, steric factors such as the difference in bulkiness between -S- and =C-C= may be responsible for this deformed structure.

The electronic spectra of 2, particularly that of 2c shown in Fig. 3, are quite different from that of an open chain reference, 2,5-divaleloylthiophene (7). The longest wavelength band of 2c exhibits a large bathochromic shift upon the solvent change from cyclohexane to chloroform, in contrast to a small hypsochromic shift of the $n-\pi^*$ band of 7 at ca. 350nm. Furthermore, this band shifts to the shorter wavelength as the electron releasing ability of Y decreases.



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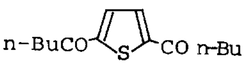

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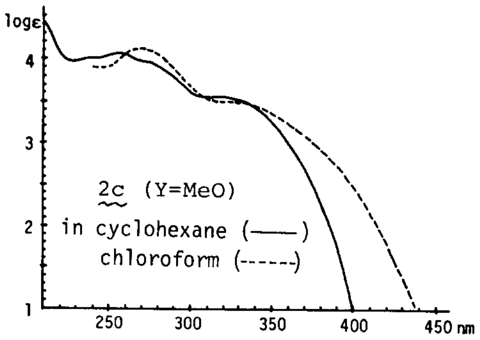
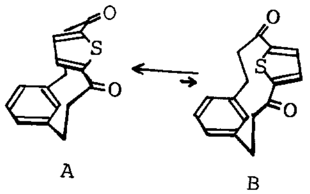


Fig. 3. The electronic spectra of 2c.

Therefore, it is attributable to the CT interaction between the electron poor thiophene-2,5-dicarbonyl moiety and the electron rich benzene ring. The absorption at ca. 270nm in Fig. 3 may then be assigned as the π-π^* band arising from the thiophene-2,5-dicarbonyl chromophore, the blue shift of which (20nm) as compared to 7 is considered to be due to the deformation of the chromophore.

Since all of **2** showed similar DNMR changes and the minor conformer was present only in a small amount, the structure of the major conformer of **2a-d** in solution must be the same as that determined by the X-ray analysis for **2c** and in a *syn* O,S,O-*cis*,*cis* conformation A. The minor conformer may then be tentatively assigned as an *anti* O,S,O-*trans*,*trans* structure B on the basis of the large downfield shift of the thiophene proton signal considering anisotropic effects of the benzene and carbonyl groups.



References and Notes

1. Y. Miyahara, T. Inazu, and T. Yoshino, Chem. Lett., 397 (1980).
2. Satisfactory elemental analyses and NMR and IR spectral data were obtained for all of the new compounds.
3. **3a**: J. S. Kipping, Ber, 21, 28 (1888); diethyl ester of **3b**: bp 164-167°C/0.4 mm; diethyl ester of **3d**: bp 174-180°C/0.01 mm.
4. M. Narayana, J. F. Dash, and P. D. Gardner, J. Org. Chem., 27, 4704 (1962).
5. **4a** (X=Cl): 60.9% yield, mp 42-43°C; **4b** (X=Cl): 62.6% yield, mp 86-87°C; **4c** (X=Br): 63.8% yield, mp 113-114°C; **4d** (X=Cl): 75.5% yield, mp 131-132°C.
6. **5a**: 45.6% yield, mp 150-151°C; **5b**: 54.6% yield, mp 216-217.5°C; **5c**: 60.4%, mp 191-192°C; **5d**: 54.0%, mp 257-259°C(dec). The molecular weights of **5a-d** were confirmed by mass spectrometry.
7. The cosolvents used were dioxane for **5a**, dichloromethane for **5b** and **5c**, and N,N-dimethylformamide for **5d**. The condensation of 5 was carried out at room temperature except for that of **5d** at 60-65°C because of its low solubility.
   2a: 63.4% yield, colorless prisms, mp 161-161.5°C; **2b**: 39.0% yield, colorless prisms, mp 208.5-209.5°C; **2c**: 55.4% yield, yellow prisms, mp 203-204°C; **2d**: 20.9% yield, colorless plates, mp 219-220°C.
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12. Submitted for publication. A preliminary X-ray analysis established the O,S,O-*trans*, *trans* conformation for **6** (n=7).

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