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ORGANOSULPHUR COMPOUNDS—XVIII[1]

A NEW AND GENERAL SYNTHESIS OF KETENE S,S- AND O,S-THIOACETALS BASED ON THE HORNER–WITTIG REACTION[2]

M. MIKOŁAJCZYK,* S. GRZEJSZCZAK and A. ZATORSKI
Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Department of Organic Sulphur Compounds, 90-362 Lodz, Boczna 5, Poland

B. MŁOTKOWSKA
Institute of Organic Chemistry, Technical University, 90-539 Lodz, Zwirki 36, Poland

and

H. GROSS and B. COSTISELLA
Zentralinstitut für Organische Chemie der Akademie der Wisserschaften der DDR, DDR-1199 Berlin-Adlershof, Rudower Chaussee 5, Deutsche Demokratische Republik

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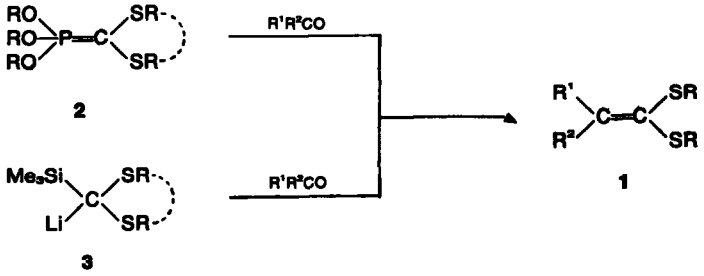
Abstract—A new and general synthesis of ketene S,S-thioacetals (1) and ketene O,S-thioacetals (6) which involves the Horner–Wittig reaction of carbonyl compounds with the metallated S,S- and O,S-thioacetals of formylphosphonates (4 and 5) is described. The Horner–Wittig reaction of 4 with aromatic aldehydes can be carried out under two-phase conditions. The generation of the carbanions from 4 and 5 as well as the course of their reaction with carbonyl compounds were studied by the low temperature ^{31}P NMR spectroscopy. It was found that S,S-thioacetals of formylphosphonates (4) are very easily metallated in contrast to O,S-thioacetals of formylphosphonates (5) which form the lithium derivatives only on treatment with t-butyllithium. No evidence was obtained from ^{31}P NMR spectra supporting the formation of the lithium derivatives of 0,0-acetals of formylphosphonates (12).

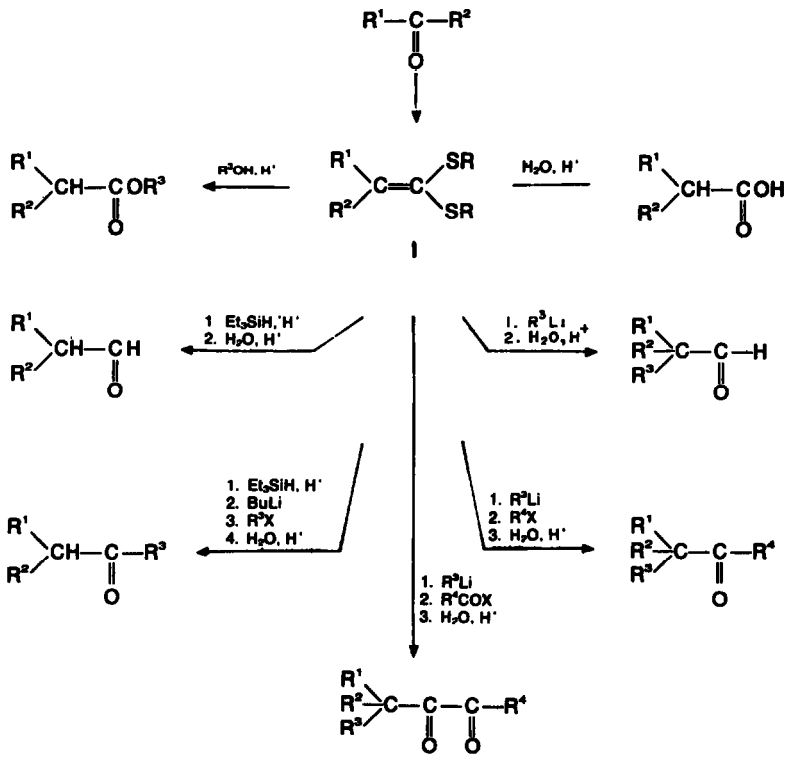
Ketene S,S-thioacetals (1) are key intermediates in a wide variety of organic syntheses.[3] Their hydrolysis[4] and alcoholysis[5] afford carboxylic acids and carboxylic acid esters, respectively. The reduction of the carbon–carbon double bond in 1 gives dithioacetals which on hydrolysis may be converted into a homologous aldehydes.[6] The addition of alkyllithium reagents to 1 results in the formation of the corresponding lithium derivatives of dithioacetals[7] which are also reactive compounds useful in further reactions. Therefore, the possibility of the conversion of a carbonyl compounds into the corresponding ketene S,S-thioacetal makes it possible to perform a large number of further transformations summarized in Scheme 1.

For this reason the synthesis of ketene S,S-thioacetals (1) from as large as possible group of aldehydes and ketones is of great importance. Although a number of methods for preparing 1 have been reported[8] only two of them utilize carbonyl compounds as the reaction substrates. The first method for converting carbonyl compounds into 1 is by way of the Wittig reaction employing the phosphite ylides (2).[9] Apart from the hard availability of 2 this method gives satisfactory results only with aldehydes but not with ketones. The second method, based on the Peterson reaction of the lithium derivatives of trimethylsilyldithioacetals (3),[8,10] is more general and efficient but also in this case sterically hindered ketones like benzophenone yield the corresponding 1 in a moderate yields.

In the course of our studies on α-phosphoryl substituted organosulphur compounds we have recently synthesized two new classes of compounds derived from formylphosphonates, $(RO)_2P(O)C(O)H$, namely S,S-thioacetals of formylphosphonates (4)[11] and O,S-thioacetals of formylphosphonates (5).[12]

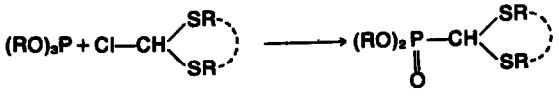
In contrast to the parent compounds, thioacetals 4 and 5 are chemically stable and can be readily prepared in a high yields by the Arbuzov reaction of trialkylphosphites



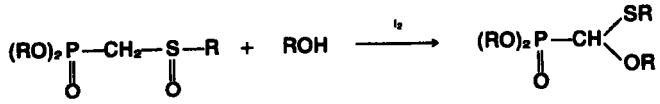


Scheme 1. Homologation of carbonyl compounds via ketene S,S-thioacetals (1).

with chlorodithioacetals and by the Pummerer-type reaction of α-phosphoryl sulphoxides with alcohols in the presence of iodine, respectively



4

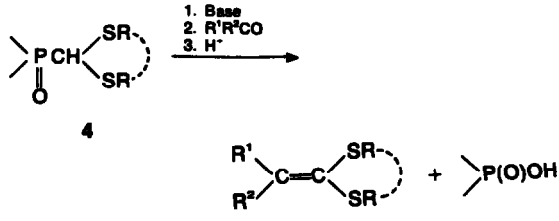


5

Since both the phosphoryl group and the S atom are known to stabilise the neighbouring carbanion one could expect that the proton elimination from 4 and 5 will readily occur and the corresponding carbanions formed should give on treatment with carbonyl compounds ketene S,S-thioacetals (1) and ketene O,S-thioacetals (6), respectively. With this consideration in mind we developed† a new and general synthesis of 1 and 6 and the full results of these studies we report in the present paper.

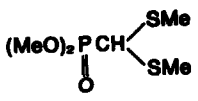
RESULTS AND DISCUSSION

Synthesis of ketene S,S-thioacetals (1). We have found that the Horner PO-olefination reaction using 4 as the phosphonate component affords ketene S,S-thioacetals (1) in high purity and yields from 70 to 96%. This novel approach for the direct conversion of carbonyl compounds into 1, in contrast to those utilizing 2 and 3 as reagents, has practically no limitations. The carbanion derived from 4 reacts smoothly with aliphatic and aromatic, acyclic and cyclic aldehydes and ketones. It is noteworthy that good results have been obtained with acetophenone and benzophenone as well as with cyclic ketones like cyclopentanone and cyclohexanone. During attempted synthesis of ketene S,S-dimethylthioacetal (1a) we found that the Horner reaction of 4 takes place with the linear polymer of formaldehyde (paraformaldehyde) but under the same experimental conditions the cyclic trimer of formaldehyde (trioxane) is unreactive.

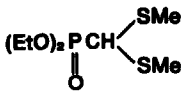


†After appearing our preliminary report on the synthesis of 1 several papers have been published on the same approach.[13]

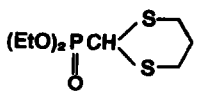
To test the generality of the present method the variously substituted S,S-thioacetals of formylphosphonates (4)[11] listed below were used as the reaction components.



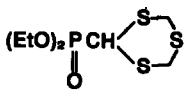
4a



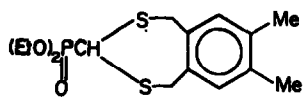
4b



4c



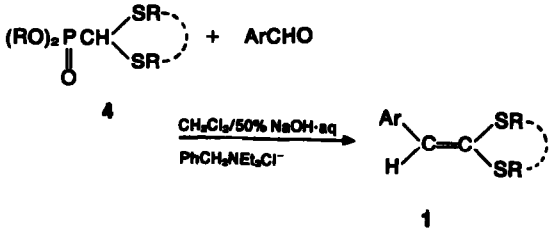
4d



4e

As expected, metalation of 4 takes place readily on treatment with a small excess of n-butyllithium in THF solution at −78°. An alternative procedure is the generation of the sodium derivatives of 4 by means of sodium hydride in DME solution at room temperature. Usually generation of the sodium derivative of 4 was carried out in the presence of carbonyl compounds. In this case, however, the resulting, crude 1 were less pure and the yields were slightly lower.

The experimental procedure can be considerably simplified by applying the phase-transfer technique for the Horner–Wittig reaction. However, as it has been found in our previous studies,[14] the range of carbonyl compounds is limited to aromatic aldehydes. Therefore, the reaction of 4 was carried out with benzaldehyde and *p*-bromobenzaldehyde under the standard two-phase system conditions using benzyltriethylammonium chloride as catalyst.



The experimental results concerning the synthesis of 1 are summarized in Table 1. Table 2 shows physical and spectroscopic data of ketene S,S-thioacetals (1) obtained in our work.

Since we have found that acetophenone reacts with the metallated 4 giving the corresponding 1 in good yield, it was of interest to carry out the Horner–Wittig reaction with other, specially substituted methylaryl ketones such as methyl-*p*-isobutyl ketone (7) and methyl-6-methoxy-naphthyl ketone (8). These ketones are used as starting materials in the industrial, multi-step synthesis of the corresponding 1α-arylpropionic acids 9 and 10 which are known as therapeutic agents[15] having the commercial names Brufen and Naproxen, respectively.

Now it has been found that both ketones can be converted in excellent yields by means of the Horner–Wittig reaction using the lithium derivative of 4a into the corresponding ketene S,S-thioacetals (1m and 1n) which in turn after hydrolysis gave the desired acids 9 and 10 in 74 and 70% yield, respectively. It is noteworthy that there is no need for the isolation of ketene thioacetals 1m and 1n before hydrolysis.

Synthesis of ketene O,S-*thioacetals* (6). The synthetic approaches to ketene O,S-thioacetals (6) are few in number and for the most part of limited applicability.

Until now thioacetals 6 have been prepared by addition of mercapto-anions to acetylenic ethers[16] or alternatively by addition of alkoxy-anions to acetylenic thioethers.[17] Another method involves alkylation of thionoesters bearing at least one α-hydrogen atom.[18,25] Thioacetals 6 can also be prepared by ligand exchange in ketene 0,0-acetals[19] or from thiadiazoles according to the method described by Raap.[20]

Therefore, with the intent of developing a general method for the synthesis of 6 from carbonyl compounds we studied the Horner–Wittig reaction of O,S-thioacetals of formylphosphonates (5)[12] which are requisite reagents for this transformation. However, as it was expected, the replacement of one sulphur atom in 4 by the oxygen atom caused a decrease in the acidity of the methine proton in 5.[21] For this reason, we were not able to generate the lithium derivative of 5 by means of n-butyllithium in THF solution at −78°C or using sodium

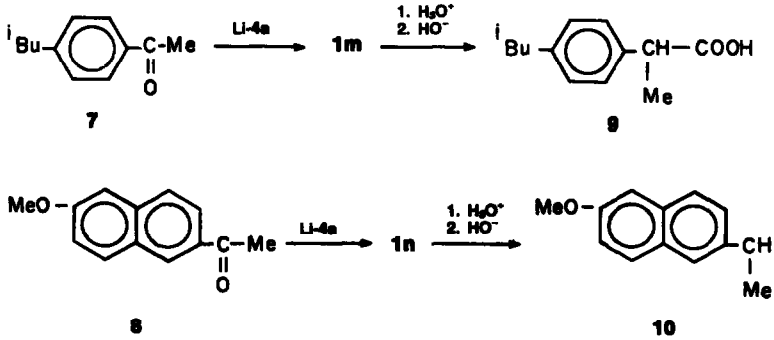
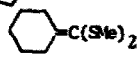
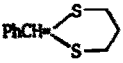
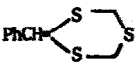
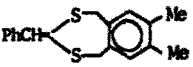
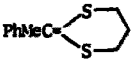
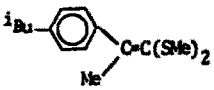
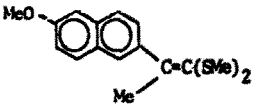
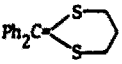
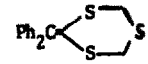
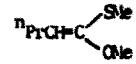
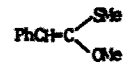
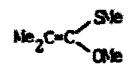


Table 1. Preparation of ketene S,S-thioacetals (1) and ketene O,S-thioacetals (6)

Ketene thioacetal[a]	Starting formylphosphate	Experimental procedure[b]	Yield(%)[c]
1a, $H_2C{=}C(SMe)_2$	4a	A	96
1b, $MeCH{=}C(SMe)_2$	4a	A	92
1c, $Me_2C{=}C(SMe)_2$	4a	A	80
1d, 	4a	A	82
1e, 	4a	A	80
1f, $PhCH{=}C(SMe)_2$	4a	A B C	90 75 88
1g, 	4c	A C	90 92
1h, 	4d	A B C	82 78 80
1i, 	4e	C	75
1j, $pBrPhCH{=}C(SEt)_2$	4b	A C	91 88
1k, $PhMeC{=}C(SMe)_2$	4a	A	81
1l, 	4c	A	86
1m, 	4a	A B	80 68
1n, 	4a	A	78
1o, $Ph_2C{=}C(SMe)_2$	4a	A	78
1p, 	4c	A	70
1q, 	4d	A	72
6a, 	5	D	82[d]
6b, 	5	D	80[e]
6c, 	5	D	79

[a] Satisfactory elemental analyses have been obtained for all compounds.
[b] A-nBuLi/THF, −78°; B-NaH/DME; C-50% NaOH/CH_2Cl_2, 5% TEBA, cool temperature; D-t-BuLi/THF, −78°.
[c] Yield of the analytically pure products.
[d] The product is a mixture of E and Z isomer (45:55).
[e] The product is a mixture of E and Z isomers (46:54).

Table 2. Physical properties, ^{1}H NMR spectral data and elemental analyses of ketene S,S-thioacetals (I)

Compound	n_D^{20} m.p. (solvent)	^{1}H NMR ($CDCl_3$, δ[ppm]; J[Hz]	Formula (Mol.wt)	Elemental Analyses	C	H	S
1a	1.5430	2.25(6H,s,SCH_3); 5.16(2H,s,H_2C=)	$C_4H_8S_2$ (120.24)	calcd.	39.96	6.71	53.33
				found	39.76	6.73	53.39
1b	1.5328	1.98(3H,d,J=7.0,CH_3-CH=); 2.38 and 2.40 (3H,s,SCH_3); 6.15(1H,q,J=7.0,CH_3-CH=)	$C_5H_{10}S_2$ (134.26)	calcd.	44.73	7.51	47.76
				found	44.70	7.40	47.61
1c	1.5225	2.02(6H,s,CH_3-C=); 2.20(6H,s,SCH_3)	$C_6H_{12}S_2$ (148.29)	calcd.	48.60	8.16	43.24
				found	48.51	8.02	43.11
1d	1.5626	1.70 and 2.50(8H,m,-$(CH_2)_4$-);2.22(6H,s,SCH_3)	$C_8H_{12}S_2$ (174.33)	calcd.	55.12	8.09	36.79
				found.	54.92	8.11	36.51
1e	1.5597	1.55 and 2.60(10H,m,-$(CH_2)_5$-);2.22(6H,s,SCH_3)	$C_9H_{10}S_2$ (188.35)	calcd.	57.39	8.56	34.05
				found	57.11	8.44	34.22
1f	1.5648	2.32 and 2.38(3H,s,SCH_3); 6.80(1H,s, C_6H_5-CH=); 7.25(5H,m,C_6H_5)	$C_{10}H_{12}S_2$ (196.34)	calcd.	61.18	6.16	32.66
				found	61.00	6.33	32.72
1g	1.6799	2.03(2H,m,α-CH_2); 2.83(4H,m,β-CH_2); 6.79 (1H,s,C_6H_5-CH=); 7.25(5H,m,C_6H_5)	$C_{11}H_{12}S_2$ (208.35)	calcd.	63.41	5.81	30.78
				found	63.45	5.60	30.91
1h	1.7005	4.05 and 4.12(2H,s,S-CH_2-S); 6.95(1H,s, C_6H_5-CH=); 7.35(5H,m,C_6H_5)	$C_{10}H_{10}S_3$ (226.38)	calcd.	53.06	4.45	42.49
				found	53.30	4.60	42.62
1i	175-176° (benzene)	2.20(6H,s,CH_3-C_6H_2); 4.18(4H,s,S-CH_2-); 6.90 (2H,s,C_6H_2); 7.10(1H,s,C_6H_5-CH=); 7.35(5H,m, C_6H_5)	$C_{18}H_{18}S_2$ (298.47)	calcd.	72.44	6.08	21.48
				found	72.27	6.04	21.46
1j	1.6422	1.20 and 1.27(3H,t,J=7.3,CH_3-CH_2); 2.81(4H, q,J=7.3,CH_3-CH_2); 6.86(1H,s,C_6H_5-CH=); 7.43 (4H,s,C_6H_4)	$C_{12}H_{15}BrS_2$ (303,29)	calcd.	47.52	4.99	21.14
				found	47.56	5.07	21.17
1k	1.6054	2.10(3H,s,CH_3-C=); 2.32(6H,s,SCH_3); 7.20 (5H,m,C_6H_5)	$C_{11}H_{14}S_2$ (210.36)	calcd.	62.81	6.71	30.48
				found	62.60	6.60	30.64
1l	1.6440	2.05(2H,m,α-CH_2); 2.18(3H,s,CH_3-C=); 2.85 (4H,m,β-CH_2); 7.25(5H,m,C_6H_5)	$C_{12}H_{14}S_2$ (222.37)	calcd.	64.82	6.35	28.84
				found	64.71	6.40	28.66
1m	1.5768	0.91(6H,d,J=6.4,$(CH_3)_2$-CH); 1.88(1H,m, $(CH_3)_2$-CH); 2.11(3H,s,CH_3-C=); 2.32(6H,s, SCH_3); 2.46(2H,d,J=6.4, CH-CH_2) 7.11(4H, s,C_6H_4)	$C_{15}H_{22}S_2$ (266.47)	calcd.	67.61	8.32	24.07
				found	67.50	8.25	23.91
1n	61-62° (benzene)	2.12(3H,s,CH_3-C=); 2.36 and 2.40(3H,s,SCH_3); 3.89(3H,s,CH_3-O); 7.02-7.80(6H,m,naphthyl)	$C_{16}H_{18}OS_2$ (290.45)	calcd.	66.17	6.25	22.08
				found	65.92	6.10	21.81
1o	83-84° (benzene)	2.20(6H,s,SCH_3); 7.20(10H,m,C_6H_5)	$C_{16}H_{16}S_2$ (272.43)	calcd.	70.54	5.92	23.54
				found	70.30	5.80	23.40
1p	133-134° (benzene)	2.08(2H,m,α-CH_2); 2.93(4H,m,β-CH_2); 7.25 (10H,m,C_6H_5)	$C_{17}H_{16}S_2$ (284.45)	calcd.	71.78	5.67	22.54
				found	71.90	5.80	22.71
1r	136-137° (benzene)	4.05(4H,s,S-CH_2-S); 7.25(10H,m,C_6H_5)	$C_{16}H_{14}S_3$ (302.48)	calcd.	63.53	4.67	31.80
				found	63.29	4.70	32.02

hydride in boiling DME. Furthermore, the Horner–Wittig reaction was observed not to occur when the mixture of 5 and n-butyllithium was treated with carbonyl compound at room temperature. We found that metalation of 5 could only be achieved when t-butyllithium was used as a base. The metallated phosphonates 5 reacted easily with aldehydes and ketones giving ketene O,S-thioacetals (6) in high yields (Table 1). This approach failed, however, in the case of benzophenone.

Crude thioacetals 6 were purified by distillation.

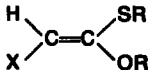
5

6a: R^1 = *n*-Pr R^2 = H
6b: R^1 = Ph R^2 = H
6c: R^1 = Me R^2 = Me

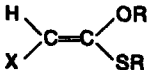
Column chromatography on silica gel was found unsuitable as a method for purification of **6** since their hydrolysis was observed to occur.[22] It resulted in the formation of methyl phenylacetate and the corresponding thiol ester in the ratio 84:16.

If aldehydes were used for the Horner–Wittig reaction with **5**, ketene O,S-thioacetals **6a** and **6b** were obtained as mixtures of E and Z geometrical isomers in a nearly 1:1 ratio. The isomeric compositions were determined from ^{1}H NMR spectra of the crude products by integrating non-equivalent signals of the methoxy- and thiomethoxy-group as well as of the olefinic proton. The latter appears in the spectrum of **6a** and **6b** as a triplet and singlet, respectively.

Our attempt to assign the configuration around the double bond in isomers of **6a** by means of the additive increments method using Pascual–Simon's table[23] was rather unsuccessful since the calculated values of chemical shift of the olefinic proton differ markedly from those experimentally found. Furthermore, limited NMR data on ketene O,S-thioacetals precluded also the application of the parent compound method proposed by Tobey.[24] In this situation, assuming, however, the general applicability of the additive increments method, one can tentatively demonstrate (see below) that the vinylic proton in the E isomers of ketene O,S-thioacetals should absorb at higher field than that in the Z isomers.



E



Z

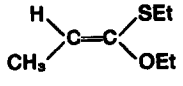
Calculations for R = CH_3, X = alkyl, aryl†

$\delta_H = 5.25 + Z_X + Z_{RS} + Z_{RO_{trans}}$ $\quad$ $\delta_H = 5.25 + Z_X + Z_{RS_{trans}} - Z_{RO_{cis}}$

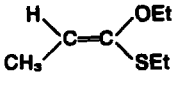
$\delta_H = 5.25 + Z_X - 0.29 - 1.21$ $\quad$ $\delta_H = 5.25 + Z_X - 0.13 - 1.07$

$\delta_H = 3.75 + Z_X$ $\quad$ $\delta_H = 4.05 + Z_X$

This reasoning is in agreement with the configurational assignments to the geometrical isomers of methylketene O,S-diethylthioacetal given by Brandsma.[25]



E, $\delta_{H_{exp}} = 4.91$

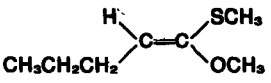


Z, $\delta_{H_{exp}} = 5.10$

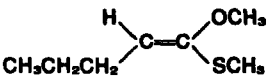
Therefore, in view of the above results it seems reasonable to propose the following assignment of configuration E and Z to the respective isomers of ketene O,S-thioacetals **6a** and **6b** obtained in our work.

Finally, it is interesting to note that the initially formed isomeric mixture of E-**6b** and Z-**6b** undergoes isomerisation to the more stable isomer E-**6b** when it is kept in chloroform solution for *ca.* 3 weeks. This observation indicates that the Horner–Wittig reaction of **5** is not stereoselective and the ratio of isomeric ketene O,S-thioacetals is most probably determined by kinetic factors.

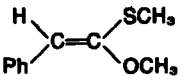
An attempt at ketene O,O-*acetals* (**11**) *synthesis.* Positive results on the conversion of carbonyl compounds



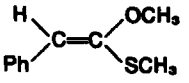
E, $\delta_{H_{exp}} = 4.72$



Z, $\delta_{H_{exp}} = 4.98$

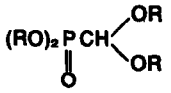


E, $\delta_{H_{exp}} = 5.78$

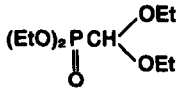


Z, $\delta_{H_{exp}} = 5.84$

into ketene S,S- and O,S-thioacetals with the aid of the Horner–Wittig reaction prompted us to extend this approach to the synthesis of ketene O,O-acetals (**11**). This was possible since the starting O,O-acetals of formylphosphonates (**12**) became also readily available.[26]



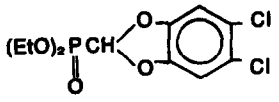
12



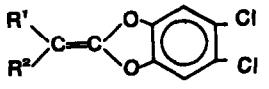
12a

Preliminary experiments showed, however, that O,O-diethylacetal of O,O-diethyl formylphosphonate (**12a**) does not undergo the metalation even if t-butyllithium is used as a base. This was not surprising in view of the commonly-known fact that the alkoxy group is much worse than the alkylthio group in stabilising the α-carbanionic centre as well as in the light of the recent results[27] on the deprotonation of benzo-1,3-oxathiolane and benzo-1,3-dioxolane. Whereas metalation of the former compound occurred at the methylene C atom, the latter was metalated in the aromatic ring.

The only limited success in the synthesis of **11** was achieved when the cyclic acetal **12b** was employed as the phosphonate component and the PO-olefination reaction was carried out in dioxane at 80–90°C using sodium hydride as a base.



12b



11a: R' = R² = Et
11b: R' = R² = Ph

Thus, from diethyl ketone and benzophenone the corresponding ketene O,O-acetals **11a** and **11b** were obtained in 19 and 32% yield, respectively.

Application of ^{31}*P NMR spectroscopy to elucidation of the Horner–Wittig reaction course.* In order to obtain additional informations on the formation of the lithium derivatives of phosphonates **4**, **5** and **12** as well as to gain an insight into the structure of the Horner–Wittig reaction intermediates[28] we monitored both the metalation process and the reaction with carbonyl compound by the low temperature ^{31}P NMR spectra using Fourier trans-

†The values of the additive increments for alkyl and aryl substituents in the *gem* position to the olefinic proton are always positive.

form technique with proton noise decoupling. Such approach was successful in the case of the typical Wittig[29] reaction and led to an experimental confirmation that the pentavalent phosphorus species (oxaphosphetanes) are relatively stable reaction intermediates.

First we investigated the Horner–Wittig reaction of the S,S-dimethylthioacetal of O,O-dimethyl formylphosphonate (**4a**) with benzaldehyde. Thus, a solution of **4a** in THF was treated at −70° with an equimolar amount of n-butyllithium. After short time the signal at δ_{31P} 20.9 ppm characteristic of **4a** disappeared in the spectrum and a single signal at δ_{31P} 46.3 ppm was observed which undoubtedly corresponds to the metalation product.† Addition of benzaldehyde at −70° caused immediate disappearance of the δ_{31P} 46.3 signal and appearance of a signal at δ_{31P} −2.1 ppm. The latter is due to the lithium salt of O,O-dimethylphosphoric acid.

A similar picture was observed with the O,S-dimethylthioacetal of O,O-dimethyl formylphosphonate (**5**). However, in this case the lithium derivative of **5** was completely formed on treatment with an equimolar amount of t-butyllithium after 1 h at −70° as evidenced by the appearance of the signal at δ_{31P} 42.0 ppm at the expense of the signal at δ_{31P} 17.0 ppm of the substrate **5**. It is interesting to note that the signal of the metallated **5** did not appear in the spectrum when n-butyllithium was used as a base. Upon adding benzaldehyde to the metallated **5** at −70° the signal at δ_{31P} −2.1 ppm immediately appeared indicating completion of the reaction.

As it could be expected, in the ^{31}P NMR spectra of the mixtures of phosphonates **12a** and **12b** with either n-butyllithium or t-butyllithium we did not observe the appropriate signals of the lithium derivatives.

For comparison purposes the Horner–Wittig reaction of O,O-diethyl methylphosphonate with benzaldehyde was monitored by the low temperature ^{31}P NMR spectra. We found that O,O-diethyl methyllithium phosphonate, δ_{31P} 60.6 ppm, is very easily formed from the starting phosphonate, δ_{31P} 31.25 ppm, at −70° (*ca.* 15 min) on treatment with n-butyllithium in THF solution and after adding benzaldehyde it affords the corresponding addition product (δ_{31P} 35.4 and 35.9 ppm) which is stable at room temperature.[31]

The results reported above demonstrate not only the usefulness of ^{31}P NMR spectroscopy in the estimation of the exact conditions of the phosphonate carbanions generation but also allow to draw some conclusions concerning the mechanism of the Horner–Wittig reaction of **4** and **5**. First of all, the fact that the signals corresponding to the expected products (A) formed by addition of the metallated **4** and **5** to benzaldehyde were not observed in the ^{31}P NMR spectra even at −70° indicates that they are very unstable reaction intermediates. For the same reason one can conclude that the decomposition of adducts (A) should be faster than their formation.

Further studies on the application of ^{31}P NMR spectroscopy to elucidate the Horner–Wittig reaction mechanism are under way.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Solvents and commercial reagents were distilled and dried by conventional methods before use; THF and DME were distilled from LAH. ^{1}H NMR spectra were recorded at 60 MHz with a R 12 B Perkin–Elmer spectrometer and at 80 MHz with a Tesla BS-487C spectrometer using TMS as an internal standard. ^{31}P NMR spectra were obtained on a Jeol-JNM-FX60 Fourier transform spectrometer at 24.3 MHz with 85% H_3PO_4 as external standard. In this paper the new convention of positive ^{31}P NMR signals to low field from H_3PO_4 is used. Column chromatography was done on silica gel Merck 100–200 mesh.

General procedures for synthesis of ketene S,S-*thioacetals* (**1**)

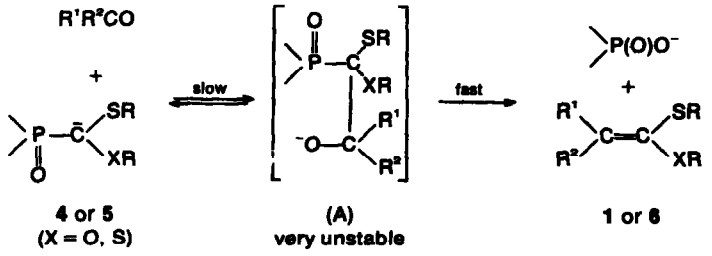
Procedure A. To a soln of S,S-thioacetal of **4** (0.01 mol) in 15 ml THF a soln of n-BuLi (0.011 mol) in hexane was added at −78° under argon atmosphere. The mixture was stirred at −78° for 0.25 hr. Then a soln of carbonyl compound (0.01 mol) in 10 ml THF was added dropwise at −78° and the mixture was stirred for 15 min at this temp. The mixture was warmed slowly to room temp. After removal of the solvents the residue was dissolved in $CHCl_3$ (15 ml). The $CHCl_3$ soln was washed with NH_4Claq, then with water, dried and evaporated to afford crude **1**. It was purified by distillation, crystallization or column chromatography.

Procedure B. NaH (0.48 g, 55% dispersion in mineral oil, 0.011 mol) was washed under argon three times with light petroleum ether and then added to a soln of **4** (0.01 mol) and carbonyl compound (0.01 mol) in 25 ml DME. With benzaldehyde the reaction was complete after 1 hr at room temp.; in the case of ketones the mixture was heated at 60° for 1 hr. After evaporation of DME the residue was dissolved in $CHCl_3$ (50 ml). The $CHCl_3$ layer was washed with NH_4Claq, then with water, dried and evaporated to afford the crude **1** which was further purified by suitable methods.

Procedure C. A soln of **4** (0.01 mol) and aromatic aldehyde (0.01 mol) in CH_2Cl_2 (5 ml) was added to the heterogeneous mixture of 50% NaOHaq (10 ml) containing triethylbenzylammonium chloride (0.1 g) and CH_2Cl_2 (5 ml). The mixture was stirred for 0.5 hr at room temp. and additional 10 ml of CH_2Cl_2 were added. The organic layer was washed with an NH_4Claq, dried and evaporated to yield the crude **1**.

α-p-Isobutylphenyl propionic acid (**9**). A soln of **1m** (1.33 g, 0.005 mol) in 10 ml EtOH and p-toluenesulphonic acid (0.1 g) was stirred for 2 hr at room temp. and then refluxed for 0.5 hr. EtOH was evaporated and the residue was dissolved in 10 ml $CHCl_3$. The $CHCl_3$ soln was washed with $NaHCO_3$aq and concentrated to give the residue which was treated with KOH (2.8 g, 0.05 mol) in 15 ml 95% EtOH. The resulting mixture was refluxed for 24 hr. After removal of EtOH the residue was dissolved in water and acidified with conc. HCl. The water phase was extracted with

†To the best of our knowledge the only work dealing with the low temperature ^{1}H and ^{13}C NMR studies of the lithium derivatives of phosphonoacetates is that published by Bottin-Strzalko, Seydon-Penne and Simonnin.[30]



$CHCl_3$ and the organic phase was dried over $MgSO_4$. Removal of $CHCl_3$ afforded crude **9** which was purified by crystallization from acetone–hexane (1:1); 0.76 g (74%), m.p. 74–75°; ^1H NMR (CCl_4) δ(ppm): 0.91 (6H, d, J = 6.4 Hz, $(CH_3)_2CH$), 1.46 (3H, d, J = 6.4 Hz, CH_3–CH), 1.84 (1H, m, $(CH_3)_2CH$), 2.42 (2H, d, J = 6.4 Hz, CH–CH_2), 3.62 (1H, q, J = 6.4 Hz, CH_3–CH), 7.08 (4H, m, C_6H_4), 12.1 (1H, s, COOH).

α-[2-(6-Methoxy)naphthyl]propionic acid (**10**). According to the procedure described above **1a** (1.45 g, 0.005 mol) was converted into **10** (0.80 g), in 70% yield; m.p. 152–154° (lit.[15] m.p. 152–154°); ^1H NMR ($CDCl_3$) δ(ppm): 1.57 (3H, d, J = 6.8 Hz, CH_3–CH), 3.84 (1H, q, J = 6.8 Hz, CH_3–CH), 3.89 (3H, s, CH_3O), 7.07–7.78 (6H, m, $C_{10}H_6$), 10.42 (1H, s, COOH).

Synthesis of ketene O,S-thioacetals (**6**)

1-Methoxy-1-thiomethoxy-pentene-1 (**6a**). To a soln of **5** (1.0 g, 0.005 mol) in THF (10 ml) a soln of 0.8 M t-BuLi (6.5 ml, 0.0052 mol) in n-pentane was added at −78° under argon atmosphere. The mixture was stirred at this temp. for 1 hr. Then a soln of n-butyraldehyde (0.36 g, 0.005 mol) in THF (5 ml) was added at −78°. The mixture was warmed to room temp. and stirred for some time. After addition of water (20 ml) the organic layer was separated and the water soln was extracted with $CHCl_3$. The combined organic solns were washed with water, dried and evaporated to give crude **6a** which was purified by distillation: 0.60 g (82%), b.p. 82–85°/50 mmHg, n_D^{20} 1.4580 (Found: C, 57.28; H, 9.60; S, 21.74. Calc. for $C_7H_{14}OS$ (146.25): C, 57.49; H, 9.65; S, 21.92%). Analysis of the ^1H NMR spectrum of crude **6a** permitted the determination of the E:Z ratio as 45:55. The spectrum showed, in addition to the aliphatic multiplets at 0.7–1.5 ppm (5H, CH_3–CH_2–CH_2–CH=) and the O-methyl protons as a singlet at 3.56 ppm, two singlets at 2.10 and 2.14 ppm (CH_3S) and two triplets at 4.72 and 4.98 ppm (J = 7.4 Hz) for the E and Z isomer, respectively.

1-Methoxy-1-thiomethoxy-2-phenyl-ethene (**6b**). The reaction of **5** (1.0 g, 0.005 mol) with benzaldehyde (0.53 g, 0.005 mol) performed in the same manner as described above gave crude **6b** which was purified by distillation; 0.72 g (80%), b.p. 80°/0.3 mmHg, n_D^{20} 1.5960 (lit. $^{22}n_D^{20}$ 1.5955). The product composition was determined by ^1H NMR to be E:Z = 46:54. E-**6b**: 2.14 (3H, s, CH_3S), 3.61 (3H, s, CH_3O), 5.78 (1H, s, Ph–CH=), 7.0–7.6 (5H, m, C_6H_5); Z-**6b**: 2.18 (3H, s, CH_3S), 3.66 (3H, s, CH_3O), 5.84 (1H, s, Ph–CH=), 7.0–7.6 (5H, m, C_6H_5).

1-Methoxy-1-thiomethoxy-2-methyl-propene-1 (**6c**). From **5** (1.0 g, 0.005 mol) and acetone (0.29 g, 0.005 mol) according to the procedure described for **6a** **6c** was obtained; 0.52 g (79%), b.p. 84°/70 mmHg, n_D^{20} 1.4640; ^1H NMR ($CDCl_3$) δ (ppm): 1.72 and 1.80 (6H, two s, CH_3–C=), 2.10 (3H, s, CH_3S), 3.52 (3H, s, CH_3O) (Found: C, 54.23; H, 8.91; S, 24.30. Calc. for $C_6H_{12}OS$ (132.23): C, 54.50; H, 9.15; S, 24.25%).

General procedure for synthesis of ketene O,O-acetals (**11**)

A mixture of **12b** (3.27 g, 0.01 mol) and NaH (0.48 g, 55% dispersion in mineral oil, 0.011 mol) in abs dioxane was heated at 60° for 0.5 hr and then treated with ketone (0.01 mol). The resulting mixture was heated at 80–90° for 2 hr and after cooling it was poured into water (50 ml). The water phase was extracted with ether (4 × 25 ml). The organic soln was dried over Na_2SO_4 and evaporated. The residue was distilled or crystallized to give pure **11**.

According to this procedure from diethylketone acetal, **11a** was obtained in 19% yield; b.p. 100–104°/0.01 mmHg, m.p. 39–40° (from MeOH); ^1H NMR ($CDCl_3$) δ (ppm): 1.03 (6H, t, CH_3–CH_2–), 2.12 (4H, q, CH_3–CH_2–), 6.98 (2H, s, aromatic) (Found: C, 55.40; H, 4.77. Calc. for $C_{12}H_{12}Cl_2O_2$ (259.13): C, 55.62; H, 4.67%).

Benzophenone and **12b** afforded acetal **11b** in 32% yield; m.p. 117–118° (from petroleum ether); ^1H NMR ($CDCl_3$) δ (ppm): 7.12 (2H, s, aromatic), 7.27 (10H, s, aromatic) (Found: C, 67.46; H, 3.32; Cl, 20.12. Calc. for $C_{20}H_{12}Cl_2O_2$ (355.22): C, 67.62; H, 3.41; Cl, 19.97%).

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