Tetrahedron Letters 56 (2015) 1894–1897

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Phosphite-mediated conversion of benzaldehydes into stilbenes via umpolung through a dioxaphospholane intermediate

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ARTICLE INFO

Article history:
Received 17 December 2014
Revised 10 February 2015
Accepted 19 February 2015
Available online 26 February 2015

Keywords:
Cruciform
Dioxaphospholane
Phosphite
Stilbene
Tetrathiafulvalene

ABSTRACT

The phosphite-mediated coupling of two benzaldehydes into 2,2,2-triethoxy-1,3,2-dioxaphospholanes was investigated using ^{13}C NMR spectroscopy and was found to be very sensitive to the nature of the *ortho*/*para* substituents, and promoted by electron-withdrawing groups (EWGs). Stilbene-extended tetrathiafulvalenes were prepared by heating the intermediate dioxaphospholane, containing aldehyde substituents at *para* positions and ethynyl groups at *ortho*/*meta* positions, with 1,3-dithiol-2-thiones in $P(OEt)_3$. While EWGs promoted dioxaphospholane formation, electron-donating groups (EDGs), generated by conversion of the aldehydes into dithiafulvenes, promoted subsequent conversion into an alkene.

The phosphite-mediated coupling of 1,3-dithiol-2-chalcogenones is a key reaction for the formation of derivatives of tetrathiafulvalene (TTF),[1] a redox-active molecule which has generated significant interest in both materials and supramolecular chemistries.[2] Serendipitously, we found that this reaction could also be used to prepare extended TTFs **1** and **2** (Fig. 1), which were coined 'H-Cruciforms' on account of the molecular shape of the central part.[3] These compounds were prepared from an acetylenic derivative **5** of terephthalaldehyde and the 1,3-dithiol-2-thiones **3**[4] and **4**,[4] respectively. Thus, not only had **3** or **4** reacted with an aldehyde functionality of the terephthalaldehyde, but more importantly, two aldehyde functionalities had coupled together under the influence of triethyl phosphite to furnish a carbon–carbon double bond as part of a stilbene moiety. Interestingly, from terephthaldehyde itself, we only isolated the extended TTF where each aldehyde group had reacted with a 1,3-dithiol-2-thione. Ramirez et al.[5] have shown that *o*- and *p*-nitrobenzaldehyde, that is, aldehydes with electron-withdrawing substituents, can react with trialkyl phosphites at 20 °C to generate 2,2,2-trialkoxy-1,3,2-dioxaphospholanes, and we hypothesize that such heterocyclic compounds could be intermediates in the formation of stilbenes **1** and **2**. To investigate this carbon–carbon bond forming reaction in further detail, we decided to study the outcome of subjecting a variety of substituted benzaldehydes to reactions with triethyl phosphite.

First, we examined the reaction between triethyl phosphite and terephthalaldehyde at 100 °C—these experiments were performed in neat phosphite in an NMR tube with a DMSO-d_6 insert tube, while recording ^{13}C NMR spectra at regular intervals. ^{13}C NMR spectroscopic analysis of the reaction mixture revealed the disappearance of the starting material and the appearance of multiple new signals in the aromatic region and two new signals at 79 and 74 ppm, assigned to the carbon atoms of the five-membered dioxaphospholane ring (*cis* and *trans* isomers; however, we were unable to make an absolute assignment). The two remaining aldehyde groups were not converted. A similar outcome was observed with 4-nitrobenzaldehyde. The reactivity of terephthalaldehyde and 4-nitrobenzaldehyde toward phosphite encouraged the investigation of the reaction in different solvents. Gratifyingly, we found that the reaction proceeded in MeCN, CH_2Cl_2, THF, and toluene at room temperature with 5–10 equiv of $P(OEt)_3$. In the case of toluene, heating to 40–60 °C increased the reaction rate substantially; in the cases of THF, CH_2Cl_2, and MeCN, ambient temperature was sufficient to affect the transformations (in agreement with the results of Ramirez et al.[5] in CH_2Cl_2). With 4-nitrobenzaldehyde, the transformation performed in MeCN at rt was virtually complete by the time the ^{13}C NMR spectrum had been recorded (within 10 min), employing two molar equivalents of $P(OEt)_3$ (Fig. 2). The screening of different molar equivalents of $P(OEt)_3$ showed that the transformation could be driven to completion with just 0.5 molar equivalents in the case of 4-nitrobenzaldehyde. The reaction rate increased dramatically, however, when an excess of $P(OEt)_3$

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http://dx.doi.org/10.1016/j.tetlet.2015.02.108
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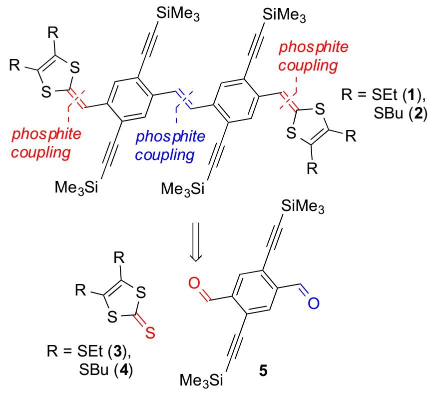
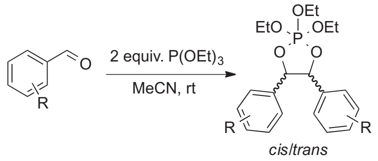


Figure 1. H-Cruciform extended TTFs—prepared by phosphite-mediated couplings.



Scheme 1. Formation of dioxaphospholanes from substituted benzaldehydes (for details, see Table 1).

Table 1
Aldehydes tested for dioxaphospholane formation (see Scheme 1)

Entry	Reactant (substituent R)	Dioxaphospholane[a]	Time
1	H	None	14 d[b]
2	*p*-O_2N	>95%[c]	<10 min
3	*o*-O_2N	>95%[c]	<30 min
4	*m*-O_2N	None	14 d[b]
5	*o*-CHO	>95%[c]	2 h
6	*p*-CHO	>95%[c]	2 h
7	*p*-CO_2Me	15–20%	14 d[b]
8	*p*-CN	80–90%	36–48 h[d]
9	C(O)Me	15–20%	>72 h
10	*p*-F	None	14 d[b]
11	*p*-I	None	14 d[b]
12	*p*-F_3C	None[e]	14 d[b]
	carbonyl reactant		
13	*p*-$O_2NC_6H_4CH{=}CHCHO$	None	14 d[b]
14	**5**	>95%[c,f]	4 h
15	*p*-$O_2NC_6H_4C(O)Me$	None	14 d[b]

[a] Estimated conversion into dioxaphospholane as determined by ^{13}C NMR (126 MHz, DMSO-d_6) spectroscopy.
[b] No conversion observed after 14 d at 80 °C.
[c] No aldehyde ^{13}C NMR signal remained.
[d] Reaction was performed in refluxing MeCN.
[e] Reaction was performed in neat P(OEt)$_3$, due to solubility issues.
[f] The product contained mainly one of the isomers.

was present. The reaction was also easily performed on preparative scale from which we isolated 2,2,2-triethoxy-4,5-bis(4-nitrophenyl)-1,3,2-dioxaphospholane in a yield of 97% (see the Supplementary material).

Our next objective was to study dioxaphospholane formation in MeCN using two equivalents of P(OEt)$_3$ and a variety of benzaldehyde derivatives, as shown in Scheme 1 and Table 1. The degree of conversion was estimated by comparing key ^{13}C NMR signals in the dioxaphospholane and in the starting material. Since signal intensities in ^{13}C NMR spectroscopy cannot be quantitatively compared, the conversion is formulated in a very conservative manner; that is, in cases where no starting material is observed, the conversion is reported as >95% (only very minor signals from unidentified by-products are present). As can be seen from Table 1, the balance for the outcome of the reaction is very subtle. First of all, we do not observe conversion of benzaldehyde itself (entry 1); only starting material was observed. It can be seen that electron-withdrawing groups (EWGs) such as NO$_2$, CHO in *ortho* or *para* positions (entries 2, 3, 5 and 6) favor the formation of the dioxaphospholane, in each case, as a mixture of *cis* and *trans* isomers. However, other electron-withdrawing *para* substituents such as F, I, and CF$_3$ (entries 10–12) do not favor the formation of the dioxaphospholane. After prolonged exposure to P(OEt)$_3$, new signals began to appear, but they were not consistent with dioxaphospholanes.

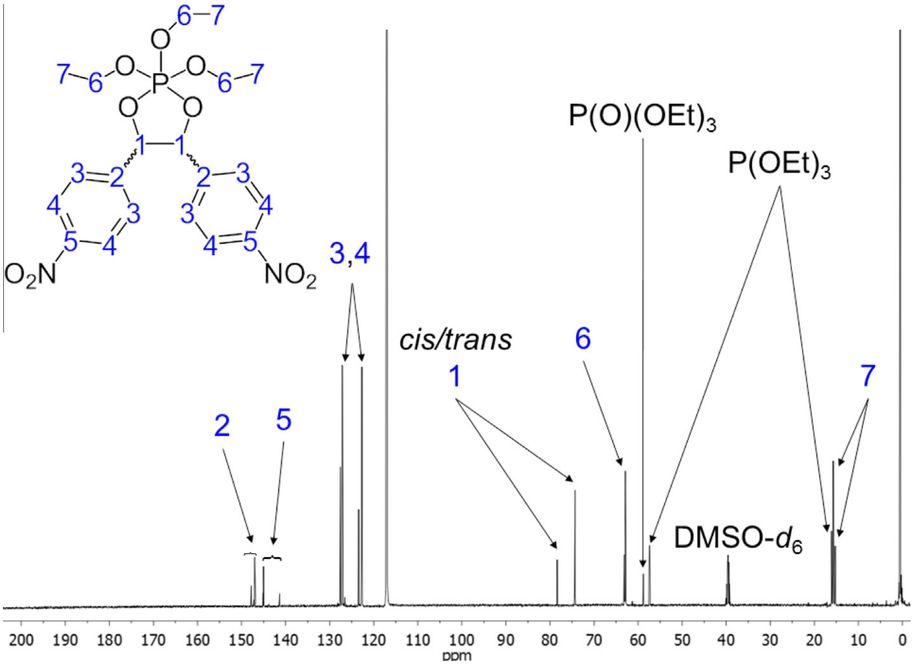


Figure 2. ^{13}C NMR (126 MHz, DMSO-d_6) spectrum of the reaction mixture obtained from heating 4-nitrobenzaldehyde with 2 equiv of P(OEt)$_3$ in MeCN. Signals split due to the presence of *cis*/*trans* isomers. As can be seen, no aldehyde resonance remained in the region around 190 ppm, and all the signals could be accounted for.