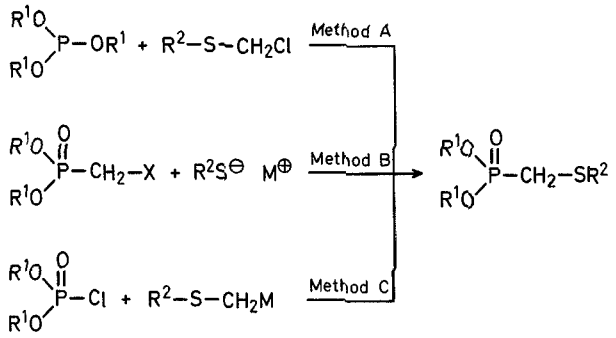
# Sulphenylation of Phosphonates. A Facile Synthesis of α-Phosphoryl Sulphides and *S,S*-Acetals of Oxomethanephosphonates[1]

Marian MIKOŁAJCZYK*, Piotr BAŁCZEWSKI, Sławomir GRZEJSZCZAK

Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Department of Organic Sulphur Compounds, 90-362 Łódź, Boczna 5, Poland

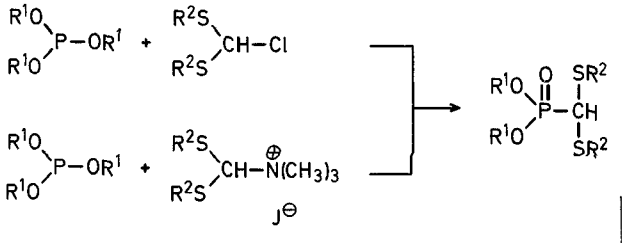
The application of α-phosphoryl sulphides[2,3,4] and *S,S*-acetals of oxomethanephosphonates[5] in organic synthesis is a subject of some current interest. They can be used as reagents in the Wittig-Horner synthesis of vinyl sulphides and ketene *S,S*-acetals which can be further transformed into various carbonyl systems.

Thus far α-phosphoryl sulphides have been obtained by the following methods: (A) Arbuzov reaction of trialkyl phosphites with α-halo sulphides[6,7], (B) condensation of dialkyl chloromethanephosphonates with alkyl or aryl mercaptides[8,9], and (C) treatment of dialkyl phosphorochloridates with metallated alkyl aryl sulphides[10] (Scheme **A**).




Scheme **A**

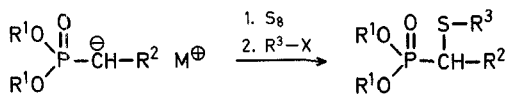
*S,S*-Acetals of oxomethanephosphonates have been synthesised by condensation of trialkyl phosphites with chlorodithioacetals or the corresponding trialkylammonium iodide as shown below[11] (Scheme **B**).



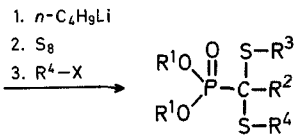
*Scheme* **B**

In the course of our studies on α-phosphoryl substituted organo-sulphur compounds, we have recently developed a new and general synthesis of **1** and **2** which involves addition of elemental sulphur to the metallated phosphonates and subsequent alkylation[4].

In an extension of this work we found now that metallated dialkyl phosphonates may be sulphenylated directly by means of dialkyl or diaryl disulphides[12] to afford substituted or unsubstituted α-phosphoryl sulphides **1** and *S,S*-acetals of oxomethanephosphonates **2** in high yields[13].



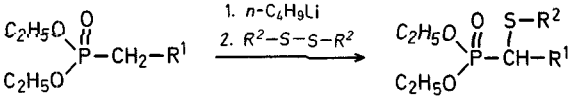
**1**



**2**

$R^2$ = H, alkyl, aryl

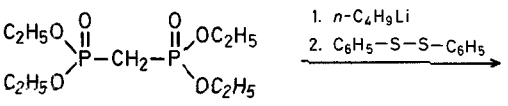
Thus, diethyl ethanephosphonate (**3**) and diethyl phenylmethanephosphonate (**4**) were transformed into the corresponding α-phosphoryl sulphides **5a-d** isolated in 60 to 90% yields.



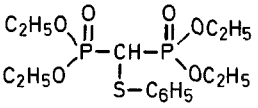
**3** $R^1$ = $CH_3$
**4** $R^1$ = $C_6H_5$

**5a** $R^1$ = $CH_3$, $R^2$ = $C_6H_5$
**5b** $R^1$ = $CH_3$, $R^2$ = 4-$H_3C$-$C_6H_5$
**5c** $R^1$ = $C_6H_5$, $R^2$ = $CH_3$
**5d** $R^1$ = $C_6H_5$, $R^2$ = $C_6H_5$

The metallated derivative of the bis-phosphonate **6** underwent facile sulphenylation with diphenyl disulphide giving **7** in 85% yield. However, our attempts to sulphenylate **6** with dimethyl disulphide failed.

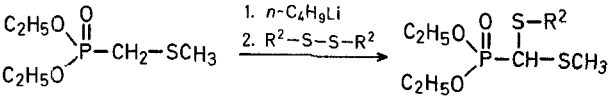


**6**



**7**

Similarly, diethyl methylthiomethanephosphonate (**8**) gave, on treatment with *n*-butyllithium and subsequently with dialkyl of diaryl disulphides, *S,S*-acetals of diethyloxomethanephosphonate **9a-d** in yields of 75–85%.



**8**

**9a** $R^2$ = $CH_3$
**9b** $R^2$ = $C_2H_5$
**9c** $R^2$ = $n$-$C_4H_9$
**9d** $R^2$ = $C_6H_5$

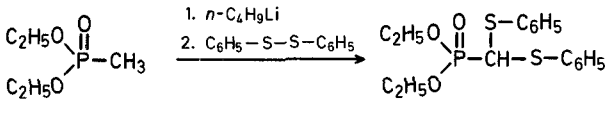
In this connection it is interesting to point out that it is possible to convert, in one-step, diethyl methanephosphonate (**10**) into the *S,S*-diphenylacetal of diethyl oxomethanephosphonate (**11**) using at least two equivalents of diphenyl disulphide.

0039-7881/80/0232-0127 $ 03.00

**Table 1.** Sulphenylated Phosphonates **5**, **7**, **9**, and **11**

| Substrate | Product | Yield[a] [%] | $n_D^{20}$ | Molecular formula[b] | $^1$H-N.M.R. ($CCl_4$) δ [ppm] | $^{31}$P-N.M.R. ($CHCl_3$) δ [ppm][c] |
|---|---|---|---|---|---|---|
| **3** | **5a** | 84 | 1.5189 | $C_{12}H_{19}O_3PS$ (274.3) | 1.31 (t, 6H, $OCH_2CH_3$, $J_{HH}$ = 7.0 Hz); 1.48 (dd, 3H, $PCHCH_3$, $J_{HH}$ = 7.0 Hz, $J_{HP}$ = 16.6 Hz); 3.18 (dq, 1H, PCH, $J_{HH}$ = 7.0 Hz, $J_{HP}$ = 15.2 Hz); 4.08 (dq, 4H, $OCH_2CH_3$, $J_{HP}$ = 7.2 Hz); 7.04–7.62 (m, 5 $H_{arom}$) | 25.6 |
| **3** | **5b** | 75 | 1.5170 | $C_{13}H_{21}O_3PS$ (288.4) | 1.29 (t, 6H, $OCH_2CH_3$, $J_{HH}$ = 7.0 Hz); 1.35 (dd, 3H, $PCHCH_3$, $J_{HH}$ = 7.5 Hz, $J_{HP}$ = 17.0 Hz); 2.29 (s, 3H, $H_3C-C_6H_4$); 3.05 (dq, 1H, PCH, $J_{HH}$ = 7.9 Hz, $J_{HP}$ = 16.2 Hz); 4.07 (dq, 4H, $OCH_2CH_3$, $J_{HP}$ = 7.2 Hz); 6.84–7.52 (m, 4 $H_{arom}$) | 25.8 |
| **4** | **5c** | 80 | 1.5288 | $C_{12}H_{19}O_3PS$ (274.3) | 1.09 + 1.28 (2t, 6H, $OCH_2CH_3$, $J_{HH}$ = 7.0 Hz); 2.02 (s, 3H, $H_3CS$); 3.86 (d, 1H, PCH, $J_{HP}$ = 20.3 Hz); 4.09 (dq, 4H, $OCH_2CH_3$, $J_{HP}$ = 7.2 Hz); 7.03–7.72 (m, 5 $H_{arom}$) | 21.1 |
| **4** | **5d** | 83 | 1.5654 | $C_{17}H_{21}O_3PS$ (336.4) | 1.06 + 1.28 (2t, 6H, $OCH_2CH_3$, $J_{HH}$ = 6.7 Hz); 3.9 (m, 4H, $OCH_2CH_3$); 4.22 (d, 1H, PCH, $J_{HP}$ = 21.3 Hz); 6.95–7.54 (m, 10 $H_{arom}$) | 20.6 |
| **6** | **7** | 85 | 1.5100 | $C_{15}H_{26}O_6P_2S$ (397.0) | 1.22 (t, 12H, $OCH_2CH_3$, $J_{HH}$ = 8.2 Hz); 3.34 (t, 1H, PCH, $J_{HP}$ = 24.0 Hz); 4.10 (dq, 8H, $OCH_2CH_3$, $J_{HP}$ = 8.2 Hz); 7.0–7.6 (m, 5 $H_{arom}$) | 16.9 |
| **8** | **9a** | 60 | 1.5196 | $C_7H_{17}O_3PS_2$ (244.3) | 1.32 (t, 6H, $OCH_2CH_3$, $J_{HH}$ = 7.3 Hz); 2.22 (s, 3H, $SCH_3$); 3.69 (d, 1H, PCH, $J_{HP}$ = 18.0 Hz); 4.18 (dq, 4H, $OCH_2CH_3$, $J_{HP}$ 8.2 Hz) | 20.0 |
| **8** | **9b** | 70 | 1.4950 | $C_8H_{19}O_3PS_2$ (258.3) | 1.22 (t, 6H, $SCH_2CH_3$, $J_{HH}$ = 7.3 Hz); 1.25 (t, 6H, $OCH_2CH_3$, $J_{HH}$ = 7.9 Hz); 2.25 (s, 3H, $SCH_3$); 2.52 (q, 4H, $SCH_2CH_3$); 3.58 (d, 1H, PCH, $J_{HP}$ = 17.7 Hz); 4.10 (dq, 4H, $OCH_2CH_3$, $J_{HP}$ = 8.1 Hz) | 18.5 |
| **8** | **9c** | 72 | 1.4913 | $C_{10}H_{23}O_3PS_2$ (286.4) | 0.8–1.9 (m, 13H, $OCH_2CH_3$ + $SCH_2-C_3H_7$-*n*); 2.22 (s, 3H); 2.72 (m, $SCH_2-C_3H_7$-*n*); 3.66 (d, 1H, PCH, $J_{HP}$ = 18.0 Hz); 4.11 (dq, 4H, $OCH_2CH_3$, $J_{HP}$ = 7.5 Hz) | 19.3 |
| **8** | **9d** | 90 | 1.5526 | $C_{12}H_{19}O_3PS_2$ (306.4) | 1.31 (t, 6H, $OCH_2CH_3$, $J_{HH}$ = 7.3 Hz); 2.30 (s, 3H, $SCH_3$); 3.98 (d, 1H, PCH, $J_{HP}$ = 17.4 Hz); 4.15 (dq, 4H, $OCH_2CH_3$, $J_{HP}$ = 7.0 Hz); 7.09–7.67 (m, 5 $H_{arom}$) | 18.4 |
| **10** | **11** | 84 | 1.5819 | $C_{12}H_{21}O_3PS_2$ (368.5) | 1.30 (t, 6H, $OCH_2CH_3$, $J_{HH}$ = 7.3 Hz); 4.26 (dq, 4H, $OCH_2CH_3$, $J_{HP}$ = 7.3 Hz); 4.42 (d, 1H, PCH, $J_{HP}$ = 14.5 Hz); 7.06–7.78 (m, 10 $H_{arom}$) | 18.2 |

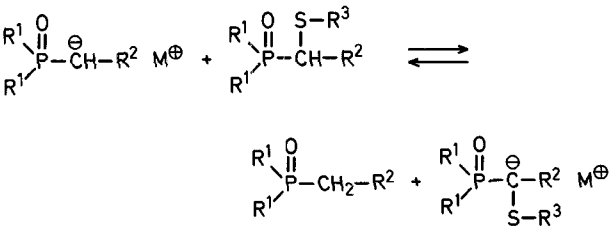
[a] Yield of analytically pure products.
[b] All products gave satisfactory microanalyses (C ±0.29, H ±0.30, P ±0.32).
[c] Signals to lower field than $H_3PO_4$.




**10** **11**

In all experiments shown above α-metallation of the phosphonates was carried out using *n*-butyllithium at −78 °C in tetrahydrofuran. Then, the metallated phosphonates were quenched with a solution of the appropriate disulphide in tetrahydrofuran. After the usual work-up, the α-phosphoryl sulphides **5** and **7** and dithioacetals **9** and **11** were purified by column chromatography on silica gel. The results obtained are summarized in Table 1.

The generation of the metallated phosphonates and their sulphenylation reactions were monitored by low temperature $^{31}$P-N.M.R. spectrometry using the Fourier transform technique with proton noise decoupling. The phosphorus chemical shifts of the starting phosphonates and the sulphenylation products as well as their lithio-derivatives are listed in Table 2. The N.M.R. experiments clearly revealed that the sulphenylation of the metallated phosphonates, as in the case of ketones or ester enolates, is reversible[14]. This is a consequence of the greater acidity of the initially formed sulphenylation product as compared with the starting phosphonate.



$R^2$ = H, alkyl, aryl, S–$R^4$

In a typical example, when a tetrahydrofuran solution of *O,O*-diethyl methylthiomethanephosphonate (**8**) in an N.M.R. tube was treated with *n*-butyllithium at −78 °C the signal at $\delta_P$ = 23.4 ppm characteristic of **8** disappeared in the spectrum and a signal at $\delta_P$ = 49.2 ppm of the lithio derivative of **8** was observed. Addition of dimethyl disulphide caused its immediate disappearence and appearence of two signals at $\delta_P$ = 42.7 and 23.4 ppm. The former is due to the lithio derivative of the sulphenylation product **9a** while the latter corresponds to the starting phosphonate **8**. Addition of

the second portion of *n*-butyllithium and then dimethyl disulphide results in the full conversion of **8** into the α-lithium derivative of **9a**. A similar pattern was observed with other phosphonates.

Based on the N.M.R. data and the results of experiments performed on a preparative scale, the most favourable reagents ratio and the order of their addition were chosen in order to obtain the optimum yield of the desired products.

Solvents and commercial reagents were distilled and dried by conventional methods before use. Reagent grade tetrahydrofuran was distilled from lithium aluminium hydride. $^1$H-N.M.R. spectra were recorded at 60 MHz with a R12B Perkin-Elmer spectrometer. $^{31}$P-N.M.R. spectra were obtained on a Jeol JNM-C-60H1 spectrometer with external $H_3PO_4$ as the standard. Column chromatography was done on Merck silica gel, 100–200 mesh using benzene/acetone (100:1) as the eluent.

**Diethyl 1-Thiophenylethanephosphonate (5a):**
To a stirred solution of phosphonate **3** (1.66 g, 0.01 mol) in tetrahydrofuran (25 ml), a solution of *n*-butyllithium (0.011 mol) in hexane is added dropwise under nitrogen at −78 °C. The solution is stirred at −78 °C for 10 min and then a solution of diphenyl disulphide (2.18 g, 0.01 mol) in tetrahydrofuran (10 ml) is added. After 30 min of stirring, the reaction mixture is treated with a solution of *n*-butyllithium (0.011 mol) and, after an additional 10 min, with a solution of diphenyl disulphide (1.09 g, 0.005 mol) in tetrahydrofuran (5 ml). The mixture is stirred for 30 min and neutralised by 10% aqueous hydrochloric acid. After evaporation of the solvents, the aqueous layer is extracted with chloroform (3 × 25 ml). The chloroform layer is washed with water, dried with anhydrous magnesium sulphate, and evaporated to give a crude product which was chromatographed to afford analytically pure **5a**; yield: 2.3 g (84%).

According to this procedure α-phosphoryl sulphides **5** and **9d** were prepared.

**Bis[diethylphosphoryl]phenylthiomethane (7):**
To a stirred solution of phosphonate **6** (2.88 g, 0.01 mol) in tetrahydrofuran (20 ml), a solution of *n*-butyllithium (0.022 mol) in hexane is added dropwise under nitrogen at −78 °C. The solution is stirred at −78 °C for 5 min and then a solution of diphenyl disulphide (2.18 g, 0.01 mol) in tetrahydrofuran (10 ml) is added. The mixture is warmed slowly to room temperature and quenched with aqueous ammonium chloride solution. After evaporation of the solvents, the aqueous layer is extracted with chloroform (3 × 25 ml). The chloroform solution is dried and evaporated to give a crude product, which is chromatographed to afford analytically pure **7**; yield: 3.37 g (85%).

**Table 2.** $^{31}$P-N.M.R. Chemical Shifts of Starting Phosphonates, Sulphenylated Phosphonates and their α-Lithium Derivatives [δ, ppm][a]

| Phosphonate | α-Lithio Phosphonate | Sulphenylated Phosphonate | α-Lithio Sulphenylated Phosphonate |
|---|---|---|---|
| **10:** 29.7 | 60.4 | **11:** 18.6 | 37.9 |
| **6:** 26.7 | 44.8 | **7:** 17.2 | 35.7 |
| **3:** 32.2 | 53.5 | **5a:** 26.8 | 45.8 |
| | | **5b:** 26.3 | 45.3 |
| *4: 25.5* | *44.6* | **5c:** 21.6 | 43.2 |
| | | **5d:** 20.9 | 38.3 |
| **8:** 23.4 | 49.2 | **9a:** 18.3 | 42.7 |
| | | **9b:** 19.0 | 41.3 |
| | | **9c:** 19.3 | 42.1 |
| | | **9d:** 18.3 | 40.9 |

[a] Spectra measured at −80 °C in tetrahydrofuran solution; signals to lower field than $H_3PO_4$.

**S,S-Dimethylthioacetal of Diethyl Oxomethanephosphonate (9a):**
To a stirred solution of phosphonate **8** (1.98 g, 0.01 mol) in tetrahydrofuran (25 ml), a solution of *n*-butyllithium (0.011 mol) in hexane is added dropwise under nitrogen at −78 °C. The reaction mixture is stirred at −78 °C for 10 min and then a solution of dimethyl disulphide (0.094 g, 0.01 mol) in tetrahydrofuran (10 ml) is added. Work-up as described above and chromatography gives analytically pure **9a**; yield: 1.46 g (60%).

According to this procedure *S,S*-acetals of oxomethanephosphonate **9b** and **9c** were obtained.

**S,S-Diphenylacetal of Diethyl Oxomethanephosphonate (11) from Diethyl Methanephosphonate (10):**
To a stirred solution of phosphonate **10** (1.52 g, 0.01 mol) in tetrahydrofuran (25 ml), a solution of *n*-butyllithium (0.011 mol) in hexane is added dropwise under nitrogen at −78 °C. The solution is stirred at −78 °C for 10 min and then a solution of diphenyl disulphide (2.18 g, 0.01 mol) in tetrahydrofuran (10 ml) is added. After 30 min of stirring, a solution of *n*-butyllithium (0.011 mol) and then a solution of diphenyl disulphide (2.18 g, 0.01 mol) in tetrahydrofuran (10 ml) are added. The mixture is stirred for 30 min and once more a solution of *n*-butyllithium (0.0055 mol) in hexane and after 10 min a solution of diphenyl disulphide (1.09 g, 0.005 mol) in tetrahydrofuran (5 ml) are added. The mixture is stirred for about 30 min and then worked up in the manner described above to afford analytically pure **11**; yield: 3.09 g (84%).

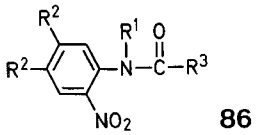
Received: October 12, 1979


[1] Part XXIV of the series: Organosulphur Compounds; Part XXIII: see Ref. [4].
[2] E. J. Corey, J. I. Shulman, *J. Org. Chem.* **35**, 777 (1970).
[3] E. J. Corey, J. I. Shulman, *J. Am. Chem. Soc.* **82**, 5522 (1970).
[4] M. Mikołajczyk, S. Grzejszczak, A. Chefczyńska, A. Zatorski, *J. Org. Chem.* **44**, 2967 (1979).
[5] M. Mikołajczyk, S. Grzejszczak, A. Zatorski, B. Młotkowska, H. Gross, B. Costisella, *Tetrahedron* **34**, 3081 (1978).
[6] N. Kreutzkamp, J. Pluhatsch, *Arch. Pharm. (Weinheim, Ger.)* **292**, 159 (1959).
[7] M. Green, *J. Chem. Soc.* **1963**, 1324.
[8] B. A. Arbuzov, N. P. Bogonostseva, *Zh. Obshch. Khim.* **26**, 2419 (1956).
[9] B. A. Arbuzov, N. P. Bogonostseva, *Zh. Obshch. Khim.* **27**, 2360 (1957).
[10] D. L. Comins, A. F. Jacobine, J. L. Marshall, M. Turnbull, *Synthesis* **1978**, 309.
[11] B. Młotkowska, H. Gross, B. Costisella, M. Mikołajczyk, S. Grzejszczak, A. Zatorski, *J. Prakt. Chem.* **319**, 17 (1977).
[12] B. M. Trost, *Chem. Rev.* **78**, 763 (1978).
[13] Recently, Grayson and Warren have described the sulphenylation of diphenylmethylphosphine oxide and its *S*-phenyl derivative: J. I. Grayson, S. Warren, *J. Chem. Soc. Perkin Trans. 1* **1977**, 2263.
[14] B. M. Trost, *Organic Sulphur Chemistry*, C. J. M. Stirling, Ed., *Butterworths, London, 1975.*


0039-7881/80/0232-0129 $ 03.00

## Errata and Addenda 1980

V. N. R. Pillai, *Synthesis* **1980** (1), 1–26;
The structure of compound **86** (p. 12) should be:

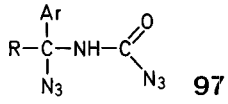


**86**

V. I. Cohen, *Synthesis* **1980** (1), 60–63;
The alternative name (in brackets) for compounds **1** (p. 62, first experimental procedure) should be ***S*-Methylpseudothiourea Hydroiodides.**

J. R. Mahajan, H. C. de Araújo, *Synthesis* **1980** (1), 64–66;
The authors have erroneously stated that "exaltolide" is a trivial name for pentadecanolide. In fact "exaltolide" is a trademark registered in the name of Firmenich SA, Geneva and should be designated as Exaltolide®.

V. I. Gorbatenko, L. I. Samarai, *Synthesis* **1980** (2), 85–110;
The structure of compound **97** (p. 99) should be:



**97**

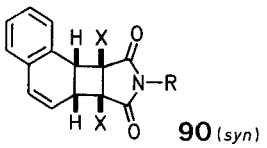
M. Mikołajczyk, P. Bałczewski, S. Grzejszczak, *Synthesis* **1980** (2), 127–129;
The correct name for compound **5a** (first procedure, p. 129) is **Diethyl 1-Phenylthioethanephosphonate.**

G. A. Olah, Y. D. Vankar, M. Arvanaghi, *Synthesis* **1980** (2), 141–142;
The correct name for compound **4** is ***N*-(Chlorosulfonyl)-dimethylsulfilimine.**

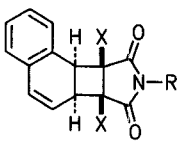
Abstract 5692, *Synthesis* **1980** (2), 159;
The title should be: **Phenols from Aryl Ethyl Ethers.**

Abstract 5698, *Synthesis* **1980** (2) 161;
The title should be: **Enals and Enones from Ketones.**

T. Wagner-Jauregg, *Synthesis* **1980** (3), 165–214;
The structures of compounds **90** (p. 175) should be:



**90** (*syn*)



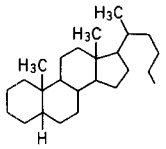
**90** (*anti*)

The correct name for compound **251** (p. 188) is **2*H*-Cyclohepta[*gh*]pyrrolizin-Derivat.**

Abstract 5724, *Synthesis* **1980** (3), 254;
The title should be: **Carbamates, Thiocarbamates, and Carbonates from Alcohols or Thiols.**
The first line under the formula scheme should be: Y = O, S.

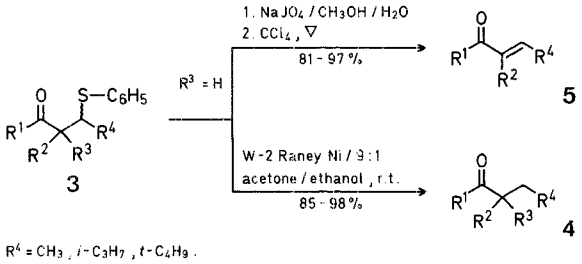
Abstract 5728, *Synthesis* **1980** (3), 256;
The title (and name for compound **3**) should be: ***N*-Sulphenylimines Derived from Amino Acids.**

C. R. Harrison, P. Hodge, *Synthesis* **1980** (4), 299–301;
The 3rd group in the Table, part B (p. 300) should have the structure:



Abstract 5745, *Synthesis* **1980** (4), 334;
The title should be: **Stereocontrolled *cis*-Addition of Organocopper Reagents to 2-Alkynals, 1-Alkynyl Ketones, 2-Alkynoic Acids, and 2-Alkynoic Esters.**

Abstract 5752, *Synthesis* **1980** (4), 336;
The title should be: **α-Alkylation and α-Alkylidenation of Carbonyl Compounds.**
The formula scheme for the conversion **3**→**4** or **5** should be:



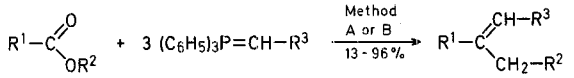

**3** **5** **4**

$R^4$ = $CH_3$, *i*-$C_3H_7$, *t*-$C_4H_9$.

Abstract 5770, *Synthesis* **1980** (4), 342;
The title should be: **Claisen Rearrangement of Ketene Allyl Ethyl Acetals.**

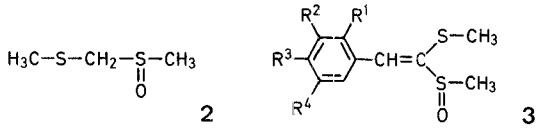
M. A. Alkhader, R. K. Smalley, B. Mohajerani, *Synthesis* **1980** (5), 381–383;
The correct name for compound **6** is **Indazolo[3,2-*b*]naphtho[2,3-*d*]-[1,3] oxazin-6-one.**

Abstract 5782, *Synthesis* **1980** (5), 418;
The formula scheme should be:



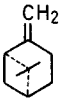

**1** **2** **3**

Abstract 5799, *Synthesis* **1980** (5), 424;
The structures of compounds **2** and **3** should be:



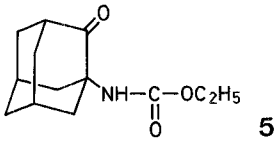
**2** **3**

L. M. Harwood, M. Julia, *Synthesis* **1980** (6), 456–457;
The structure of compound (−)-**7** should be:



(−)-**7**

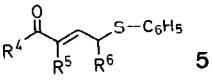
T. Sasaki, S. Eguchi, T. Okano, *Synthesis* **1980** (6), 472–475;
The structure of compound **5** should be:



**5**

Abstract 5804, *Synthesis* **1980** (6), 498;
The title should be: **Allylic Funtionalisation of Exomethylene Compounds.**

Abstract 5817, *Synthesis* **1980** (6), 503;
The structure of compound **5** should be:



**5**