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Atropisomerism in 2-(2,2-Dicyano-1-methylethenyl)benzoic Acid and 3-(2,2-Dicyano-1-methylethenyl)thiophene-2-carboxylic Acid Studied by Solid-State ^{13}C NMR Spectroscopy and X-Ray Crystallography

Christian Rømming,[a] Per Kolsaker,[a] Are Wiberg[a] and Tore Skjetne[b]

[a]Department of Chemistry, University of Oslo, PO Box 1033 Blindern, N-0315 Oslo, Norway and [b]MR-Center, SINTEF-UNIMED, N-7034 Trondheim, Norway

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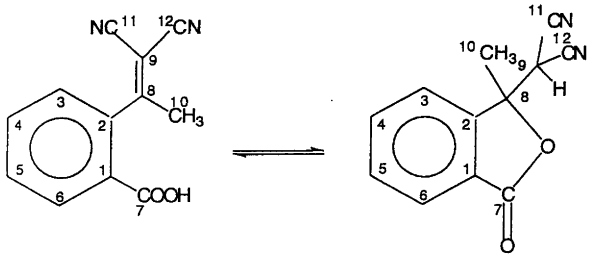
The title compounds have been studied in solution by FTIR, UV, ^{1}H and ^{13}C NMR spectroscopy, which indicate atropisomerism where the two enantiomers exist as a centrosymmetric dimer. In solid-state ^{13}C NMR two sets of resonance signals are observed indicating diastereoisomerism in the dimer due to rotational restriction. Crystal structures for both acids and the methyl ester of the benzoic acid analogue (**1b**) have been determined. Compound **1a** crystallizes in the orthorhombic space group $P2_12_12_1$ with cell dimensions $a = 8.945(2)$, $b = 10.644(2)$ and $c = 22.458(5)$ Å, $Z = 8$, R-value 5.2%, 2159 reflections; **2** and **1b** both crystallize in monoclinic space groups with cell dimensions $a = 11.058(2)$, $b = 14.628(3)$, $c = 12.713(2)$ Å and $\beta = 97.98(1)°$, space group $P2_1/n$, $Z = 8$, R-value 3.8%, 5599 reflections; $a = 14.076(4)$, $b = 6.153(1)$, $c = 14.437(2)$ Å and $\beta = 110.92(2)°$, space group $P2_1/c$, $Z = 4$, R-value 4.8%, 2504 reflections, respectively.

The Knoevenagel condensation product from 2-acetylbenzoic acid and malononitrile has been shown to exhibit ring-chain tautomerism[1] in solution, as indicated by IR, ^{1}H and ^{13}C NMR spectroscopy.[2]

so that distinct and separate ^{13}C NMR spectra could be recorded for **1a** (Table 1) and the ring tautomer.

A comparison of the UV spectrum of **1a** ($\lambda_{max} = 283$ nm, $\varepsilon = 5540$ M^{-1} cm^{-1}) with those of (phenylmethylene)propanedinitrile ($\lambda_{max} = 309$ nm, $\varepsilon = 20400$ M^{-1} cm^{-1}) and (1-phenylethylidene)propanedinitrile ($\lambda_{max} = 292$ nm, $= 12800$ M^{-1} cm^{-1})[4] indicates a successive decrease in planarity around the bond between the ring and the dicyanoethenyl group, allowing for atropisomerism.



1a

The parent compound, 2-acetylbenzoic acid, also exhibits the same type of isomerism. The interconversion is fast compared with the NMR timescale, thus showing only averaged resonance positions for the methyl protons.[3] On the other hand, the interconversion of the condensation product is much slower at room temperature,

Table 1. ^{13}C NMR shifts (in ppm) of 2-(2,2-dicyano-1-methylethenyl)benzoic acid (**1a**) in tetrachloroethane-d_2 at 25 °C.[a]

C1	C2	C3–C6	C7	C8	C9	C10	C11–C12
139.3	125.7	134.4, 132.4 130.6, 127.2	180.5	169.4	86.4	25.7	111.9, 111.7

[a] Spectrum of the open-chain form recorded shortly after dissolution of the compound.

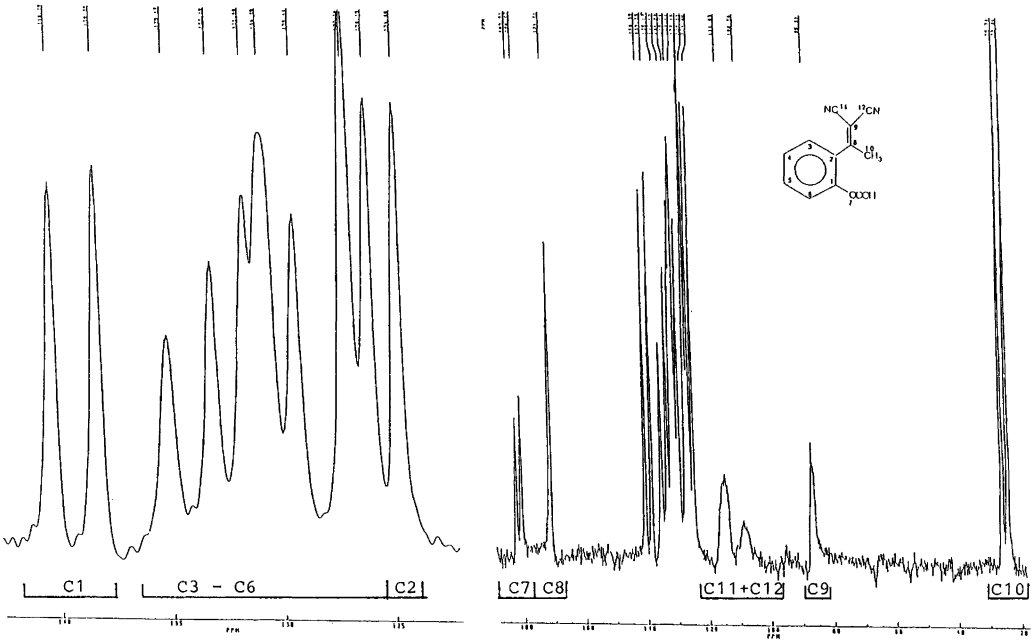


Fig. 1. Solid-state ^{13}C NMR spectrum of 2-(2,2-dicyano-1-methylethenyl)benzoic acid (**1a**). Left-hand side: spectral region 122–142 ppm enlarged.

The IR spectrum recorded for samples in KBr pellets shows that only the open form **1a** is present. In solution (tetrachloroethane-d_2) the IR spectrum taken shortly after dissolution shows the characteristics of a carboxylic acid dimer with the broad OH stretch at 3000 cm^{-1} (half-intensity bandwidth 580 cm^{-1})[5] and the C = O stretch at 1695 cm^{-1}. This observation, together with the above-mentioned set of single ^{13}C resonance signals, indicating a centre of symmetry in the dimer, shows that if atropisomerism is present, the two monomeric acids must be enantiomers.

Solid-state ^{13}C NMR spectra (MAS) (Fig. 1) gave 15 well resolved resonance signals, two poorly resolved signals (C9) at 86.8 ppm and two non-resolved multiplets, the latter representing the carbons of the nitrile groups, a phenomenon often observed and due to quadrupole effects from the ^{14}N directly bonded to ^{13}C in the nitrile groups.[6] Since the pivotal bond is between C2 and C8, these carbons should give only one signal each; thus, allowing for an overlap of two resonance signals from the benzene carbon atoms, the rest of the carbon atoms of the dimer give separate signals.[†]

[†] 2-Acetylbenzoic acid was shown by us to exist as the ring tautomer by solid-state ^{13}C NMR spectroscopy.

The existence of two separate sets of ^{13}C signals excludes normal enantiomerism and must allow for different torsion angles, both in sign and magnitude, i.e., two diastereoisomers must be present in the crystals. It was therefore decided to undertake a crystal structure determination using X-ray diffraction methods.

The thiophene analogue of **1a** (**2**) was also synthesized[7] and in contrast with **1a** did not show any ring-chain tautomerism in solution. However, solid-state C^{13} NMR (data not shown) also indicated two diastereomeric forms in the crystals and therefore its crystal structure determination is included in this study.

Upon treatment of an ethereal solution of **1a** with diazomethane the normal open methyl ester (**1b**) was formed.[2] The solid-state ^{13}C NMR spectrum is normal, i.e., only one set of carbon resonance peaks is observed. For comparison, its crystal structure was determined.

Experimental

Preparations. 2-(2,2-Dicyano-1-methylethenyl)benzoic acid (**1a**) was synthesized by condensation of 2-acetylbenzoic acid with malononitrile,[2] its methyl ester (**1b**) by treatment of the acid with diazomethane,[2] and 2-(2,2-

dicyano-1-methylethyl)thiophene-2-carboxylic acid (**2**) by condensation of 3-acetyl-2-thiophenecarboxylic acid with malononitrile.[7]

FTIR spectra were recorded on a Nicolet Magna spectrometer equipped with a Dell 433/L for samples either in tetrachloroethane-d_2 solution or KBr tablets.

UV spectra were recorded on a Shimadzu UV-260 spectrophotometer.

NMR. Solution spectra (^{1}H and ^{13}C) were recorded on a Gemini 200 (Varian) spectrometer, resonance frequency 50 MHz for ^{13}C, and solid state ^{13}C spectra on a Brucker MSL 200 spectrometer, resonance frequency 50 MHz. The acquisition was done using a CP/MAS technique with a contact time for cross polarization of 1 ms, spectral width 350 ppm for ^{13}C and averaging over 2800 scans.

X-Ray crystal structure determination. The experiments were carried out using a Nicolet P 3/F four-circle diffractometer. The radiation was Mo Kα (λ = 0.71069 Å) and the crystals were cooled by a cold nitrogen stream to 138 K. Unit cell parameters were determined from the settings of 25 carefully centred general reflections by a least-squares procedure. Crystal data and the conditions for the data collection are given in Table 2.

The intensity data were corrected for Lorentz and polarization effects but not for absorption and extinction. Standard deviations for the intensities were based on intensity statistics with an addition of 2% of the net intensity.

Atomic coordinates of all non-hydrogen atoms were determined by direct methods (MITHRIL).[8] Refinements were performed by least-squares calculations.[9] Hydrogen positions were all found from difference syntheses and included in the refinements with isotropic thermal parameters. Final figures of merit are included in Table 2. Positional parameters of the non-hydrogen atoms are listed in Table 3 together with their equivalent isotropic thermal parameters. List of structure factors, anisotropic thermal parameters and hydrogen parameters, and a complete list of bond lengths, bond angles and torsion angles may be obtained from C.R. upon request.

Description of the structures

Discussion. PLUTO plots of the molecules are presented in Figs. 2(a) and 2(b) (compound **1a**), 3 (compound **1b**) and 4 (compound **2**). Bond lengths and angles for all the structures are as expected unless specified in the following discussion. With the bulky 2,2-dicyano-1-methylethenyl group and the acid or ester group bonded to neighbouring carbon atoms in the ring the molecules cannot be planar. The former group and the rest of the molecule are, however, each almost planar, and the strain is relieved mainly by rotation about the bond connecting the ring and the ethenyl group, the rotation being of the order 90°; the aromatic ring is unconjugated with the double bond.

Table 2. Crystal and experimental data.

	1a	**1b**	**2**
Formula	$C_{12}H_8N_2O_2$	$C_{13}H_{10}N_2O_2$	$C_{10}H_6N_2O_2S$
M.p./°C	156–157	95–96	141–142
Crystal dimensions/mm	0.3×0.3×0.2	0.3×0.2×0.2	Sphere ϕ=0.4
Crystal system	Orthorhombic	Monoclinic	Monoclinic
a/Å	8.945(2)	14.076(4)	11.058(2)
b/Å	10.644(2)	6.153(1)	14.628(3)
c/Å	22.458(5)	14.437(2)	12.713(2)
β/°		110.92(2)	97.98(1)
V/Å	2138.3(7)	1167.9(4)	2036.5(7)
T/K	136	136	136
Space group	$P2_12_12_1$	$P2_1/c$	$P2_1/n$
M	212.21	226.23	218.23
Z	8	4	8
D_x/g cm^{-3}	1.318	1.287	1.423
Scan mode	ω	ω/2θ	ω/2θ
Scan speed/°min^{-1}	3.0	2.0	3.0
Scan range/°	2.6	1.7	1.8
Maximum (sinθ/λ)/Å^{-1}	0.80	0.80	0.80
No. of indep. meas.	5280	5123	9060
No. with $I>3.0\sigma(I)$	2159	2504	5599
No. of parameters ref.	353	194	319
$R=\Sigma\|\|F_o\|-\|F_c\|\|/\Sigma\|F_o\|$	0.052	0.048	0.038
$R_w=[\Sigma w(F_o-F_c)^2/\Sigma wF_o^2]^{1/2}$	0.038	0.054	0.042
$S=[\Sigma w(F_o-F_c)^2/(n-m)]^{1/2}$	1.59	2.60	2.16
Max. $\Delta\rho$/e Å^{-3}	0.52	0.26	0.45
Min. $\Delta\rho$/e Å^{-3}	−0.38	−0.23	−0.24

Table 3. Final fractional coordinates and equivalent temperature factors with estimated standard deviations for non-hydrogen atoms.

Atom	x	y	z	U_{eq} [a]
1a 2-(2,2-Dicyano-1-methylethenyl)benzoic acid				
O1	0.6453(3)	0.4591(2)	0.2376(1)	0.034
O2	0.6053(2)	0.2745(2)	0.1925(1)	0.030
O21	0.1852(3)	0.6513(2)	0.2540(1)	0.041
O22	0.1609(3)	0.8236(2)	0.1976(1)	0.032
N1	0.4922(4)	−0.0513(2)	0.0525(1)	0.048
N2	0.6348(3)	0.3181(2)	−0.0121(1)	0.034
N21	−0.1623(3)	1.1391(2)	0.0964(1)	0.037
N22	−0.3313(4)	0.8418(3)	0.2107(1)	0.050
C1	0.4035(4)	0.3876(3)	0.1109(1)	0.025
C2	0.3229(4)	0.4533(3)	0.0681(1)	0.030
C3	0.3225(4)	0.5843(3)	0.0677(1)	0.035
C4	0.4002(4)	0.6492(3)	0.1108(2)	0.034
C5	0.4787(4)	0.5861(3)	0.1540(1)	0.031
C6	0.4830(3)	0.4546(3)	0.1543(1)	0.024
C7	0.5818(4)	0.3867(3)	0.1966(1)	0.027
C8	0.4029(3)	0.2466(3)	0.1080(1)	0.026
C9	0.4792(3)	0.1908(3)	0.0635(1)	0.025
C10	0.3048(4)	0.1767(3)	0.1502(1)	0.035
C11	0.4845(4)	0.0553(3)	0.0575(1)	0.031
C12	0.5654(3)	0.2616(3)	0.0213(1)	0.024
C21	−0.0479(3)	0.6903(3)	0.1223(1)	0.025
C22	−0.1323(4)	0.6126(3)	0.0863(1)	0.035
C23	−0.1380(4)	0.4840(3)	0.0952(1)	0.038
C24	−0.0589(4)	0.4319(3)	0.1415(2)	0.036
C25	0.0252(4)	0.5067(3)	0.1785(1)	0.032
C26	0.0323(3)	0.6355(3)	0.1695(1)	0.025
C27	0.1310(3)	0.7134(3)	0.2083(1)	0.028
C28	−0.0420(3)	0.8273(3)	0.1066(1)	0.028
C29	−0.1431(4)	0.9066(3)	0.1292(1)	0.028
C30	0.0682(4)	0.8655(3)	0.0604(2)	0.036
C31	−0.1523(4)	1.0373(3)	0.1104(1)	0.030
C32	−0.2488(4)	0.8699(3)	0.1745(1)	0.031
1b Methyl 2-(2,2-dicyano-1-methylethenyl)benzoate				
O1	0.65716(8)	0.02391(20)	0.56172(8)	0.032
O2	0.81394(9)	0.08384(22)	0.67186(9)	0.037
N1	0.73676(12)	0.12156(27)	0.93953(12)	0.041
N2	1.06306(12)	0.23548(26)	1.00043(13)	0.041
C1	0.74072(11)	0.45675(28)	0.74506(11)	0.025
C2	0.69935(13)	0.64166(30)	0.77130(12)	0.031
C3	0.59708(14)	0.69276(33)	0.72220(13)	0.036
C4	0.53601(13)	0.56043(34)	0.64695(13)	0.036
C5	0.57695(12)	0.37757(31)	0.61958(12)	0.031
C6	0.67962(11)	0.32467(27)	0.66739(11)	0.025
C7	0.72501(12)	0.13311(29)	0.63563(11)	0.027
C8	0.85079(12)	0.41298(27)	0.80184(12)	0.026
C9	0.87604(11)	0.29427(26)	0.88546(12)	0.025
C10	0.92586(14)	0.52334(38)	0.76715(16)	0.038
C11	0.79940(12)	0.19723(27)	0.91649(12)	0.028
C12	0.98040(12)	0.25920(27)	0.94897(12)	0.029
C13	0.69642(16)	−0.15933(34)	0.52412(15)	0.038
2 3-(2,2-Dicyano-1-methylethenyl)thiophene-2-carboxylic acid				
S1	0.89589(3)	0.27334(2)	0.20316(3)	0.022
S11	0.92836(3)	0.55266(3)	−0.36434(3)	0.024
O1	0.75698(10)	0.49823(7)	0.07374(8)	0.025
O2	0.87292(11)	0.38869(7)	0.01507(8)	0.030
O11	0.90328(11)	0.47477(8)	−0.15863(9)	0.033
O12	0.76654(10)	0.57455(7)	−0.11046(8)	0.025
N1	0.39520(13)	0.60008(10)	0.20981(12)	0.035
N2	0.49809(12)	0.36435(10)	0.03615(10)	0.030
N11	0.49098(12)	0.65784(10)	−0.47356(10)	0.032
N12	0.42725(13)	0.83689(10)	−0.20992(11)	0.033
C1	0.80388(12)	0.36787(9)	0.17986(10)	0.018
C2	0.74086(12)	0.38599(9)	0.26460(10)	0.018
C3	0.77191(13)	0.32247(10)	0.34848(11)	0.023
C4	0.85335(14)	0.25787(10)	0.32533(12)	0.025
C5	0.81308(12)	0.41992(10)	0.08247(10)	0.020

Table 3. (continued)

Atom	x	y	z	U_{eq} [a]
C6	0.65131(12)	0.45997(9)	0.27271(10)	0.018
C7	0.55074(12)	0.46979(9)	0.19934(10)	0.018
C8	0.46400(13)	0.54226(10)	0.20605(11)	0.023
C9	0.52332(12)	0.41046(10)	0.10845(11)	0.020
C10	0.67593(15)	0.52170(11)	0.36695(12)	0.027
C11	0.83990(12)	0.59489(10)	−0.27391(10)	0.020
C12	0.78030(12)	0.67450(9)	−0.30989(10)	0.018
C13	0.80905(13)	0.70038(10)	−0.41141(11)	0.023
C14	0.88809(14)	0.64119(11)	−0.44904(11)	0.025
C15	0.83309(13)	0.54687(10)	−0.17401(11)	0.021
C16	0.69659(12)	0.72858(9)	−0.25296(10)	0.019
C17	0.57995(13)	0.73994(10)	−0.29938(10)	0.020
C18	0.53182(13)	0.69491(10)	−0.39762(11)	0.023
C19	0.49436(13)	0.79436(10)	−0.25029(11)	0.024
C20	0.74153(14)	0.77347(11)	−0.14884(11)	0.025

[a] $U_{eq}=(U11+U22+U33)/3$.

In the subsequent discussion we follow the numbering of Figs. 2–4, which differ from the IUPAC convention used in the formulae and Table 1.

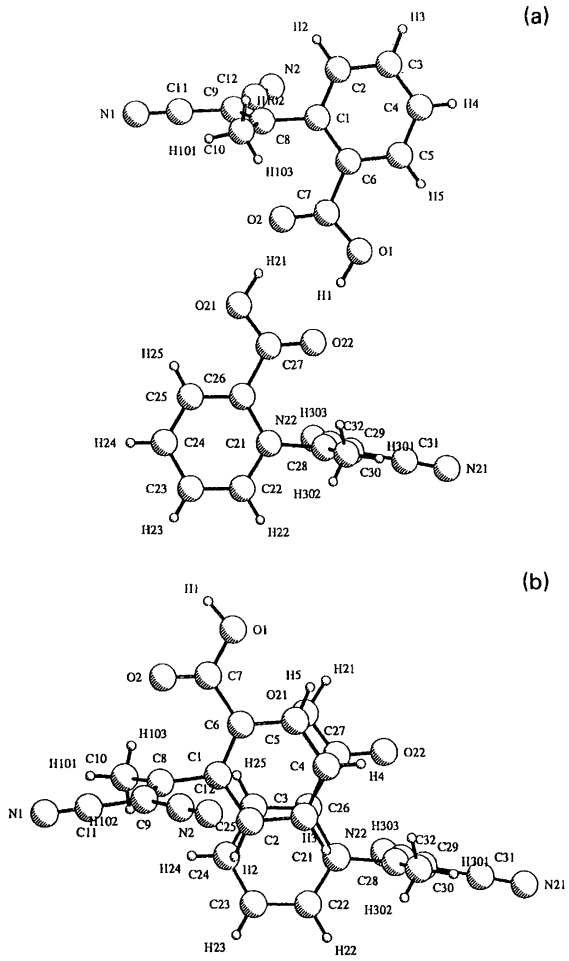


Fig. 2. PLUTO plot of **1a** showing (a) the non-centrosymmetric acid dimer and (b) the overlap diagram of the stacked molecules.

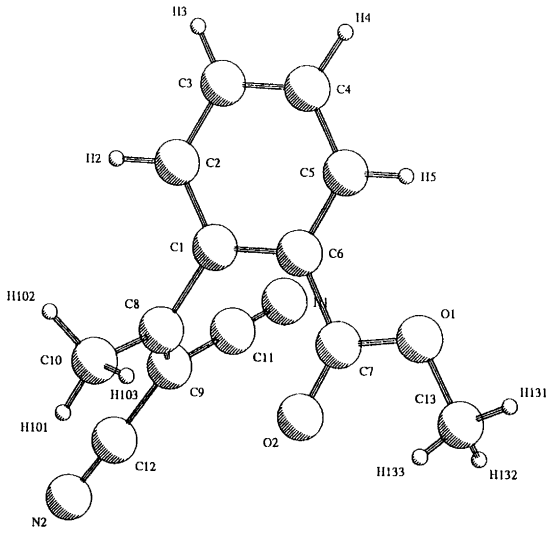


Fig. 3. PLUTO plot of **1b**.

1a, *2-(2,2-Dicyano-1-methylethenyl)benzoic acid.* The molecules form non-centrosymmetric hydrogen bonded pairs in the crystal as depicted in Fig. 2(a). The hydrogen bonds are of medium strength, O1–O22 and O21–O2 equal to 2.685(3) Å and 2.584(3) Å, respectively. The centrosymmetric arrangement often encountered in carboxylic acid dimers is destroyed by the different arrangement of the two dicyanomethylethenyl groups. As may be seen from the figure, the methyl groups of the dimer point to the same side of the general dimer plane as do the dicyanoethenyl groups. The situation may be characterized by the single bond torsion angles: C6–C1–C8–C9 = −107.9(4)°, C6–C1–C8–C10 = 78.7(4)°, C26–C21–C28–C29 = −93.3(4)°, and C26–C21–C28–C30 = 93.6(4)°. The two parts of the dimer thus have different geometries as also demonstrated by the solid-state ^{13}C NMR spectra. The torsion angles about the C1–C8 and C21–C28 is too close to 90° for any conjugation to be possible; the single bonds of length 1.502(5) Å and 1.501(5) Å and the double bonds, 1.349(5) Å and 1.337 Å are close to the values expected for a non-conjugated system.[10]

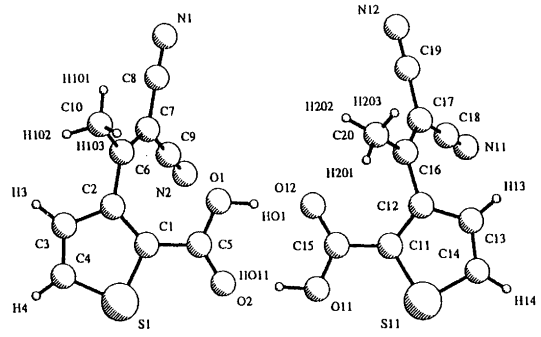


Fig. 4. PLUTO plot of **2** showing the non-centrosymmetric acid dimer.

There is a very short intramolecular distance between the carbonyl oxygen atom and the carbon of the ethenyl group closest to the phenyl ring; the O2–C8 distance is 2.685(3) Å and the O22–C28 distance 2.733(3) Å. The strain has to some degree been compensated by opening of the angles at C1 and C7 (C21 and C27), but the separations are still well within the van der Waal's distance. This is probably the reason for the ease of the ring closure reaction in solution (*vide infra*).

Fig. 2(b) shows another part of the unit cell illustrating other intermolecular contacts within the structure. The benzoic acid planes are nearly parallel with a separation corresponding to a stacking sequence; the C4–C27 separation is only 3.327(4) Å and other contacts are C3–C26, 3.501(5) Å; C4–C26, 3.549(5) Å and C5–O21, 3.523(4) Å.

1b, *Methyl 2-(2,2-dicyano-1-methylethenyl)benzoate.* There are no possibilities for strong intermolecular interactions in the solid-state in this molecule and it is expected to have a structure much like that in the free state. The plane of the dicyanomethylethenyl group is nearly normal to the phenyl plane, the torsion angles corresponding to those given for **1a** being C6–C1–C8–C9 = −92.2° and C6–C1–C8–C10 = 93.3°. The carbon and oxygen atoms of the ester group are situated in the plane of the phenyl ring. The C1–C8 bond length is 1.496(3) Å and the C8–C9 bond 1.346(3) Å, not far from the unconjugated values.[10] Also in this molecule the O2–C8 distance is very short, 2.633(2) Å, as found for the acid. The strain is relieved by opening of the angles at C1 and C7.

2, *3-(2,2-Dicyano-1-methylethenyl)thiophene-2-carboxylic acid.* The molecules form non-centrosymmetric hydrogen-bonded dimers in the crystal, the hydrogen bonds being O1–O12 [2.610(1) Å and 011–02 [2.604(2) Å]. Since the substituents in this molecule are connected to a five-membered ring, the bonds to the ring form a larger angle than in the case of the phenyl ring and the bulky dicyanomethylethenyl group is not required to be rotated as much as in the phenyl analogue. In this case the two methyl groups also point to the same side of the general plane of the dimer. There are thus two different molecules in the crystals as found by the MAS measurements. The torsion angles are as follows: C1–C2–C6–C7 = 56.1(2)°, C1–C2–C6–C10 = −125.3(2)°, C11–C12–C16–C17 = −119.4(2)° and C11–C12–C16–C20 = 63.5(2)°. They are appreciably further from 90° than found for the phenyl analogue **1a** and the ester **1b**; the C2–C6 and C12–C16 single bonds were found to be 1.480(2) and 1.481(2) Å, respectively, and the C6–C7 and C16–C17 double bonds 1.356(2) Å and 1.352(2) Å. The shorter single bond and longer double bond suggest a higher degree of conjugation than in **1a** and **1b**.

It should be noted that in the present dimer the carboxy groups are rotated 180° relative to the ring; in one molecule the hydroxy group is *trans* to the sulfur atom in the other it is *cis* to this atom. It follows then that for one

of the molecules the hydroxy oxygen atom is closest to the ethenyl carbon atom with the O1–C6 distance being 2.983(2) Å, whereas in the other molecule the carbonyl oxygen atom is closest to the ethenyl carbon atom C16, the separation O12–C16 being 2.927(2) Å. Compared with the phenyl analogue the separations are larger by 0.25 Å, which might be the reason for the thiophene analogue's inability to undergo ring closure in solution.

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