Enols and thioenols of substituted cyanomonothiocarbonylmalonamides: structures, enolization *vs.* thioenolization, equilibria and conformations †‡§

Ahmad Basheer and Zvi Rappoport*

Received 13th November 2007, Accepted 18th January 2008 First published as an Advance Article on the web 14th February 2008 DOI: 10.1039/b717556f

Condensation of organic isothiocyanates with cyanoacetamides gave 24 *N*- and *N'*-substituted cyanomonothiocarbonylmalonamides in different tautomeric ratios *i.e.*, amide–thioamides (TMA) R³NHCSCH(CN)CONR¹R² (12), thioamide–enols of amides (E) R³NHCSC(CN)=C(OH)NR¹R² (11) or amide–thioenols (TE) R³NHC(SH)=C(CN)CONR¹R² (13). The equilibrium constants ($K_{thioenol} = [TE]/[TMA]$ and $K_{enol} = [E]/[TMA]$) in solution depend on R¹, R², R³ and the solvent. The %(E + TE) for NR¹R² increases in the order NMe₂ < NHMe < NH₂. The ($K_{thioenol} + K_{enol}$) in various solvents follows the order CCl₄ > CDCl₃ > C₆D₆ > THF-d₈ > (CD₃)₂CO > CD₃CN > DMF-d₇ > DMSO-d₆. The δ (OH) values are 16.46–17.43 and the δ (SH) values are 3.87–5.26 ppm in non polar solvents, *e.g.*, CDCl₃ and 6.34–6.97 ppm in THF-d₈ and CD₃CN. An intramolecular O–H ··· O hydrogen bond leads to the preferred *Z*-configuration of the enols, and an N–H ··· O bond stabilizes the thioenols' preferred *E*-configuration with a non-bonded SH in solution. X-Ray crystallography revealed that systems with high %(E + TE) in solution mostly display the enols 11 in the solid state and systems with lower %(E + TE) in solution display structure 12. The differences in δ (OH), δ (NH), K_{enol} and crystallographic data for analogous enol and thioenol systems are compared.

Introduction

Enols and keto–enol equilibria for mono-carbonyl and 1,3dicarbonyl compounds have been extensively investigated over the last hundred years.¹ In contrast, enols of carboxylic acids, their esters, anhydrides, amides, thioamides or halides have been scarcely investigated until recently.² In the last decade we have extensively investigated these species,^{3,4} especially the enols of amides,^{3a-c,4} which are usually unobservable, *i.e.*, the equilibrium constant $K_{enol} = [enol]/[amide]$ is <0.01. The computed K_{enol} for acetamide is 10^{-21.6}.⁵ The reason for this is that mesomeric electron donation by X stabilizes the acid derivative **2a** *via* contributing structure **2b** which is favored by the negative charge on its oxygen atom (eqn (1)).



A similar electron donation by X and OH to C_{α} of the enol 1a creates a negative charge on C_{β} , which only slightly stabilizes

the enol when Y,Y' are not electron-withdrawing groups (EWGs). Consequently, the acid derivative is much more stabilized than the enol with a drastic reduction in K_{enol} compared with those for simple carbonyl derivatives.⁶

Our approach to stabilized enols of carboxylic acid derivatives is by increased stabilization of structure **1b** by substituting C_{β} with resonatively negative charge EWGs Y and Y'.^{3,4} The stabilized **1b** is zwitterionic with delocalized positive charge on C_a , X and OH and negative charge on C_{β} , Y and Y'. This implies a relatively long C_a – C_{β} formal double bond with a significant single bond character. The acid derivatives are presumably also destabilized by Y,Y'/CO dipole–dipole repulsion.^{3b}

By applying this approach we observed by NMR spectroscopy >100 enols of amides YY'C=C(OH)NHX (4) either exclusively or as mixtures with the isomeric amides Y'YCHCONHX (3) in solution, and determined the solid structures of >25 enols by X-ray crystallography. Combinations of Y,Y' for which only the enol is observed in CDCl₃ ($K_{enol} \ge 50$) include amides where Y'Y is the cyclic diester Meldrum's acid (MA) moiety,^{3a} Y = CN, Y' = CO₂R, R = CH₃^{3b} or CH₂CCl₃,^{4d} or Y = CO₂CH(CF₃)₂, Y' = CO₂CH₂CF₃. The K_{enol} value is low when Y = Y' = CO₂Me.^{3a}

A problem is that Y or Y' can serve as an enolization site. Although ester groups do not compete with an amide, a ketonic CO at C_{β} , *e.g.*, in PhNHCOCH(*COMe*)CO₂Et (**5**),³⁶ serves as an enolization site. Substituted 2-amidoindandiones can form enol isomers on both the amide and the ring CO.⁷

Cyanomalonamides display in solution both the amide **6** and one of the enols 7or **8** (eqn (2)). The enolic hydrogen forms a strong intramolecular hydrogen bond to the carbonyl of the second amide group and apparently migrates rapidly between the two oxygens.⁸ The K_{enol} and $\delta_{\rm H}$ (OH) values in moderate and polar solvents are relatively high.

Department of Organic Chemistry and the Lise Meitner Minerva Center for Computational Quantum Chemistry, The Hebrew University, Jerusalem 91904, Israel. E-mail: ZR@vms.huji.ac.il

[†] Presented in part in the 11th Kyushu International Symposium on Physical Organic Chemistry (KISPOC XI), Fukuoka, September 12–15, 2005

[‡] CCDC reference numbers 667545–667551. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b717556f

[§] Electronic supplementary information (ESI) available: Tables S1–S6 (spectral and analytical data). See DOI: 10.1039/b717556f

R¹R²NCOCH(CN)CONHR³ R¹R²NCOC(CN)=C(OH)NHR³ or R¹R²NC(OH)=C(CN)CONHR³ 7

> a: R¹= R² = Me; R³ = Ph, *p*-MeOC₆H₄, C₆F₅, i-Pr, *t*-Bu (K_{Enol} (CDCl₃) = 2.2-4.0) (2)b: R¹= Me, R² = H; R³ = Ph, *p*-MeOC₆H₄, C₆F₅, i-Pr, *t*-Bu (K_{Enol} (CDCl₃) = 5.3-11.5) $\textbf{c} \colon \mathsf{R}^1 = \ \mathsf{R}^2 = \mathsf{H}; \ \mathsf{R}^3 = \mathsf{Ph}, \ \rho \cdot \mathsf{MeOC}_6\mathsf{H}_4, \ \mathsf{C}_6\mathsf{F}_5, \ i \cdot \mathsf{Pr}, \ t \cdot \mathsf{Bu} \quad (\mathsf{K}_{\mathsf{Enol}} \ (\mathsf{CDCl}_3) \geq 50)$ **d**: $R^1 = H$, $R^2 = R^3 = i$ -Pr (K_{Enol} (CDCl₃) = 8.09)

8

CH₂(CN)CONR¹R² + R³NCS 10 9 Na/dry THF

R³NHCSC(CN)=C(OH)NR¹R² \rightarrow R³NHCSCH(CN)CONR¹R² $\xrightarrow{K_{\text{thioenol}}}$ R³NHC(SH)=C(CN)CONR¹R²

Enol (E)	Amide/Thioamide (TMA)	Thioenol (TE)
11	12	13
11a: R ¹ = R ² = Me; R ³ = Ph	12a	13a
11b: R ¹ = R ² = Me; R ³ = <i>p</i> -MeOC ₆ H ₄	12b	13b
11c: R ¹ = R ² = Me; R ³ = 1-Np (1-Naphthyl)	12c	130
11d: R ¹ = R ² = Me; R ³ = Me	12d	13d
11e: R ¹ = R ² = Me; R ³ = Et	12e	13e
11f: R1= R ² = Me; R ³ = i-Pr	12f	13 f
11g: R ¹ = R ² = Me; R ³ = <i>t</i> -Bu	12g	13g
11h: R ¹ = H; R ² = Me; R ³ = Ph	12h	13h
11i: R ¹ = H; R ² = Me; R ³ = <i>p</i> -MeOC ₆ H ₄	12i	13i
11j: R ¹ = H; R ² = Me; R ³ = 1-Np	12j	13j
11k: R ¹ = H; R ² = Me; R ³ = Me	12k	13k
11I: R ¹ = H; R ² = Me; R ³ = Et	121	131
11m: R ¹ = H; R ² = Me; R ³ = i-Pr	12m	13m
11n: R ¹ = H; R ² = Me; R ³ = <i>t</i> -Bu	12n	13n
11o: R ¹ = R ² = H; R ³ = Ph	120	130
11p: R ¹ = R ² = H; R ³ = <i>p</i> -MeOC ₆ H ₄	12p	13p
11q: R ¹ = R ² = H; R ³ = 1-Np	12q	13q
11r: R ¹ = R ² = H; R ³ = i-Pr	12r	13r
11s: R ¹ = R ² = H; R ³ = <i>t</i> -Bu	12s	13s
11t: R ¹ = H; R ² = i-Pr; R ³ = Ph	12t	13t
11u: R ¹ = H; R ² = R ³ = i-Pr	12u	13u
11v: R ¹ = H; R ² = CHPh ₂ ; R ³ = i-Pr	12v	13v
11w: R ¹ = H; R ² = CHPh ₂ ; R ³ = <i>t</i> -Bu	12w	13w
11x: R ¹ = H; R ² = Ph; R ³ = <i>t</i> -Bu	12x	13x

In the present work we replaced one carbonyl group in 6 by a thiocarbonyl group, obtaining cyanomonothiocarbonylmalonamides R3NHCSCH(CN)CONR1R2, in order to investigate the following goals: (i) to extend the scope of stable enols of amides with a β -thioamido group; (ii) to study the intramolecular competition between amide and thioamide enolization sites as a function of R^1 - R^3 ; (iii) to probe the role of hydrogen bonding on the configuration and conformation of the enols and thioenols; (iv) to determine the solid state structure of these species, and whether it is the same as in solution.

6

Results

Synthesis

The 24 "formal"⁹ cyanomonothiocarbonylmalonamides 11/ 12/13 (a-x) were prepared by reacting the anion of a substituted cyanoacetamide (9) with an organic isothiocyanate (10) (eqn (3)). The products are the amide-thioamide (TMA, 12), the enol (E, 11) and/or the thioenol (TE, 13), or a mixture. Three equilibrium constants are defined: K_{enol} , $K_{thioenol}$ and K_{total} (eqn (4)). Compounds, 12e,^{10a} 12h,^{10b} 12k,^{10c} 11k,^{10c} 11o,^{10d} 11p^{10e,f} and 12r¹¹ were prepared previously. The stereochemistries of 11 and 13 are discussed below. Compounds 11/12/13 are much more reactive than 6/7/8. Several of them react on crystallization in a variety of ways, mostly to give heterocyclic compounds.11

$$K_{\text{enol}} = [\text{E}]/[\text{TMA}], K_{\text{thioenol}} = [\text{TE}]/[\text{TMA}],$$
$$K_{\text{total}} = ([\text{E}] + [\text{TE}])/[\text{TMA}] \quad (4)$$

(3)

Solid state structures

Solid state structures of eight systems were determined by X-ray diffraction.[‡] Four of them display the enol structures 11h–11k. 11h and 11i were crystallized from EtOAc and 11j was crystallized from EtOAc under nitrogen. Fig. 1a displays the ORTEP drawing of 11j which shows both intramolecular $O-H\cdots S$ and intermolecular $CN \cdots H-N$ hydrogen bonds. The four derivatives **12d** (Fig. 1b), 12f, 12k, 12v display amide structures. 12d, 12f and 12v were crystallized from CDCl₃.

Table 1 gives selected crystallographic data for enols 11h-11j. Data for 11k, which was crystallized from CDCl₃, was reported earlier.^{10c} The differences between the relevant parameters for the four compounds are small, considering the standard deviations. The C(1)–O(1) bond lengths of 1.301-1.307 Å, the C(2)–C(4) bond of 1.402–1.417 Å, the small difference of ≤ 0.011 Å between the bond lengths of C(1)-C(2) and C(2)-C(3) for the three compounds, and the doubly bonded C=S moiety (1.687–1.700 Å), indicate a highly delocalized enol structure. The variable O-H bond length of 0.98–1.18 Å is in line with the difficulty in locating hydrogens by X-ray diffraction. The O · · · S non-bonding distance of 2.836-2.865 Å, and the non-linear C=S \cdots H–O hydrogen bond of



Fig. 1 ORTEP drawing of (a) **11j** and (b) **12d** (thermal ellipsoids scaled to include 50% probability).

1.70–1.93 Å indicate a weaker hydrogen bond than the O ··· H– O bond in enols **7/8**.⁸ Bond angles around the C(1)–C(2) bond are 120 ± 5° (Table 1), and their sum of 359.8–360.0° indicate planarity around C(2). The structures are dimeric: one cyano nitrogen in each molecule is intermolecularly hydrogen bonded to the amide H–N–CO of a second molecule. These bonds cause a C(4)–N(2) bond elongation from 1.136–1.137 Å for the C_{sp}1≡N bond¹² to 1.148–1.151 Å. The non-bonding N····N[#] (N[#] belongs to a second molecule) and H····N[#] distances, the N–H bond lengths and the N(1)–H···N(2)[#] angles indicate an asymmetric and bent intermolecular hydrogen bond.

Fig. 1b, Table 2 and the ESI§ give structural data for the amides **12d**, **12f** and **12v** and of the "amide" part of **12r** (see below; those of **12k** was reported earlier^{10c}), with normal bond lengths: C=O 1.228–1.236 Å, C=S 1.646–1.659 Å, C=N 1.129–1.137 Å and C(1)–C(2) 1.535–1.543 Å. The 107.6–113.6° angles around C2 indicate an sp³ carbon. The structures are "polymeric" where the C=O carbonyl is intermolecularly hydrogen bonded to the H–N–C=S of another molecule.

Crystallization of **12r** from CD₃CN gave an associate with an "apparent" amide structure **12r** intermolecularly hydrogen bonded *via* one water molecule to 3,5-bis(isopropylamino)-[1,2]dithiolane-4-carbonitrile (Fig. 1 in ref. 11). The C(1)–C(2), C(2)–C(3) and C(2)–C(4) bonds of **12r** are shorter, and the C(1)– O(1), C(3)–N(3) and C(4)–N(2) bonds are longer, than those of the other amides (Table 2). The H–N–C=S is intramolecularly hydrogen bonded to the C=O group with an N–H bond length and O···H and O···N distances of 0.82(2) Å, 2.01(2) Å and 2.667(2) Å, respectively, and an OHN angle of 137.7(17)°. It was suggested that the species is a radical derived from **12r**.¹¹ System 11k/12k/13k, $R^3 = Me$ was crystallized either as the amide 12k or as the enol 11k, depending on the solvent polarity.^{10c}

Structures in solution. NMR spectra and K_{enol} values in solution

¹H and ¹³C NMR spectra were recorded for **11/12/13** in several solvents. Selected ¹H spectral parameters are given in Table 3 and the complete data are in Table S1. The ¹³C NMR data are in Table S2 in the supplementary data.§

On dissolving a sample of the X-ray analyzed crystals of either 11 or 12 or the formal⁹ TMA, the substituent- and solventdependent spectra of the tautomeric system 11 (E)/12 (TMA)/13 (TE) were instantaneously observed. The composition did not change with time, *i.e.*, equilibria between the various species is rapidly established, as found for other enols of amides.^{3,4}

Both the E and TE species can *a priori* exist in both *E* and *Z* configurations. For the analogous 7/8 only the isomer whose enolic OH is intramolecularly hydrogen bonded to the *cis* amido carbonyl is usually observed.⁸ The linear CN cannot form an intramolecular CN \cdots H–O hydrogen bond and the isomer with the *cis*-CN/OH configuration is not observed.

For all enois **11** the δ (OH) signals at > 16 ppm in CDCl₃ indicate the presence of hydrogen bonding. Most derivatives (except for NR¹R² = NMe₂, R³ = Alk) also showed a relatively high field singlet at *ca.* 3.9–7.0 ppm ascribed to a non-hydrogen bonded SH group of **13**.

Fig. 2a displays the low field region of a CDCl₃ solution of formal⁹ *t*-BuNHCSCH(CN)CONHMe **12n**. The lowest field very narrow doublet at δ 16.88 is ascribed to the hydrogen bonded OH signal of **11**, by analogy with many systems.^{3,4} There are two relatively sharp NH signals for each species, with reliable position and integration for assignment and for determination of the K_{enol} values; *e.g.*, the signals at δ 6.55 and 6.05 with 99% intensities of the δ (OH) are the NH signals of **11**. The NH signals at δ 11.61 and 5.81 with 40 \pm 1% intensity of δ (OH), are ascribed to **13**. Its SH signal almost overlaps the amide CH signal at δ 4.79. The signals of **12** at δ 8.75 and 7.05 have 81% intensity of δ (OH).

The ¹H NMR spectrum in DMSO-d₆ displays only the CH, CSNH and CONH signals of **12n** at δ 5.13, 8.00 and 9.77 ppm, respectively (Fig. 2b). In the ¹³C NMR spectrum in CDCl₃ (Fig. 2c), three pairs of signals appear in the high ppm region: at *ca*. δ 185 for the C=S groups of **11n** and **12n**, at δ 172 and 168 for C_a of the **11n** and **13n**, and at δ 162 and 164 for the C=O signals of **13n** and **12n**. The coupled C_β signals are singlets at 66.7 (**11n**) and 70.7 (**13n**) ppm and a doublet at 56.1 ppm for **12n**. Simpler ¹H NMR spectra are observed for systems **11a–g/12a–g/13a–g**, having only three NH signals; *e.g.*, for **11c/12c/13c** the δ (NH) values resemble those observed in Fig. 2a. The separated CH and SH signals are at 5.49 and 4.50 ppm, respectively.

The δ (OH), δ (SH) and δ (CH) for selected R³NHCSCH(CN)-CONR¹R² systems in several solvents where all three species are observed are given in Table 3. In all the solvents and for all R's δ (OH) is at 16.46–17.43, δ (SH) is at 3.87–6.97 and δ (CH) is at 4.09–5.79. Changes due to combinations of R¹, R² and R³ are not systematic. The highest δ (OH) and δ (SH) values are in THF-d₈ or C₆D₆, for each group.

In the δ_c values of the C=S, C=O, C_a(11), C_a(13), C=N and C_β signals for the three isomers of all systems soluble in CDCl₃ (Table S3 in the ESI§), each isomer displays pairs of low field

Compound	$11h (R^3 = Ph)^b$	$11i (R^3 = p-An)$	11j ($R^3 = 1$ -Np)
Bond length/Å			
C(1)-C(2)	1.426(2), 1.425(2)	1.424(5)	1.412(3)
C(1) - N(1)	1.318(2), 1.317(2)	1.314(4)	1.319(3)
C(1)–O(1)	1.301(2), 1.302(2)	1.301(4)	1.307(2)
C(2) - C(3)	1.427(2), 1.427(2)	1.427(4)	1.423(3)
C(3) - N(3)	1.352(2), 1.345(2)	1.346(4)	1.344(3)
C(3)-S(1)	1.693(1), 1.700(1)	1.687(3)	1.694(2)
C(2) - C(4)	1.415(2), 1.414(2)	1.402(5)	1.417(3)
C(4) - N(2)	1.151(2), 1.149(2)	1.151(4)	1.148(3)
O(1)–H(O1)	1.06(3), 1.05(3)	1.18(5)	0.98(3)
$S(1) \cdots H(O1)$	1.85(3), 1.84(3)	1.70(5)	1.93(3)
$O(1) \cdots S(1)$	2.857(1), 2.849(1)	2.836(3)	2.865(2)
N(1)–H(N1)	0.82(2), 0.77(2)	0.83(3)	0.87(2)
N(3)–H(N3)	0.75(2), 0.76(2)	0.83(4)	0.78(2)
$N(2) \cdots H(N1)^c$	2.23(2), 2.30(2)	$2.23(4)^{\#1}$	$2.14(2)^{\#2}$
$N(1) \cdots N(2)^{c}$	2.999(2), 2.975(2)	2.976(5)#1	2.947(3)#2
Bond angle/°			
O(1)-C(1)-C(2)	122.7(1), 123.0(1)	122.5(3)	122.9(2)
O(1)-C(1)-N(1)	115.3(1), 115.3(1)	115.4(3)	115.3(2)
N(1)-C(1)-C(2)	122.0(1), 121.7(1)	122.2(3)	121.8(2)
C(1)-C(2)-C(3)	124.9(1), 125.1(1)	124.9(3)	125.1(2)
C(1)-C(2)-C(4)	116.1(1), 116.3(1)	116.0(3)	116.7(2)
C(4) - C(2) - C(3)	118.9(1), 118.6(1)	119.0(3)	118.0(2)
C(2)-C(3)-S(1)	123.7(1), 122.9(1)	123.1(3)	124.2(2)
N(3)-C(3)-S(1)	120.5(1), 120.3(1)	119.8(3)	119.2(2)
C(2)-C(3)-N(3)	115.8(1), 116.7(1)	117.1(3)	116.7(2)
C(2)-C(4)-N(2)	178.5(2), 179.3(2)	179.3(5)	178.4(3)
C(1)–O(1)–H(O1)	108(2), 104(2)	104(2)	107(2)
$O(1)-H\cdots S(1)$	156(2), 160(2)	161(3)	158(2)
$N(1)-H(N1)\cdots N(2)^{c}$	150(2), 151(2)	151(3)#1	$153(2)^{\#2}$

 Table 1
 Selected crystallographic data (bond lengths, hydrogen bond distances and angles) for the enois $R^3NHCSC(CN) = C(OH)NR^1R^2$ 11h–11j, ($R^3 = Ph, p-An(p-MeOC_6H_4), 1-Np$) at room temperature^{*a*}

^{*a*} Measured at 173(1) K. ^{*b*} Two independent molecules. ^{*c*} Symmetry transformations used to generate equivalent atoms: ^{*m*1}, -x + 2, -y + 1, -z + 1; ^{*m*2}, -x, -y + 1, -z + 1.

Compound	$12d (R^3 = Me)$	$12f(R^3 = i-Pr)$	$12v (R^3 = i-Pr)$	$12r (R^3 = i - Pr)$
Bond length/Å				
C(1) - C(2)	1.535(6)	1.542(2)	1.543(6)	1.447(2)
C(1) - N(1)	1.315(5)	1.310(2)	1.333(6)	1.340(2)
$\vec{C}(1) = O(1)$	1.236(5)	1.229(2)	1.228(5)	1.253(2)
C(2) - C(3)	1.540(5)	1.544(2)	1.524(6)	1.425(2)
C(3) - N(3)	1.308(5)	1.315(2)	1.300(7)	1.333(2)
C(3) - S(1)	1.646(4)	1.659(1)	1.646(5)	1.713(2)
C(2) - C(4)	1.456(7)	1.467(2)	1.460(7)	1.418(2)
C(4) - N(2)	1.129(6)	1.137(2)	1.133(6)	1.149(2)
C(2)-H(C2)	0.98	0.98	0.98	_ ``
N(3) - H(N3)	0.81(5)	0.82(2)	0.65(5)	0.82(2)
$H(N3) \cdots O(1)^b$	2.07(5)#1	$2.15(2)^{\#2}$	$2.45(5)^{\#3}$	$2.01(2)^{c}$
$N(3) \cdots O(1)^{b}$	2.871(5)#1	$2.910(2)^{\#2}$	$3.064(5)^{\#3}$	$2.667(2)^{c}$
Bond angle/°		()		
O(1) - C(1) - C(2)	118.8(4)	119.7(1)	122.6(5)	122.4(2)
O(1) - C(1) - N(1)	123.9(4)	122.7(1)	124.2(5)	119.0(2)
N(1) - C(1) - C(2)	117.3(4)	117.6(1)	112.9(4)	118.6(2)
C(1)-C(2)-C(3)	111.6(3)	112.3(1)	107.6(4)	124.9(1)
C(1) - C(2) - C(4)	109.9(4)	108.2(1)	110.2(4)	116.6(1)
C(4) - C(2) - C(3)	109.5(3)	107.7(1)	113.6(4)	118.5(1)
C(2) - C(3) - S(1)	121.0(3)	119.06(9)	120.8(4)	120.5(1)
N(3)-C(3)-S(1)	124.4(3)	126.9(1)	125.8(4)	121.4(1)
C(2) - C(3) - N(3)	114.6(4)	114.05(1)	113.1(4)	118.1(1)
C(2) - C(4) - N(2)	176.1(5)	177.7(2)	175.8(5)	174.9(2)
$N(3)-H(N3)\cdots(O1)^{b}$	172(5) ^{#1}	$154(2)^{\#2}$	158(7)#3	138(2) ^c

^{*a*} Measured at 173(1) K. ^{*b*} Symmetry transformations used to generate equivalent atoms: ^{*ii*1} x - 1, -y + 1/2, z - 1/2; ^{*ii*2} x, -y + 1/2, z + 1/2; ^{*ii*3} x, -y + 2, z + 1/2. ^{*c*} The N–H is intramolecularly hydrogen bonded to oxygen O(1).



Fig. 2 ¹H NMR spectra for the **11n/12n/13n** system: (a) OH, NH, CH and SH regions (inset Me and *t*-Bu signals) in CDCl₃ at rt; (b) in DMSO-d₆ at rt. Only **12n** is observed, and no signals are at <10 ppm. (c) ¹³C NMR spectrum in CDCl₃ at rt.

signals with similar intensities. For **12** the C=S and C=O signals are at 183.16–187.67 ppm and 158.78–162.37 ppm, respectively; for **11** the C=S and C_a(E) are at 184.75–189.88 ppm and 170.41–173.26 ppm, respectively. Mostly, δ (C=S, **11**) > δ (C=S, **12**). The

C=O and C_a signals of **13** are at 164.80–169.38 ppm (**13k** at 173.26 ppm). The C=N signals are doublets (J = 9.5–11.0 Hz) at 113.85–114.64 ppm for **12** and at 117.93–120.04 ppm for **11**, and are singlets at 120.21–121.78 ppm for **13**. The coupled C_β signals are doublets at 50.15–58.65 ppm (J = 139.2–143.2 Hz) for **12**, and the C_β signals are singlets for **11** and **13** at 65.93–68.09 and 69.82–73.04 ppm, respectively.

Substituent and solvent effects

The substituents R^1 – R^3 have an effect on the distribution of the three species, and the derived K_{enol} for R^1R^2NCOCH -(CN)CSNHR³ in different solvents at rt is given in Table 4.

For NMe₂ systems the %(12) in CDCl₃ is much higher for the aliphatic $R^3 = Alk$, when 13 is not observed, than when $R^3 = Ph$, *p*-An, 1-Np, where **13** is present in 16–29%. When $R^3 = Ph$, *p*-An, %(11) > %(13), whereas the %(11 + 13) is higher when $R^3 = 1$ -Np, but the %(13) slightly exceeds the %(11). A similar trend was observed for other NR^1R^2 systems (Table 4). The effects of R^1-R^3 on the % and the K's of the various species are shown in Table 4. The %(11 + 13) increases by successively replacing the Me groups in NR¹R² by hydrogens, as was observed for the 7/8/9 system and in calculations.⁸ Thus, for $R^3 = Alk$, the %(12) is 88–96%, 22–37% and 7–24% for NR¹R² = NMe₂, NHMe and NH₂, respectively, and a similar trend was found for $R^3 = Ar$. Systematically, $K_{enol} >$ K_{thioenol} for $\mathbb{R}^3 = \text{Alk}$, Ph. In both CDCl₃ and THF-d₈, **12** is the major species for the NMe2 derivative, a minor component for NHMe and is absent for the NH₂ derivative. For the NHMe and NH₂ derivatives 11h/12h/13h and 11o/12o/13o, the %(13)/%(11) in CDCl₃ is ca. 1.1 and 1.5, respectively. However, in THF-d₈ $K_{\text{enol}}/K_{\text{thioenol}} = 11$ for NHMe, and 49 for NH₂ when R³ = Ph. For 11h-n/12h-n/13h-n, the %(11) decreased on increasing the bulk of R³: Me (71) > Et (68) \approx i-Pr (66) > t-Bu (45) \approx Ph (46) > p-An (43) > 1-Np (31). The %(12) and %(13) increase on increasing the steric effect according to t-Bu > i-Pr \approx Et > Me (Table 4).

The percentage of enolization and thioenolization decreases on increasing the solvent polarity from CCl₄ to DMSO-d₆ (Table 4), as found earlier for enols of amides.^{34,8} In the highly polar DMSO-d₆ and DMF-d₇, and also for several systems in CD₃CN, only **12** is observed. The highest %(**13**) for all systems is in CDCl₃. In CDCl₃ and CCl₄, K_{thioenol} resembles or is higher than K_{enol} for aromatic R's. In the other solvents $K_{\text{enol}} > K_{\text{thioenol}}$.

Discussion

Comparison of the solid state structures of 6/7/8 and 11/12/13

The X-ray solid state structures of three analogous pairs of the two series can be compared: (i) i-PrNH(C=Z)CH(CN)CONMe₂ (I), in which Z = O, S have amide structures with small bond length differences ($\Delta_{os} = 0.003-0.0096$ Å) between Z = O and Z = S. For I in CDCl₃, Z = O is 80% enol and Z = S is 12% enol; (ii) PhNH(C=Z)CH(CN)CONHMe (II), in which Z = O displays an amide structure, whereas for Z=S it crystallized as an enol, although in CDCl₃ the %(enol) is 90% (Z = O) and 46% (Z = S); (iii) *p*-AnNH(C=Z)CH(CN)CONHMe (III), in which Z = O, S are both enols, with small bond length differences ($\Delta_{os} = 0.004-0.03$ Å). The C(1)–C(2) bond lengths of 1.401 Å for Z = O and 1.422 Å for Z = S indicate a lower single bond character for the

Со	mpound	R ³	Solvent	$\delta(\mathrm{OH})(\mathrm{E},11)$	$\delta(\text{CH})$ (TMA, 12)	$\delta(\mathrm{SH})$ (TE, 13)
11a	a/12a/13a	Ph	CDCl ₃	16.64	5.33	4.58
111	b/12b/13b	<i>p</i> -An	CDCl ₃	16.61	5.33	4.53
110	c/12c/13c	1-Np	CCl_4	16.56	5.01	4.29
			CDCl ₃	16.64	5.49	4.50
			C_6D_6	17.29	5.09	4.27
			THF-d ₈	16.89	5.79	5.17
			CD_3CN	16.52	5.65	5.11
11ł	h/12h/13h	Ph	CDCl ₃	16.85	5.05	4.45
			THF-d ₈	17.09	5.03	6.89
			CD_3CN	16.85	5.05	6.80
11i	i/12i/13i	<i>p</i> -An	CDCl ₃	16.85	4.94	4.36
			THF-d ₈	17.12	5.01	4.85
			CD_3CN	16.86	5.01	4.55
11j	/12j/13j	1-Np	CDCl ₃	16.83	a	4.34
			THF-d ₈	17.11	5.30	6.97
			CD_3CN	16.79	5.36	6.34
111	k/12k/13k	Me	CDCl ₃	16.59	4.88	4.55
111	/121/131	Et	CDCl ₃	16.64	4.87	4.54
11r	m/12m/13m	i-Pr	CDCl ₃	16.68	4.85	5.84
11r	n/12n/13n	t-Bu	CCl_4	16.57	4.21	4.47
			CDCl ₃	16.88	4.79	4.79
			$C_6 D_6$	17.43	4.09	5.44
110	o/12o/13o	Ph	CDCl ₃	16.61	a	4.47
11r	r/12r/13r	i-Pr	CDCl ₃	16.46	4.68	5.22
11s	s/12s/13s	t-Bu	CDCl ₃	16.66	4.75	4.88
			$C_6 D_6$	17.02	4.29	3.87
11t	t/12t/13t	Ph	CDCl ₃	16.82	5.17	4.70
			THF-d ₈	17.11	5.04	6.35
11u	u/12u/13u	i-Pr	CDCl ₃	16.64	4.83	5.26
11v	v/12v/13v	i-Pr	CDCl ₃	16.94	4.81	4.63
11v	w/12w/13w	t-Bu	CDCl ₃	17.09	4.79	4.83
115	x/12x/13x	t-Bu	CDCl ₃	17.31	4.86	4.90

Table 3 Selected ¹H NMR δ values (in ppm) for 11/12/13 systems in several solvents at room temperature

" The CH or other signals of the TMA were not observed.

latter. For III in CDCl₃, Z = O is 90% enol, and Z = S is 43% enol. We conclude that there is no correlation between the %(enol) in solution and the structure of the crystallized species. The data are reported in Table S4 in the ESI.§

Enolization on C=O vs. thioenolization on C=S

A main theme of this work is the intramolecular competition between enolization on C=O and thioenolization on C=S. Both processes have been previously compared in terms of both intermolecular and intramolecular competition as shown below. For single enolization sites thioenolization is qualitatively much more facile than enolization. Simple thioenols are observable species¹³ but the corresponding enols are usually unobservable.⁶ Recent measurements illustrate this point: $K_{\text{thioenol}}/K_{\text{enol}} \ge 10^6$, *ca.* 10^4 , 10^6 and 10^5 when X = S, O for Ph₂CHC(=X)Ph,¹⁴ 9-C(=X)OMe-fluorenes,¹⁵ mesityl-C(=X)Me^{16a} and benzo[*b*]-2,3dihydrothiophene-2-(=X).^{16b}

The higher extent of thioenolization is ascribed¹⁷ to the much weaker C=S bond than the C=O bond (115 *vs.* 177 kcal mol⁻¹),¹⁸ which is not compensated by the smaller C-S and S-H bond energies than those of C-O and O-H bonds (61, 82, 88 and 110 kcal mol⁻¹).¹⁸ From these values thioenolization is 7 kcal mol⁻¹ more favored than the enolization, as reflected in the experimental values. However, these O-H and S-H bond energies

are for saturated systems, and for triarylethenols the O–H BDE is *ca.* 80 kcal mol⁻¹.¹⁹ Extensive calculations¹⁷ for the CH₃CH=X systems (X = S, O) show that thioenolization ($\Delta H = -5.5-8$ kcal mol⁻¹) is always favored over enolization ($\Delta H = 5-17$ kcal mol⁻¹). For (CH₃)₂C=X, the $\Delta(\Delta H)$ value is 8.8 kcal mol⁻¹ at B3LYP/6– 31G**. In less extensive calculations $\Delta(\Delta H) = 8-11$ kcal mol⁻¹.²⁰

These large differences do not apply for intramolecular competitive enolization in an O=C-CH-C=S system. Our systems are the first where such competition involves C=O and C=S sites of amides and thioamides. A competitive intermolecular enolization on esters strongly favors the C=S site.^{15,21} However, for 1,3thioxoketones R'C(=O)CHRC(=S)R'' (R', R'' = Alk, Ar),²² the situation is more complex. The many techniques used to determine whether enolization or thioenolization is preferred gave different answers.²² Complications arise from the simultaneous presence of thioxoketone, cis (with an O–H···S=C hydrogen bond) and trans enols, and cis (with a S-H \cdots O=C hydrogen bond) and trans thioenols. The observation of only one NMR (OH/SH) signal at rt is ascribed to a rapid prototropic equilibrium between few species, especially the cis enol and thioenol, which average the NMR signals. Indeed, in a low temperature dynamic NMR study^{22h} both species plus a minor percentage of the non-hydrogen bonded Z-thioenol were observed. The large intermolecular preference of enolization over thioenolization had disappeared, presumably due to a counter-effect of intramolecular $O-H\cdots S$ and

Table 4 Effect of \mathbb{R}^1 , \mathbb{R}^2 , \mathbb{R}^3 and the solvent on K_{enol} , K_{thioenol} and K_{total} for	11/12/13 systems ^a
---	-------------------------------

Compound	R ³	Solvent	% 12	% 11	% 13	$K_{ m total}$	K_{enol}	$K_{ m thioenol}$
11a/12a/13a	Ph	CDCl ₃	60	24	16	0.67	0.40	0.27
		THF-d ₈	91	9	0	0.10	0.10	0
		CD ₃ CN	96	4	0	0.04	0.04	0
11b/12b/13b	<i>p</i> -An	CDCl ₃	61	23	16	0.63	0.38	0.25
	-	THF-d ₈	94	6	0	0.06	0.06	0
		CD_3CN	97	3	0	0.03	0.03	0
$11c/12c/13c^{b}$	1-Np	CCl_4	33	35	32	2.03	1.06	0.97
		CDCl ₃	44	27	29	1.27	0.61	0.66
		C_6D_6	58	28	14	0.72	0.48	0.24
		THF-d ₈	86	12	2	0.16	0.14	0.02
		$(CD_3)_2CO$	92	7	1	0.09	0.08	0.01
		CD_3CN	94	5	1	0.06	0.05	0.01
11d/12d/13d ^c	Me	CDCl ₃	88	12	0	0.14	0.14	0
		$THF-d_8$	96	4	0	0.05	0.05	0
$11e/12e/13e^{c}$	Et	CDCl ₃	92	8	0	0.09	0.09	0
	. –	THF-d ₈	96	4	0	0.05	0.05	0
$11f/12f/13f^{c}$	i-Pr	CCl_4	72	28	0	0.039	0.39	0
		CDCl ₃	88	12	0	0.14	0.14	0
	_	THF-d ₈	97	3	0	0.03	0.03	0
$11g/12g/13g^{c}$	<i>t</i> -Bu	CCl_4	89	11	0	0.13	0.13	0
		CDCl ₃	96	4	0	0.04	0.04	0
		THF-d ₈	100	0	0	≤0.02	≤ 0.02	≤ 0.02
11h/12h/13h	Ph	CDCl ₃	4	46	50	24.00	11.50	12.50
		THF-d ₈	19	74	7	4.17	3.81	0.36
		CD ₃ CN	38	54	8	1.66	1.45	0.21
11i/12i/13i	<i>p</i> -An	CDCl ₃	4	43	53	25.89	11.73	14.16
		THF-d ₈	20	75	5	4.07	3.8	0.27
	1.3.5	CD ₃ CN	39	53	8	1.58	1.37	0.21
11j/12j/13j	I-Np	CDCl ₃	0	31	69	\geq 50	5.04	0.60
		THF-d ₈	15	76	9	5.66	5.04	0.62
		$(CD_3)_2CO$	29	65	6	2.43	2.23	0.20
		CD ₃ CN	33	55	12	2.08	1.70	0.38
11k/12k/13k	Me	CDCl ₃	22	71	7	3.54	3.23	0.31
		THF-d ₈	34	66	0	1.97	1.97	0
111/101/101	T.	CD ₃ CN	67	33	0	0.50	0.50	0
111/121/131	Et	CDCl ₃	22	68	10	3.64	3.14	0.50
		THF-d ₈	38	62	0	1.62	1.62	0
11 (12 (12	· D	CD ₃ CN	/0	30	0	0.44	0.44	0
11m/12m/13m	1-Pr	CDCl ₃	23	66	11	3.35	2.8/	0.48
		$1 \text{HF-}d_8$	47	23	0	1.13	1.13	0
11 /12 /12 /	(D	CD ₃ CN	14	23	0	0.30	0.30	0 0.07
$11n/12n/13n^{\circ}$	<i>t</i> -Bu		14	/4	12	6.19	5.32	0.87
		C_6D_6	31	62	10	2.23	2.02	0.21
		CDCl ₃	51	45	18	1.04	1.18	0.46
		$1 \text{HF-}d_8$	66	34	0	0.51	0.51	0
110/120/120	Dh	CD ₃ CN	89	11	0	0.12	0.12	0
110/120/130	гn		0	40	2	≥ 50		
11n/12n/12n		$1 \Pi \Gamma - u_8$	0	20	ے 1	≥ 50		
11p/12p/13p 11a/12a/12a	<i>p-A</i> n 1 N-		0	39 100	01	≤ 30		
11y/12y/13y 11r/13r/12n	1-INP ; Dr	CDC^1	24	100	10	≤ 30 3 17	2 75	0.42
111/121/131 $11e/13e/12e^{b}$	1-11 1 Du		2 4 0	00	10	>50	2.13	0.42
115/ 128/ 138	<i>i</i> -Bu	C_6D_6	7	90 70	23	$\frac{250}{14.12}$	10.6	3 53
		THE-d	17	83	23	5.01	5.01	0
		$CD_{1}CN$	67	33	0	0.49	0.40	0
11+/17+/12+	Ph	CDC1	54	0	37	0.49	0.49	0.60
111/121/131	1 11	THE A	31	7 64	5	2.00	2.10	0.09
		$CD_{1}CN$	<u>4</u> 9	45	6	2.23	2.00	0.17
11n/12n/13n	i-Dr	CDC1	72	70	7	2 47	3.15	0.12
11u/ 12u/ 13u	1-1 1	THE-d	61	30	ó	0.64	0.64	0.52
		$CD_{1}CN$	85	15	0	0.04	0.04	0
$11v/12v/13v^{c}$	i Dr	CDC1	11	65	24	0.10 8 15	6.16	2 20
111/121/131	1-1 1	THE-4	80	20	2 4 0	0.45	0.10	0
11w/12w/12w ^c	t. Bu	CDC^1	31	20 42	27	2.23	1.25	0.86
11W/12W/13W	<i>i</i> -Du	THE A	90	10	<u>_</u> /	0.11	0.11	0.80
	. D		20	22	18	0.11	0.11	2 46
$11v/12v/12v^{c}$	<i>t</i> D ¹¹							
$11x/12x/13x^{c}$	<i>t</i> -Bu	CDCI ₃	20	32	40	4.15	5.01	2.40

" For all systems only 12 was observed in DMSO-d₆. ^b Only 12 was observed in DMF-d₇. ^c Only 12 was observed in CD₃CN.

 $O \cdots H$ -S hydrogen bonds of different strengths, whose magnitudes were disputed.²³

β-Oxothioacetamides, which were also investigated by NMR, are written as the enols R'C(OH)=CRC(=S)NR'R''', displaying only one (presumably OH) signal at δ 14.2–15.2.²⁴

Structures of enols 11 and thioenols 13 in solution

Potential enol and thioenol structures (Chart 1 and 2) are the Z-syn thioenol 14 with an S-H \cdots O=C bond and a Z-syn enol 18 with an $O-H \cdots S=C$ hydrogen bond. In both the two double bonds are in an s-syn arrangement. These 6-membered ring structures are analogous to the most stable structures for the cyanomalonamides $7/8^8$ where the NR¹R² and NHR moieties are not involved in hydrogen bonding. Rotation around the C-C(=X) bond (X = O, S)gives the Z-anti structures with an S-H \cdots NR¹R² hydrogen bond for 15 or an $O-H \cdots NHR^3$ bond for 19. Formal rotation around the C=C bond generates the *E*-isomers. In the *E*-syn enol, if the *cis*-NR¹R² to the C=S contains no hydrogen there is no hydrogen bond, but if R^1 and/or $R^2 = H$, an N–H····S=C hydrogen bond exists in 20. Since in all the cyanomonothiocarbonylmalonamides the thioamide nitrogen carries one hydrogen, there is an N- $H \cdots O = C$ hydrogen bond in the *E-syn* thioenol **16**. An N-H \cdots N bond exists in both the E-anti enol and thioenol isomers (17 and **21**) and if R^1 and/or $R^2 = H$, there are several options for such a bond. Consequently, the combination of dipole-dipole attraction and repulsion interactions, and different hydrogen bonds in the various structures, make it difficult to unequivocally determine the structure in solution. The solid state structure is not necessarily identical to that in solution and analogy with 7/8 is useless since the C=O \rightarrow C=S change affects the nature of the hydrogen bond. In 12 there are intramolecular $N-H \cdots O=C$ bonds if one of the R groups = H.

 $R^{3}HN \longrightarrow NR^{1}R^{2}$ $R^{3}HN \longrightarrow S \longrightarrow NR^{1}R^{2}$ Z-syn (14) $R^{3}HN \longrightarrow S \longrightarrow NR^{1}R^{2}$ Z-syn (14) Z-anti (15) $HS \longrightarrow R^{3}$ $HS \longrightarrow R^{3}$ $R^{3} \longrightarrow H$ $R^$

Chart 1 Possible structures for the thioenols of cyanomonothiocarbonylmalonamides.

In our systems the nitrogen adjacent to the C=S is connected to one hydrogen and only in the *E-syn* enols is there no C=S····H– N bond when \mathbb{R}^1 , $\mathbb{R}^2 \neq \mathbb{H}$. In analysing the relative stabilities



Chart 2 Possible structures for the enols of cyanomonothiocarbonylmalonamides.

of the various configurations/conformations of **14–21** arising from the contribution of the hydrogen bonds, we assume that the C=S \cdots H–N and the S–H \cdots N hydrogen bonds are weaker than the C=O \cdots H–N and O–H \cdots N bonds.

A valuable probe is the difference in the two δ (N–H) values for each species when R¹ or R² = H. We expect a large difference when only one, low field hydrogen participates in a hydrogen bond and a relatively small difference when both N–H bonds do not form hydrogen bonds. Analysis shows that the N–H bond is involved in hydrogen bonding for the *E-anti* enol and thioenol and for the *E-syn* thioenols. If R¹ = H, a large value is also predicted for the *E-syn* enol.

When $\mathbb{R}^1 = \mathbb{R}^2 = \mathbb{M}e$ each species displays only one NH signal: at δ 12.14–13.19 for **13**, at δ 10.45–11.13 ($\mathbb{R}^3 = \operatorname{Ar}$) and 8.65–9.00 ($\mathbb{R}^3 = \operatorname{Alk}$) for **12**, and at $\delta = 8.33$ –8.49 ($\mathbb{R}^3 = \operatorname{Ar}$) and 6.81–7.26 ($\mathbb{R}^3 = \operatorname{Alk}$) for **11** (Table 5). When $\mathbb{R}^1 = \mathbb{H}$, $\mathbb{R}^2 = \mathbb{M}e$, the order of δ values is retained, but each species display two signals. The $\Delta\delta(\mathbb{N}-\mathbb{H})$ values of 4.20–7.08 for **13** > $\Delta\delta$ 2.97–3.52 ($\mathbb{R}^3 = \operatorname{Ar}$) and 1.69–2.50 ($\mathbb{R}^3 = \operatorname{Alk}$) for **12** > $\Delta\delta$ 1.59–2.17 ($\mathbb{R}^3 = \operatorname{Ar}$) and 0.27–1.16 ($\mathbb{R}^3 = \operatorname{Alk}$) for **11** (Table 5). For $\mathbb{R}^1 = \mathbb{R}^2 = \mathbb{H}$, $\Delta\delta =$ 6.19–7.21 for **13**, 2.50 for **12** and 1.13–2.76 for **11**.

Consequently, the large $\Delta\delta$ values for **13** indicate an *E*configuration (**16** or **17**) and the significantly lower $\Delta\delta$ values for **11** indicate a *Z* configuration (**18** or **19**). This conclusion is consistent with the δ (OH) of >16.5 ppm (Table 3) observed for other hydrogen bonded enols,^{3,4,8} and hence **18** is the preferred conformation for the enol; *e.g.*, for enols ArNHC(OH)=C(CN)CO₂R (R=CF₃CH₂ and (CF₃)₂CH),^{4c} δ (OH) for the *Z*-isomers is mostly at δ 13.2–14.5, and moves 2–3 ppm to a higher field for the *E*isomers. The NH values are at *ca*. δ 8.3–10.0 for the *Z*-enols and at δ 10.2–10.9 for the *E*-enols.

The low field δ (SH) signals at 4.3–4.8 in CDCl₃ (Table 3) are consistent with a non-hydrogen bonded SH group in the *E*-thioenols. Since an N–H···O is a stronger hydrogen bond than an N–H···N bond, the structure should be *E*-syn **16**. The δ of 6.3–6.9 for the NHMe derivatives in CD₃CN and THF-d₈ is

6	
0	
0	
÷	
-	
- 77	
Z	
5	
0	
õ	
-	
×.	
2	
E	
8	
- 5	
\circ	
2	
Ē	
29	
÷.	
-13	
E	
,0	
1	
ਕ	
\circ	
£	
2	
_₽	
.:	
- 13	
Š	
nive	
Unive	
y Unive	
by Unive	
d by Unive	
led by Unive	
aded by Unive	
oaded by Unive	
nloaded by Unive	
wnloaded by Unive	
ownloaded by Unive	
Downloaded by Unive	
3. Downloaded by Unive	
18. Downloaded by Unive	
008. Downloaded by Unive	
2008. Downloaded by Unive	
ry 2008. Downloaded by Unive	
ary 2008. Downloaded by Unive	
ruary 2008. Downloaded by Unive	
bruary 2008. Downloaded by Unive	
⁷ ebruary 2008. Downloaded by Unive	
¹ February 2008. Downloaded by Unive	
14 February 2008. Downloaded by Unive	
1 14 February 2008. Downloaded by Unive	
on 14 February 2008. Downloaded by Unive	
1 on 14 February 2008. Downloaded by Unive	
ed on 14 February 2008. Downloaded by Unive	
shed on 14 February 2008. Downloaded by Unive	
lished on 14 February 2008. Downloaded by Unive	
blished on 14 February 2008. Downloaded by Unive	
⁹ ublished on 14 February 2008. Downloaded by Unive	

Table 5 δ (NH) values and their differences $\Delta\delta$ (in ppm) for each of the **11/12/13** systems in several solvents at room temperature

			× 11 ×		,		-				
			Enol 11			Amide-thioami	de 12		Thioenol 13		
Compound	\mathbf{R}^3	Solvent	NHR ³ /ppm	$NR^{1}R^{2}/ppm$	∆ð/ppm	NHR ³ /ppm	$NR^{1}R^{2}/ppm$	$\Delta\delta/\text{ppm}$	NHR ³ /ppm	$NR^{1}R^{2}/ppm$	$\Delta\delta/\mathrm{ppm}$
11a/12a/13a	Ph	CDCI,	8.49			10.60			12.40		
11b/12b/13b	p-An	CDCI,	8.43			10.51			12.14		
11c/12c/13c	I-Np	CCI4	8.33			10.45			12.77		
	•	CDCI,	8.71			11.13			12.72		
		C_6D_6	8.86			11.13			13.19		
11d/12d/13d	Me	CDCI,	7.26			9.00					
11e/12e/13e	Et	CDC1 ₃	7.00	I		8.73	[[
11f/12f/13f	i-Pr	CDC1,	6.81			8.65					
11g/12g/13g	<i>t</i> -Bu	CDC1,	6.97			8.67					
11h/12h/13h	\mathbf{Ph}	CDC1,	8.21	6.32	1.89	10.90	7.75	3.15	12.80	5.97	6.83
		$THF-d_s$	9.20	7.60	1.60	11.29	7.84	3.36	13.19	6.87	6.32
		CD ₃ CN	8.61	6.80	1.81	10.53	7.01	3.52	12.80	6.30	6.50
11i/12i/13i	p-An	CDC1 ₃	8.10	6.08	2.02	10.54	7.61	2.93	12.52	5.88	6.64
		$THF-d_s$	9.11	7.52	1.59	11.15	7.82	3.33	12.88	6.83	6.05
		CD ₃ CN	8.51	6.73	1.78	10.38	6.96	3.42	12.59	6.23	6.36
11j/12j/13j	1-Np	CDCI,	8.37	6.20	2.17				13.05	5.97	7.08
		$THF-d_s$	9.53	7.66	1.87	11.55	8.07	3.48	13.51	6.98	6.53
		CD ₃ CN	8.84	6.83	2.01	10.92	7.43	3.49	13.12	a	a
11k/12k/13k	Me	CDC1 ₃	6.90	6.13	0.77	9.17	7.06	2.11	11.02	5.82	4.20
		C_6D_6	6.40	5.24	1.16	8.35	5.78	2.57	11.04	5.51	5.53
111/121/131	Еt	CDCI,	6.70	6.18	0.52	9.07	7.10	1.97	11.07	5.85	5.22
11m/12m/13m	i-Pr	CDCI,	6.44	6.17	0.27	8.91	7.05	1.86	11.14	5.84	5.30
11n/12n/13n	t-Bu	CDCI,	6.55	6.05	0.5	8.74	7.05	1.69	11.61	5.81	5.80
110/120/130	\mathbf{Ph}	CDCI,	8.31	5.55	2.76				12.70	5.49	7.21
11s/12s/13s	<i>t</i> -Bu	CDC1 ₃	6.73	5.60	1.13	8.36	5.86	2.50	11.58	5.93	6.19
" Signal not observed.											

consistent with intermolecular hydrogen bonds of the SH with the hydrogen bond accepting solvents. Indeed, in β -thioxoesters HSC(R¹)=CHCO₂R² the intramolecular S–H···O=C hydrogen bonded Z-isomer displays δ (SH) at 5.68–8.19 ppm, which is at *ca.* δ 3.80 for the *E*-isomer.^{22a} A structure related to **20** with a "free" SH group was detected earlier in solution.^{22h,J}

Comparison of δ (OH) and K_{enol} values of the enols 11 and 7/8

A qualitative comparison between the 11/12/13 and 6/7/8 systems show, in CDCl₃, a 0.69–1.69 ppm lower field δ (OH) in the latter, ascribed to a better O–H····O=C than an O–H····S=C hydrogen bond. K_{enol} and K_{total} values are significantly higher for 6/7/8. The ratios for PhNH(C=Z)CH(CN)CONRMe (Z = O, S) are >10-fold higher for R = Me than for R = H (4.01–4.5 for R³ = Alk and 0.77–0.78 for R³ = Ar). For i-PrNH(C=Z)CH(CN)CONHPr-i the ratio is 2.57. Hence, the extent of enolization is strongly structure-dependent. The corresponding data are reported in Table S5 in the ESI.§

Solvent and substituent effects on K_{enol} and $K_{thioenol}$

 K_{enol} and K_{thioenol} are strongly solvent- and substituent-dependent (Table 4). K_{enol} values increase on decreasing the solvent polarity, following the order $\text{CCl}_4 > \text{CDCl}_3 > \text{C}_6\text{D}_6 > \text{THF-d}_8 > (\text{CD}_3)_2\text{CO} > \text{CD}_3\text{CN} > \text{DMF-d}_7 > \text{DMSO-d}_6$. The same trend was observed for K_{thioenol} , except that $\text{CDCl}_3 > \text{CCl}_4$. In contrast with compounds 6/7/8, where the NHMe and NH₂ derivatives display the enol in DMSO-d₆.⁸ for compounds 11/12/13, 12 is the exclusive tautomer in DMSO-d₆.

For a constant NHR³, both K_{enol} and $K_{thioenol}$ decrease for NR¹R² in the order NH₂ > NHMe > NMe₂. Thus, for **11h-j/12hj/13h-j** and **11o-p/12o-p/13o-p**, **13** predominates in CDCl₃, and **12** predominates for **11a-g/12a-g/13a-g** systems. Moreover, for NMe₂ systems no **13** was observed for R³ = Alk and a small to moderate %(**13**) was observed when R³ = Ar. The %(**13**) for NHMe and NH₂ systems was independent of R³.

Conclusions

Replacing one C=O with a C=S group in R³NHCOCH(CN)-CONR¹R² leads to seven changes: (i) both enolization and thioenolization are observed in solution. (ii) The intramolecular $O-H\cdots O$ hydrogen bonded Z-enol structures in the 6/8 and 11/13 systems are analogous, whereas the thioenol structure has the E-configuration, no intramolecular H-bonded SH group and an intramolecularly N–H · · · O H-bonded moiety. (iii) δ (OH) values in 7 are at a lower field than in analogs 11. (iv) K_{enol} values for 11/12/13 are lower than in 6/7/8. (v) The thioenol 13 is less stable than enol 11 for S=C-N-Alk-substituted systems, but the stabilities are much closer and even slightly reversed for N-aryl systems. An increased number of N-H bonds adjacent to the C=O strongly increases the K_{thioenol} and K_{enol} values. (vi) Compounds 11/12/13 are more reactive, giving an array of different reactions.¹¹ (vii) The intramolecular hydrogen bond strengths are important in determining the structures of the enols and thioenols and the differences between them.

Experimental section

General methods, NMR and analytical data

Melting points, ¹H and ¹³C NMR and IR spectra were measured as described previously.^{2f} All the commercial precursors and solvents were purchased from Aldrich.

 δ values are relative to $\rm Me_4Si.\,J$ values are given in Hz. Analytical data, mps and yields are given in Table S6 in the ESI.§

Reaction of *N*,*N*-dimethylcyanoacetamide with phenyl, *p*-anisyl, 1-naphthyl, methyl, ethyl, isopropyl and *tert*-butyl isothiocyanates to form 11a–g/12a–g/13a–g

The procedure for isopropyl isothiocyanate was also used with the other isothiocyanates.

To a suspension of Na (0.25 g, 11 mmol) in dry THF (50 mL) was added N,N-dimethylcyanoacetamide (1.12 g, 10 mmol) and the mixture was stirred overnight giving a white precipitate. A solution of isopropyl isothiocyanate (1.08 mL, 10 mmol) in dry THF (20 mL) was added dropwise to the stirred mixture over 20 min. After stirring overnight at rt the dissolved white precipitate gave a yellow solution. The solvent was evaporated, the remaining Na salt was dissolved in DMF (5 mL) and the solution was added slowly to a cold 2 N HCl solution (100 mL). The formed yellowish precipitate was filtered, washed with cold water (30 mL) and dried in air to give 1.96 g (92%) of 12f, mp 147-9 °C. Anal. calcd for C₉H₁₅N₃OS: C, 50.70; H, 7.04; N, 19.72; found: C, 50.30; H, 7.06; N, 19.42%. Crystals for X-ray diffraction were obtained by keeping a solution of **12f** in THF-d₈ or CDCl₃ at rt for 2–3 weeks. Detailed NMR spectra of 11f/12f and the analogous preparation and spectra of 11c are given in the ESI.§ Spectral data, mps, yields and analyses are given in Tables 3, S1-S3 and S6.

Reaction of *N*-methylcyanoacetamide with phenyl, *p*-anisyl, 1-naphthyl, methyl, ethyl, isopropyl and *tert*-butyl isothiocyanates to form 11h–n/12h–n/13h–n

The procedure is demonstrated for phenyl isothiocyanate. Very small Na pieces (0.25 g, 11 mmol) were added to an Nmethylcyanoacetamide (0.98 g, 10 mmol) solution in dry THF (50 mL) under nitrogen. The mixture was stirred for 48 h until complete Na disappearance, giving a white precipitate in an orange solution. A solution of phenyl isothiocyanate (1.2 mL, 10 mmol) in dry THF (20 mL) was added dropwise over 30 min and during 6 h reflux the precipitate dissolved to give a dark orange solution. Removal of the solvent left the brown salt [PhNHCSC(CN)CONHMe]⁻Na⁺. $\delta_{\rm H}$ (400 MHz, 298 K, DMSO d_6): 2.61 (3H, d, J = 4.5, NMe), 6.94 (1H, t, J = 7.8, p-H), 7.21 (2H, t, J = 7.8, m-H), 7.79 (2H, d, J = 7.2, o-H), 13.20 (1H, s, NH). $\delta_{\rm C}$ (100.133 MHz, 298 K, DMSO-d₆): 26.43 (q, J = 136.7, Me), 76.76 (s, C[anion]), 122.18 (d, J = 160.4), 122.75 (d, J =162.4), 125.56 (s, CN), 128.32 (d, J = 161.1), 142.26 (s), 169.66 (s, C=O), 185.96 (s, C=S).

The salt was dissolved in DMF (5 mL) and the orange solution was added dropwise to a cold 2 N HCl solution (100 mL). The yellow precipitate was filtered, washed with cold water (200 mL) and dried in air to give 1.87 g (80%) of **11h**, mp 153–5 °C. Anal. calcd for $C_{11}H_{11}N_3OS$: C, 56.65; H, 4.72; N, 18.03; found: C, 56.72;

H, 4.86; N, 17.79%. Crystals for X-ray diffraction were obtained by slow evaporation of the EtOAc solution at rt.

Attempts to obtain the 1-naphthyl derivative, **11j**, gave a product in 89% yield, mp 158–60 °C. However, crystallization from EtOAc at rt gave a 5-membered ring compound resulting from an oxidation reaction, apparently by air oxygen.¹¹ Crystallization from EtOAc under nitrogen revealed the enol structure **11j**. Compounds **11i**, **11l–n** were obtained similarly. The reaction of **11n** and the spectra of the **11n/12n/13n** obtained, and spectral and analytical data of all the compounds are given in Tables 3, S1–S3 and S6.

Reaction of cyanoacetamide with phenyl, *p*-anisyl, 1-naphthyl, isopropyl and *tert*-butyl isocyanates to form 110-s/120-s/130-s

The procedure for all the derivatives is similar. To a heated solution of cyanoacetamide (0.84 g, 10 mmol) in dry THF (100 mL) at 60 °C was added Na (0.25 g, 11 mmol) and the mixture was stirred at 60 °C for 4 days, giving a white precipitate. The organic isothiocyanate (10 mmol) in dry THF (30 mL) was added dropwise during 30 min at rt. The mixture was refluxed for 48 h and then stood at rt for 1 h to give a brown solution and a white precipitate which was filtered and washed with dry ether giving the salt [R³NHCSC(CN)CONH₂]⁻Na⁺. The salt solution in DMF (5 mL) was added dropwise to a cold 2 N HCl solution (100 mL), the solid obtained was filtered, washed with cold water (500 mL) and dried in air or in vacuum to give the pure product. Attempts to crystallize the products gave different heterocycles.¹¹ Their spectral and analytical data are given in Tables 3, S1–S3 and S6.

Reaction of *N*-isopropylcyanoacetamide with phenyl and isopropyl isothiocyanates to form 11t and 11u

The procedure resembles that of the reaction of *N*-methylcyanoacetamide with phenyl isothiocyanate. **11t**, mp 128–30 °C, was prepared from *N*-isopropyl cyanoacetamide (1.26 g, 10 mmol) and phenyl isothiocyanate (1.2 mL, 10 mmol) in 80% yield. **11u**, mp 157–8 °C, was prepared from *N*-isopropyl cyanoacetamide (1.26 g, 10 mmol) and isopropyl isothiocyanate (1.07 mL, 10 mmol) in 74% yield. The spectral and analytical data are in Tables 3, S1–S3 and S6

Reaction of *N*-benzhydrylcyanoacetamide with isopropyl and *t*-butyl isothiocyanates to form 12v and 12w

The procedure resembles the reaction of *N*,*N*-dimethylcyanoacetamide with isopropyl isothiocyanate. The isopropyl derivative **11v** (0.78 g, 89%), mp 162–4 °C, was obtained by reacting *N*benzhydrylcyanoacetamide (0.625 g, 2.5 mmol) with isopropyl isothiocyanate (0.27 mL, 2.5 mmol). Crystals of **12v** for X-ray diffraction were obtained after long-term standing in CDCl₃. The *t*-butyl derivative **12w** (0.67 g, 73%), mp 166–8 °C, was obtained from *N*-benzhydrylcyanoacetamide (0.625 g, 2.5 mmol) and *t*-butyl isothiocyanate (0.29 mL, 2.5 mmol). The spectral and analytical data are in Tables 3, S1–S3 and S6.

Reaction of N-phenylcyanoacetamide with t-butyl isothiocyanate

The procedure resembles the reaction of N-methylcyanoacetamide with *t*-butyl isothiocyanate. N-Phenylcyanoacetamide (0.8 g,

5 mmol) reacted with *t*-butyl isothiocyanate (0.58 mL, 5 mmol) to yield 1.29 (87%) of 11x, mp 147–8 °C (dec.). The spectral and analytical data are in Tables 3, S1–S3 and S6.

Crystal data

12d: $C_{21}H_{33}N_9O_3S_3$, M = 555.74, monoclinic, a = 14.6537(11) Å, b = 14.1922(11) Å, c = 14.9966(12) Å, $a = 90^{\circ}$, $\beta = 108.8310(10)^{\circ}$, $\gamma = 90^{\circ}, U = 2951.9(4) \text{ Å}^3, T = 295(1) \text{ K}, \text{ space group } P2(1)/c,$ Z = 4,29673 reflections collected, 5779 independent reflections [R(int) = 0.0635]. The final $wR(F2) = 0.1972 [I > 2\sigma(I)]$. 12f: $C_9H_{15}N_3OS$, M = 213.30, monoclinic, a = 7.3690(4) Å, b =15.9322(8) Å, c = 10.1036(5) Å, $a = 90^{\circ}$, $\beta = 98.6260(10)^{\circ}$, $\gamma = 90^{\circ}$, $U = 1172.79(10) \text{ Å}^3$, T = 295(1) K, space group P2(1)/c, Z = 4, 12869 reflections collected, 2557 independent reflections [R(int) =0.0210]. The final $wR(F2) = 0.1003 [I > 2\sigma(I)]$. 12v: C₂₀H₂₁N₃OS, M = 351.46, monoclinic, a = 12.321(2) Å, b = 18.376(3) Å, c =9.3465(16) Å, $a = 90^{\circ}$, $\beta = 116.339(3)^{\circ}$, $\gamma = 90^{\circ}$, U = 1896.5(6) Å³, T = 295(1) K, space group Cc, Z = 4, 10385 reflections collected, 4082 independent reflections [R(int) = 0.1157]. The final wR(F2) =0.0973 $[I > 2\sigma(I)]$. 11h: C₁₁H₁₁N₃OS, M = 233.29, triclinic, a =9.4637(5) Å, b = 9.9527(6) Å, c = 13.2117(8) Å, $a = 81.3100(10)^{\circ}$, $\beta = 79.1780(10)^{\circ}, \gamma = 68.9710(10)^{\circ}, U = 1136.10(11) \text{ Å}^3, T =$ 295(1) K, space group P-1, Z = 4, 12684 reflections collected, 4900 independent reflections [R(int) = 0.0172]. The final wR(F2) =0.1267 [$I > 2\sigma(I)$]. 11i: C₁₂H₁₃N₃O₂S, M = 263.31, monoclinic, a = 10.5904(6) Å, b = 26.0342(14) Å, c = 9.6563(5) Å, $a = 90^{\circ}$, $\beta = 99.0470(10)^{\circ}, \gamma = 90^{\circ}, U = 2629.2(2) \text{ Å}^3, T = 295(1) \text{ K},$ space group P2(1)/c, Z = 8, 30 522 reflections collected, 6255 independent reflections [R(int) = 0.0845]. The final wR(F2) = $0.1344 [I > 2\sigma(I)]$. 11j: C₁₅H₁₃N₃OS, M = 283.34, monoclinic, a =4.9892(4) Å, b = 19.2928(14) Å, c = 14.7103(12) Å, $a = 90^{\circ}$, $\beta =$ 99.0450(10)°, $\gamma = 90°$, $U = 1398.34(18) \text{ Å}^3$, T = 295(1) K, space group P2(1)/n, 15798 reflections collected, 3056 independent reflections [R(int) = 0.0569]. The final $wR(F2) = 0.0865 [I > 2\sigma(I)]$. 12r: $C_{8.50}H_{14}N_3OS_{1.50}$, M = 222.32, orthorhombic, a = 8.4053(5)Å, b = 14.8272(9) Å, c = 18.2296(11) Å, $a = 90^{\circ}$, $\beta = 90^{\circ}$, $\gamma =$ 90°, U = 2271.9(2) Å³, T = 293(1) K, space group P2(1)2(1)2(1), Z = 8,26066 reflections collected, 4961 independent reflections [R(int) = 0.0344]. The final $wR(F2) = 0.0689 [I > 2\sigma(I)]$.

Acknowledgements

We are indebted to the Israel Science Foundation for support, and to Dr Shmuel Cohen for the X-ray structure determination.

References

- 1 (a) J. Emsley, Struct. Bonding, 1984, **57**, 1148; (b) The Chemistry of Enols, ed. Z. Rappoport, Wiley, Chichester, 1990.
- 2 (a) A. F. Hegarty and P. J. O'Neill, J. Chem. Soc., Chem. Commun., 1987, 744; (b) B. M. Allen, A. F. Hegarty, P. O'Neill and M. T. Nguyen, J. Chem. Soc., Perkin Trans. 2, 1992, 927; (c) B. M. Allen, A. F. Hegarty and P. O'Neill, J. Chem. Soc., Perkin Trans. 2, 1997, 2733; (d) J. Frey and Z. Rappoport, J. Am. Chem. Soc., 1995, 117, 1161; (e) J. Frey and Z. Rappoport, J. Am. Chem. Soc., 1996, 118, 3994; (f) J. Frey and Z. Rappoport, J. Am. Chem. Soc., 1996, 118, 5169; (g) J. Frey and Z. Rappoport, J. Am. Chem. Soc., 1996, 118, 5169; (g) J. Frey and Z. Rappoport, J. Am. Chem. Soc., 1996, 118, 5169; (g) J. Frey and Z.
- 3 (a) J. K. Mukhopadhyaya, S. Sklenak and Z. Rappoport, J. Am. Chem. Soc., 2000, 122, 1352; (b) J. K. Mukhopadhyaya, S. Sklenak and Z. Rappoport, J. Org. Chem., 2000, 65, 6856; (c) Y. X. Lei, G. Cerioni and

Z. Rappoport, J. Org. Chem., 2000, **65**, 4028; (d) Z. Rappoport, Y. X. Lei and H. Yamataka, *Helv. Chim. Acta*, 2001, **84**, 1405; (e) J. Song, Y. X. Lei and Z. Rappoport, J. Org. Chem., 2007, **72**, 9152.

- 4 (a) Y. X. Lei, G. Cerioni and Z. Rappoport, J. Org. Chem., 2001, 66, 8379; (b) Y. X. Lei, D. Casarini, G. Cerioni and Z. Rappoport, J. Phys. Org. Chem., 2003, 16, 525; (c) Y. X. Lei, D. Casarini, G. Cerioni and Z. Rappoport, J. Org. Chem., 2003, 68, 947; (d) A. Basheer and Z. Rappoport, J. Org. Chem., 2004, 69, 1151; (e) M. Mishima, M. M. Mishima, M.
- Matsuoka, Y. X. Lei and Z. Rappoport, J. Org. Chem., 2004, 69, 5947.
 5 S. Sklenak, Y. Apeloig and Z. Rappoport, J. Am. Chem. Soc., 1998, 120, 10359.
- 6 J. Toullec, in *The Chemistry of Enols*, ed. Z. Rappoport, Wiley, Chichester, 1990, ch. 6, p. 323.
- 7 J. Song, M. Mishima and Z. Rappoport, Org. Lett., 2007, 9, 4307.
- 8 A. Basheer, H. Yamataka, S. C. Ammal and Z. Rappoport, J. Org.
- *Chem.*, 2007, **72**, 5297. 9 "Formal" is written in order to emphasize that the compound is a
- mixture.
 10 (a) W. Schwede, V. Schulze, K. Eis, B. Buchmann, H. Briem, G. Siemeister, U. Boemer, and K. Parczyk, PCT Int. Appl., 2003, WO 2003093249 A1 20031113; Chem. Abstr., 2003, 139, 381496; (b) R. Laliberte, U.S. Patent, 1970, US 3506669 19700414; Chem. Abstr., 1970, 73, 3785; (c) A. Basheer and Z. Rappoport, Org. Lett., 2006, 8, 5931; (d) J. Goerdeler and U. Keuser, Chem. Ber., 1964, 97, 3106; (e) C. V. N. S. Varaprasad, D. Barawkar, H. El Abdellaoui, S. Chakravarty, M. Allan, H. Chen, W. Zhang;, J. Z. Wu, R. Tam, R. Hamatake, S. Lang and Z. Hong, Bioorg. Med. Chem. Lett., 2006, 16, 3975; (f) I. M. Bazavova, R. G. Dubenko and P. S. Pel'kis, Zh. Org. Khim., 1976, 12, 69; Chem. Abstr., 1976, 84, 105468.
- 11 A. Basheer and Z. Rappoport, J. Org. Chem., 2008, 73, 1386.
- 12 F. H. Allen, J. E. Davies, J. E. Galloy, J. J. Johnson, O. Kennard, C. F. Macrae, G. F. Mitchell, J. M. Smith and D. G. Watson, J. Chem. Inf. Comput. Sci., 1991, 31, 187.
- 13 F. Duus, in *Comprehensive Organic Chemistry*, ed. D. H. R. Barton and W. D. Ollis, Pergamon Press, Oxford, 1979, vol. 3, ch. 11.22, pp. 373–487.
- 14 T. Seltzer and Z. Rappoport, J. Org. Chem., 1996, 61, 5462.

- 15 Y. Chiang, J. J. Jones, Jr. and A. J. Kresge, J. Am. Chem. Soc., 1994, 116, 8358.
- 16 (a) A. J. Kresge and O. Meng, J. Am. Chem. Soc., 1998, 120, 11830; (b) A. J. Kresge and O. Meng, J. Am. Chem. Soc., 2002, 124, 9189.
- 17 S. Sklenak, Y. Apeloig and Z. Rappoport, J. Chem. Soc., Perkin Trans. 2, 2000, 2269.
- 18 (a) J. March, Advanced Organic Chemistry, 4th edn, Wiley, New York, 1992, p. 24; (b) C. C. Price and S. Oae, Sulfur Bonding, Ronald Press Co., New York, 1962, pp. 1–7; (c) E. Schaumann, in The Chemistry of Double Bonded Functional Groups, Supplement A, ed. S. Patai, Wiley, Chichester, 1977, vol. 2, ch. 17, pp. 1269–1274.
- 19 F. G. Bordwell, I. Zhang, I. Eventova and Z. Rappoport, J. Org. Chem., 1997, 62, 5371.
- 20 X.-M. Zhang, M. Malick and G. A. Petersson, J. Org. Chem., 1998, 63, 5314.
- 21 P. E. Allegretti, D. Asens, M. M. Schiavoni, R. D. Bravo, E. A. Castro and J. J. P. Furlong, *Arkivoc*, 2003, XV, 134.
- 22 (a) B. Floris, in *The Chemistry of Enols*, ed. Z. Rappoport, Wiley, Chichester, 1990, ch. 4, pp. 285–296; (b) F. Duus, J. Am. Chem. Soc., 1986, **108**, 630; (c) F. Duus, J. Org. Chem., 1977, **42**, 3123; (d) G. Klose, E. Ludwig and E. Uhlemann, Org. Magn. Reson., 1977, **10**, 151; (e) L. Carlsen and F. Duus, J. Am. Chem. Soc., 1981, **100**, 281; (f) J. Gebicki and A. J. Kranz, J. Am. Chem. Soc., 1981, **103**, 4521; (g) U. Berg, J. Sandstrom, L. Carlsen and F. Duus, J. Chem. Soc., 1981, **132**; (h) B. Andersen, F. Duus, S. Bolvig and P. E. Hansen, J. Mol. Struct., 2000, **552**, 45; (i) F. S. Jorgensen, L. Carlsen and F. Duus, J. Am. Chem. Soc., 1981, 1321; (k) Y. Posokhov, A. Gorski, J. Spanget-Larsen, F. Duus, P. E. Hansen, and J. Waluk, ChemPhys. Chem. Chem. Phys., 1999, **1**, 1249; (k) Y. Posokhov, A. Gorski, J. Spanget-Larsen, J. Waluk and J. Spanget-Larsen, Vib. Spectrosc., 2007, **43**, 53.
- 23 (a) S. Millefiori and A. Millefiori, J. Chem. Soc., Faraday Trans. 2, 1989, 85, 1465; (b) S. Millefiori and S. Di Bella, J. Chem. Soc., Faraday Trans. 2, 1991, 87, 1297; (c) J. S. Craw and G. B. Bacskay, J. Chem. Soc., Faraday Trans. 2, 1992, 88, 2315.
- 24 J. Goerdeler and F. Zander, Chem. Ber., 1980, 113, 2814.