Cycloaddition of 3-thioxo-1,2-dithioles onto Acetylenedicarbaldehyde and its Mono-diethylacetal : Ready Access to Intermediates in the Tetrathiafulvalene (TTF) Series

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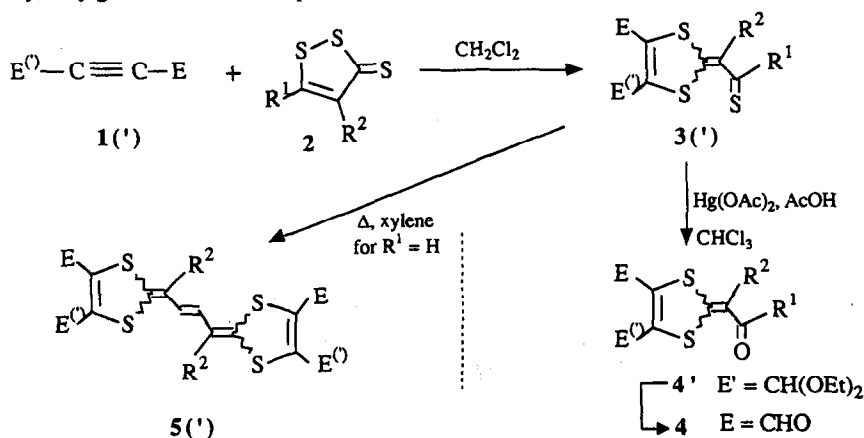[b] Laboratoire de Synthèse Organique associé au CNRS, Université de Nantes, 2 rue de la Houssinière, 44072 Nantes, France
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Abstract : The 4,5-diformyl-1,3-dithiol-2-ylidene ethanals and ethanones 4 are prepared by a three-step sequence from acetylenedicarbaldehyde mono-diEt-acetal and 3-thioxo-1,2-dithioles. Their X-ray diffraction structure, ^{1}H nmr and IR properties, reveal a δ-cis conformation in the solid state and in solution, due to strong S...O 1,5-internal bonding interactions.

The 3-thioxo-1,2-dithioles 2, unsubstituted at the 5-position (R^1= H, Scheme 1) are known to react with electrophilic alkynes (E and/or E'= electron withdrawing group) to afford cycloadducts which, by virtue of their thial functional group, readily dimerize with loss of sulphur, on simple heating, to produce highly substituted vinylogs of tetrathiafulvalene 5.[1]

We have recently reported the use of acetylenedicarbaldehyde (ADCA) 1 (E = CHO) or its mono-diEt-acetal 1' (E= CHO, E'= CH(OEt)$_2$) as the starting alkyne to obtain tetraformyl-substituted derivatives of 5 (E= CHO) of significant synthetic interest : on fourfold Wittig olefination with P-ylids bearing the 1,3-dithiol-2-ylidene moiety, they give rise to the most powerful π-donors of the TTF series achieved so far.[2]

Scheme 1

Taking into account the high synthetic potential of compounds 3, 3', 4' and 4 in the field of 1,3-dithioles and TTF chemistry[3], we have decided to generalize their preparation, with a focus on the structural features of latter compounds.

Synthesis

Cycloaddition step   The instantaneous reaction of the free dialdehyde 1 with 2b (R^1= H, R^2= Ph) in CH_2Cl_2 solution below 0°C confirms the tremendous electrophilicity of this alkyne. As a matter of fact, with dimethyl acetylenedicarboxylate, the same reaction requires 3hrs at 20°C for completion. Almost quantitative yields of 3b are thus obtained, provided that a 10% molar excess of 2b is used to prevent further (4 + 2) cycloaddition of the enethial onto 1. Under similar conditions, the cycloaddition of 1' proceeds at a slower rate as expected (1hr at 20°C), but results in almost quantitative production of the (E) and (Z) isomers of 3'b in approximately equal amounts. In view of the problems inherent to the preparation of 1 and to the handling of its aprotic solutions,[4] as well as the fact that 1 is derived from its more stable monoacetal 1',[5] this latter compound has been chosen for subsequent generalization work (Table). All the thials 3'a-c and the thiones 3'd-h, produced in fairly good yields, were isolated from the raw reaction mixture after evaporation *in vacuo* and crystallization from diethylether, as stable (when stored below 0°C) black crystals composed of a mixture of (Z) and (E)-isomers that we did not try to separate.(*)

<u>Table</u>   Preparation of 3' by cycloaddition of 1' onto 2a-h

(Z) + (E) mixture of compounds 3'	Thials			Thiones				
	3'a	3'b	3'c	3'd	3'e	3'f	3'g	3'h
R_1	H	H	H	Me	Ph	p-MeOPh	p-BrPh	α-Thienyl
R_2	H	Ph	p-MePh	Me	H	H	H	H
% yield[a]	57	71	60	79	75	80	72	65
m.p. (decomp)°C	98[b]	110[b]	90-2[b]	33-4	87-90	120-1	128	110-1

(a) Given yields correspond to similar experimental conditions : for 1-5 g of 3', CH_2Cl_2 solution, 10% excess of 2 with respect to 1' over a 1hr period, evaporation in vacuo and crystallization from Et_2O.

(b) Even such thials are stable enough in the solid state and can be stored below 0°C.

C=S to C=O conversion   Following the known procedure,[6] treatment of 3' with $Hg(OAc)_2$/AcOH in refluxing $CHCl_3$ gives the corresponding aldehydes or ketones 4' in 80%-90% yields. By performing this reaction at room temperature in the case of 3'a, we could isolate an intermediate *gem*-diacetate 6'a (Scheme 2) suggesting, as the likely mechanistic pathway, a prior soft-soft interaction between $\underline{Hg}(OAc)_2$ and -CH=$\underline{S}$, followed by the exchange S^-/ 2 AcO^- with loss of HgS, and finally hydrolysis of 6'a to give 4'a.[7]

<u>Scheme 2</u>

Deketalization   The conditions of deketalization were mainly dependent upon the substituents R^1 and R^2. Formolysis proceeds very fast at 20°C (10 min., $HCO_2H/CHCl_3$, 1/1 vol.) in the case of the aromatic ketones **4'e-h**, and much slower (10 hrs) when starting from the aldehydes **4'b,c** and the ketone **4'd**, more dilute formic solutions being required in these cases (1/3 vol.). Compounds **4** were finally obtained in 60-70% overall yields with respect to starting material **1'**. However, only poor yields (c.a. 20%) of the unstable and acid sensitive **4a** could be obtained by hydrolysis catalyzed with Amberlyst-15.[8]

Structure of tricarbonyl derivatives 4

As may be expected from preceding structural studies devoted to *i)* analogs of **4** possessing a 1,3-dithiole ring differently substituted,[9] or replaced by a 1,2-dithiole ring,[10] and *ii)* trithiapentalene and its corresponding dioxygenated analogues,[11] compounds **4** (or **4'**) are likely to exist in their δ-*cis* conformation, because of the occurrence of a strong S...O bonding internal 1,5-interaction. In order to confirm such a geometry in compouds **4** (or **4'**), their structure was analysed by X-ray diffraction and ^1H nmr and IR spectroscopy.

X-ray structure[12]

The ORTEP of **4g** (Figure) reveals a strong S...O bonding interaction, since the distance d = 2.570 Å, between the ketonic oxygen atom O(1) and S(2), is lower than the sum (3.3 Å) of the Van der Waals radii of S (1.8 Å) and O (1.5 Å), and larger than the single covalent S-O bond (1.75 Å).[13]

Figure : X-ray molecular structure of **4g**

^1H nmr and IR spectra

The ^1H nmr spectrum of **4a** exhibits a ^3J= 1.5 Hz for the =CH-CH=O system, a ^3J value related to a δ-*trans* conformation would be expected to be much higher (7-8 Hz).[14] For all other compounds **4** devoid of such conformational nmr landmarks, the stereochemistry was studied by IR spectroscopy according to previous works by Mollier *et al.*[9] By comparison of the spectra recorded in CH_2Cl_2 or $CHCl_3$ solution and in the solid state, only the vC=O are changed while the ethylenic and aromatic vC=C do not change. In the case of **4 a-c**, both dithiolic CH=O have their coupled absorption band in a different range (1660 cm^{-1}) compared with the conjugated ethanal group CH=O (1630 cm^{-1}), the low frequency of the latter resulting from the strong CH=O...S internal interaction due to the δ-*cis* conformation of the C=CH-CH=O moiety. Similar shifts are also observed in the case of the methyl ketone **4d**. For compounds **4e-h**, the extremely low frequencies of ketonic C=O absorptions at 1590-1570 cm^{-1} in KBr, easily discriminated from the aromatic and ethylenic vC=C near 1604 (and 1550 cm^{-1}) in the dry state, are also indicative of the δ-*cis* conformation.

Conclusion

The sterically crowded δ-*cis* enone or enal conformation suggests an attenuation of the electrophilicity of this moiety. Further elaboration of these compounds **4** towards the preparation of novel TTF derivatives is now in progress and will be reported in future publications.
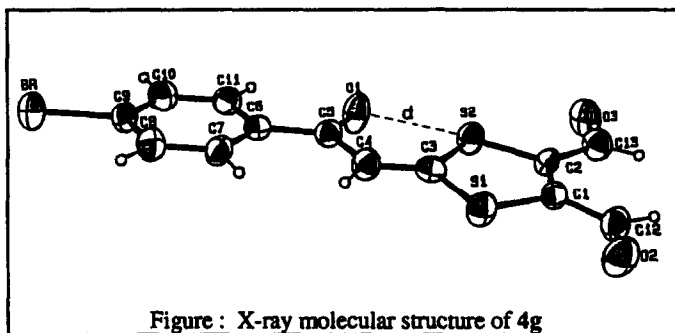
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7   It should be noted that, in this case, the E'=CH(OEt)$_2$ functionality remains untouched, its deketalization requiring more drastic conditions.

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12 Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Cristallographic Data Centre.

13 Such a d value is very close to that found in related rigid cyclic systems, e.g.; Coffin, M. A.; Bryce, M. R. and Clegg, W. *J. Chem. Soc., Chem. Commun.* 1992, 401-402.

14 =CH-CH=O ^{3}J = 7 Hz , see the Aldrich Library of NMR Spectra, Vol. II, Ed. 1974, pp 99-100.

(*) All new compounds gave satisfactory spectral data and/or elemental analyses; ^{1}H and^{13}C high field nmr as well as hrms were recorded by the CRMPO (Rennes) and analyses by the CNRS (Vernaison). Selected examples:

3'b   Black crystals, m.p. 110°C (decompn); hrms (C$_{17}$H$_{18}$O$_3$S$_3$) calcd 366.0418, found 366.0415; anal. calcd (found) C 55.70 (55.91), H 4.95 (4.98), O 13.09 (13.23), S 26.24 (26,07); IR (CHCl$_3$) 1660 (C=O), 1580 (arom.); 270 MHz ^{1}H nmr (CDCl$_3$) mixture of two isomers (maj./min.) 10.67/10.61 (s, 1 H, H-C=S), 10.23/10.18 (s, 1 H, H-C=O), 7.44 (m, 4 H, arom.), 5.97/5.91 (s, 1 H, C<u>H</u>(OEt)$_2$), 3.65 (m, 4 H, 2 OCH$_2$), 1.24 (t, 6 H, 2 CH$_3$), 75 MHz ^{13}C nmr (CDCl$_3$) for the major isomer 203.3 (HC=S), 182.(HC=O), 158.7 (S$_2$C), 151.2 ((EtO)$_2$CH-<u>C</u>=), 134.0 (OCH-<u>C</u>=), 136.3 (SCH-<u>C</u>=), 140.7, 129.6, 128.8, 128.6 (Ph), 96.5 (<u>C</u>H(OEt)$_2$), 62.3 (O-CH$_2$), 15.0 (CH$_3$).

4a   Orange powder, m.p. 188-190°C; hrms (C$_7$H$_4$O$_3$S$_2$) calcd 199.9601, found 199.9608; IR (KBr) 1662-1652 (HC=O dithiolic), 1625 (HC=O), 1552 (C=C); 270 MHz ^{1}H nmr (CDCl$_3$) 10.41 (s, 1 H, HC=O), 10.37 (s, 1 H, HC=O), 9.54 (d , J = 1.5Hz, 1 H, =CH-C<u>H</u>=O), 6.72 (d, J = 1.5Hz, 1 H, =C<u>H</u>-CH=O); 75 MHz ^{13}C nmr (CDCl$_3$) 183.84 (=CH-<u>C</u>H=O), 179.10 and 178.90 (2 <u>C</u>HO), 155.36 (CS$_2$), 149.34 and 145.85 (2 OCH-<u>C</u>=), 109.74 (=<u>C</u>H-C<u>H</u>=O)

4e   Red crystals, m.p. 206°C; hrms (C$_{13}$H$_{10}$O$_3$S$_2$) calcd 275.9914, found 275.9911; anal. calcd (found) C 56.50 (56.47), H 2.91 (2.80), O 17.36 (17.38), S 23.20 (23.49); IR (KBr) 1672-1656 (HC=O), 1605 (arom.), 1595 (arom.), 1573 (Ph-C=O), 1546 (C=C); 270 MHz ^{1}H nmr (DMSO-d_6) 10.48 (s, 2 H, CH=O), 8.04 (s, 1 H, S$_2$C=C-H), 7.78 (m, 5 H, arom.)

6'a   Orange oil; IR (CHCl$_3$) 1760 (C=O acetyl) 1660 (C=O ald.); 60 MHz ^{1}H nmr (CDCl$_3$) mixture of two isomers (maj./min.) 9.8/9.7 (s, 1 H, CH=O), 7.1/7.0 (d, J = 7Hz, 1 H, S$_2$C=C<u>H</u>-CH(OAc)$_2$), 5.5 (d, J = 7Hz, 1 H, =CH-C<u>H</u>(OAc)$_2$), 5.8 (s, 1 H, C<u>H</u>(OEt)$_2$), 3.6 (m, 4 H, 2 OCH$_2$), 2.0 (s, 6 H, 2 CH$_3$CO),1.2 (m, 6 H, C<u>H</u>$_3$-CH$_2$)