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Synthesis of Unsymmetrically Substituted TTF Derivatives *via* the "Phosphonate Way". Limitations Due To The Instability of Some Metalated 1,3-Dithiol-2-Yl-Phosphonates.

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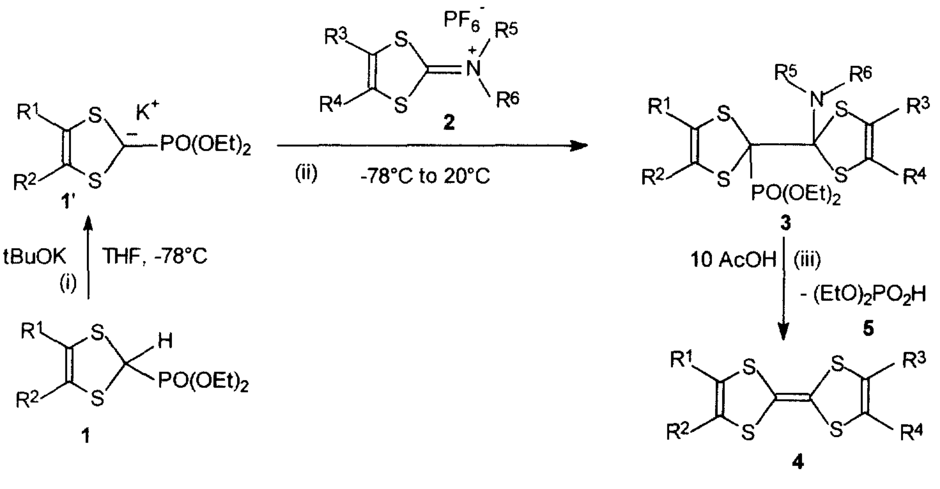
Abstract: The poor results in the syntheses of unsymmetrically substituted TTF derivatives carried out with *mono* or *un*substituted diethyl 1,3-dithiol-2-yl-phosphonates is here explained by the existence of an equilibrium between the cyclic and open forms of their corresponding carbanionic salt, with possible dimerisation of the open form. The monomeric cyclic form can react with a high reactive iminium salt, affording then the corresponding TTF derivative in moderate yield.

In our last report,[1] concerning the scope and limitations of the "phosphonate way" (scheme 1), for the synthesis of unsymmetrically substituted TTF derivatives, we pointed out a special behaviour of *mono-* or *un*substituted diethyl 1,3-dithiol-2-yl-phosphonates **1** (R^1 = H, R^2 = H, CH_3) which give very poor results for the synthesis of compounds **4**.



1a) $R^1 = R^2 =$ H; **1b**) $R^1 = CH_3$, R^2 = H.
2a) $R^3 = R^4 = CH_3$, R^5, $R^6 = (CH_2)_5$; **2b**) R^3, R^4 = S-$(CH_2)_2$-S; $R^5 = R^6 = CH_3$; **2c**) R^3, R^4 = O-$(CH_2)_2$-S; R^5,= $R^6 = CH_3$;
4aa) $R^1 = R^2$ = H, $R^3 = R^4 = CH_3$; **4ab**) $R^1 = R^2$ = H, $R^3 = R^4$ = S-$(CH_2)_2$-S; **4ac**) $R^1 = R^2$ = H, $R^3 = R^4$ = O-$(CH_2)_2$-S;
4ba) $R^1 = CH_3$, R^2=H, $R^3 = R^4 = CH_3$;; **4bb**) $R^1 = CH_3$, R^2=H, $R^3 = R^4$ = S-$(CH_2)_2$-S; **4bc**) $R^1 = CH_3$, R^2=H,
$R^3 = R^4$ = O-$(CH_2)_2$-S.

Scheme 1

Indeed, when the starting materials are the diethyl 1,3-dithiol-2-yl-phosphonate **1a**[2] and the 4,5-dimethyl-1,3-dithiol-2-yliden piperidinium hexafluorophosphate **2a**,[3] the corresponding TTF **4aa**,[4] is isolated in pure form in

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only 30% yield. Whereas, the expected TTF derivatives **4ab**,[4] and **4ac**[5] are not detected in the final mixture when the same phosphonate **1a** is reacting with the N,N-dimethyl iminium salts **2b** (R^3, R^4 = $S(CH_2)_2S$; $R^5 = R^6 = CH_3$)[6] or **2c** (R^3, R^4 = $O(CH_2)_2S$; $R^5 = R^6 = CH_3$)[7] respectively.

In fact such a failure seems to be due to the limited stability of the phosphonate anion **1'a** ($R^1 = R^2 = H$), as demonstrated by the following studies of the reactions monitored by ^{31}P-NMR and ^{1}H-NMR spectroscopies.

In a first experiment, the stability of the phosphonate **1a**, placed in anhydrous acidic medium (in presence of benzoic acid) for one hour, was clearly established. Then, the metalation of the phosphonate **1a** by tBuOK was studied between –60°C and –20°C. The ^{31}P-NMR analysis of the resulting reaction mixtures showed a single signal at δ = 16.40 ppm, very near that one observed for the starting phosphonate **1a** (δ = 16.31 ppm) (but separated from it, as shown by addition of **1a** to the solution of **1a'**).

In a reprotonation reaction, the previous mixtures were then treated by anhydrous benzoic acid and analyzed:

-By ^{31}P-NMR: two signals, in the ratio 2/98, were observed. The first one at 16.31 ppm (2%) was clearly attributed to the phosphonate **1a.** The second one at 17.66 ppm, broad (98%), disclosed under high resolution, three different peaks respectively at 17.65, 17.64, and 17.63 ppm..

-By ^{1}H-NMR: the spectrum appears similar to the spectrum of the starting phosphonate **1a**: The characteristic signals of the $P(O)(OEt)_2$ group were observed as well as the singlet of a vinylic protons (δ = 6.59 ppm) with a deshielding of 0.74 ppm (with regard to the corresponding signal for **1a**), and the doublet of the C_2-H proton [δ = 4.91 ppm ($^2J_{PH}$ = 3.43 Hz)], with a shielding of 0.64 ppm. It is worthy to note that this C_2-H proton was not found acidic, (on the contrary to the corresponding signal in **1a**), since no deuterium exchange was observed by addition of CD_3OD.

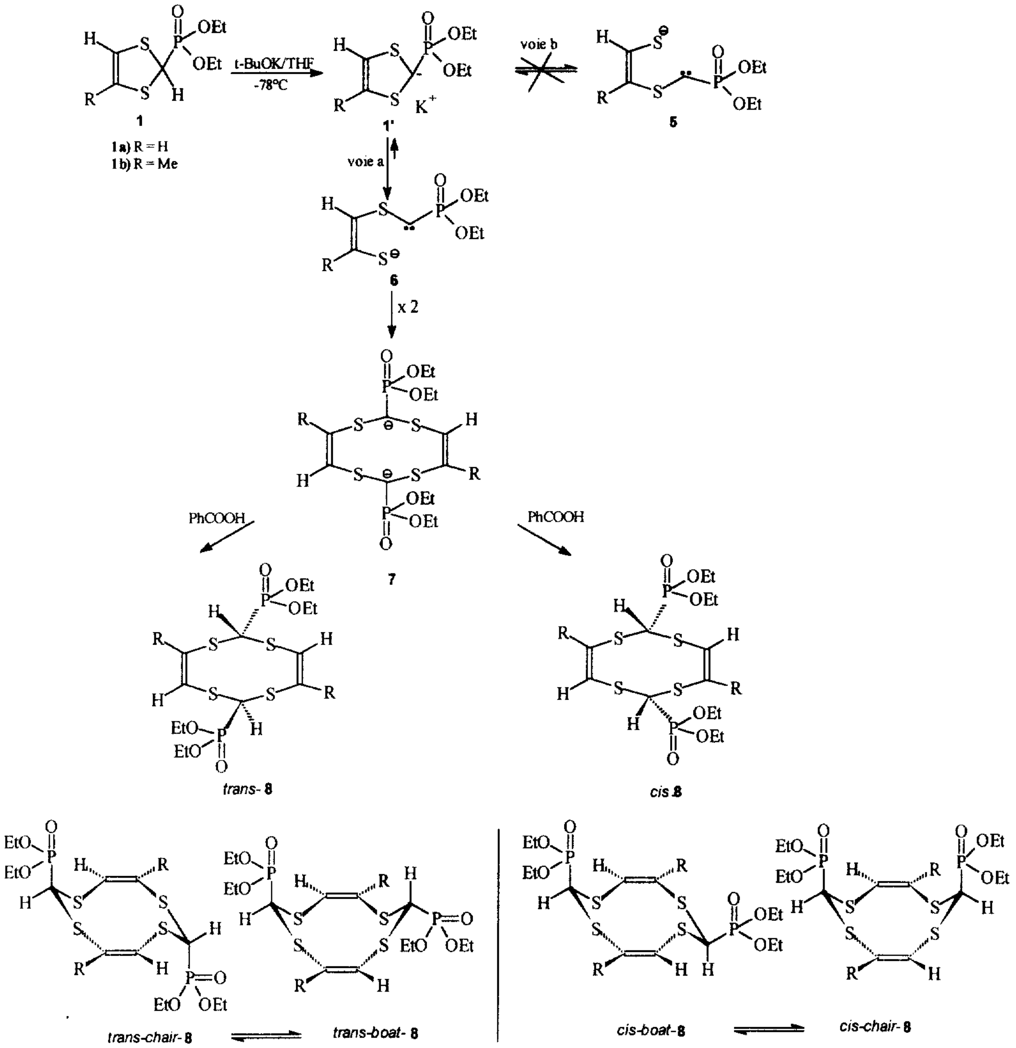
-By ^{13}C-NMR: the spectrum also indicated a great similarity with the spectrum of the phosphonate **1a**, nevertheless the vinylic carbons appear downfield as a multiplet at δ = 123.27 ppm, and not as a singlet at δ = 116.90 ppm as seen for **1a**.

Finally the new compound analyzed by mass spectroscopy displayed a peak at 509 $[M+H]^+$ corresponding likely to a dimer of **1a** (scheme 2).

Similar statements can be made on the behaviour of the diethyl 3-methyl-1,3-dithiol-2-yl-phosphonate **1b** reacting respectively with the hexafluorophosphates **2a**, **2b**, and **2c**. Since only the resulting TTF **4ba**[9] is obtained in 30% yield. while TTF **4bb**,[2] **4bc**[4] are not synthesized at all.

As in the precedent case, the deprotonation of the phosphonate **1b** ($R^1 = CH_3$; $R^2 = H$) by tBuOK followed by acidification with anhydrous benzoic acid leads to the starting phosphonate **1b** in only 4% yield, as shown by ^{31}P-NMR analysis. The signal of **1b**, at δ = 16.71 ppm, is accompanied by three signals, of about the same intensity (ca 32%), at respectively 18.26, 18.24, and 18.20 ppm.

The ^{1}H-NMR spectrum is found different, except for the signals corresponding to the $P(O)(OEt)_2$ group, from the spectrum of the phosphonate **1b**. The vinylic proton and the vinylic methyl group giving rise to two broad singlets at 6.62 and 2.13 ppm respectively, instead of a quartet and a triplet observed respectively at 5.49 and 1.93 ppm for **1b**. Moreover the doublet observed at δ = 4.27 ppm ($^2J_{PH}$ = 4.15 Hz) does not correspond with an acidic proton (non affected by CD_3OD addition on the contrary to the doublet at δ = 5.23 ppm ($^2J_{PH}$ = 4.15 Hz) in the spectra of **1b**).



Scheme 2

The ^{13}C-NMR spectrum exhibits a tertiary carbon as a multiplet at 44.34 ppm, resulting in the superposition of three doublets ($^1J_{PC}$ = 152.0 Hz, $^2J_{PC}$ = 11.5 Hz, and $^3J_{PC}$ = 8.0 Hz). Down field, instead of the singlet observed for **1b** at δ = 116. 90 ppm, the vinylic carbons gave rise to two multiplets between 126.83 and 127.19 ppm, and between

127.34 and 127.49 ppm respectively). The new compounds analyzed by mass spectroscopy, is characterized by a peak at 537 $[M+H]^+$. All these spectroscopic data are clearly in favour for a dimer (scheme 2).

Discussion: The carbanionic species **1'a**, and **1'b**, bearing a good leaving thioenolate group α to the phosphonate group, a ring opening might occur by two routes in the case of the methylated species **1'b** (scheme 2). The route (b) seems to be unfavorable, because of the inductive effect of the methyl group on the vinylic carbon of the dithiole ring.[9] A such ring opening might lead, according to the proposed mechanism described in scheme 2, to a dimerisation of the carbanionic intermediates giving, after acidification, the *trans* and *cis* dimers **8**. The unsaturated ten membered ring of isomers **8**, would adopt *boat* or *chair*-like conformations in which the cyclic strain is reduced. Among the four possible conformers depicted, the steric transannular hindrance between the two axial phosphonate groups prevents probably the formation of the *cis-boat*-**8**. Consequently, the diphosphonates **8** would exist as three preferred conformers: *trans-chair*-**8**, *trans-boat*-**8**, and *cis-chair*-**8** which are in agreement with the three different and very close signals shown by the ^{31}P-NMR spectra and also with the corresponding ^{13}C- and ^{1}H-NMR spectra described above. Moreover, as expected, a thermal interconversion between the two *trans* conformers of **8** might occur: Indeed, in a ^{31}P-NMR study a reversible coalescence of the three signals into two broad peaks (in the ratio 2/1) is effectively observed between 30°C and 130°C.

Nevertheless, the route (a), depicted in scheme 2, is very likely an equilibrium between the open and cyclic forms of **1'a**, or **1'b**. This equilibrium can be shifted to the cyclic form in presence of a strong reactive iminium salt as **2a**,[2] and in such a case, the corresponding TTF derivative **4aa** is formed in moderate yields (30%) from **1a**.

In conclusion, the established dimerisation of intermediates **1'a** or **1'b** can explain the unsuccess of most of the synthesis of unsymmetrically substituted TTF derivatives carried out from *mono* or *un*substituted phosphonates **1**.

References and notes

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9. In the same way, the donor effects of both substituents could prevent the opening of the metalated *di*substituted 1,3-dithiol-2-yl phosphonates, affording then high yields in TTF derivatives.[1b]