A General Procedure for the Conversion of a Carbonyl Group into a Thione Group with Tetraphosphorus Decasulfide

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A New Synthesis of 1,2-Benzocyclohepta-1,3-diene

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The recent publication of a new synthesis of homophthalaldehyde1 (1) prompts us to report the synthesis of 1,2-benzocyclohepta-1,3-diene (3) using a method already described for the cyclization of heptatrienes2. o-Allylstyrene (2), obtained from homophthalaldehyde by a Wittig reaction, undergoes cyclization in isopropylamine in the presence of a small amount of suspended sodium to give 1,2-benzocyclohepta-1,3-diene (3) in 55% yield (based on o-allylstyrene). Benzocycloheptene (4) is obtained as a side product in 7% yield3.

The reaction described makes possible the synthesis of 3 from indene in 3 steps, whereas the usual method starting with cinnamaldehyde requires 4 steps and the method starting with benzosuberone (5) requires two steps.

\[
\begin{align*}
\text{1} & \quad \text{2} & \quad \text{3} \\
\text{o-allylstyrene (2):} & \quad \text{The compound is obtained by reaction of homophthalaldehyde (1) with methyltriphenylyphosphonium bromide and sodium amide according to Ref.}^6; \text{ yield: 50%}; \text{ purity (G.L.C.): >99%}. \\
\text{1H-N.M.R. (CDCl}_3\text{:} & \quad \delta = 3.4 \text{ (d, 2H, J=6.0 Hz, 4.7-5.1 (m, 2H), 5.22 and 5.38 (dd, 2H, J=11 Hz and J=17 Hz), 5.7 (m, 1H), 6.95 (dd, 1H, J=17 Hz and J=11 Hz), 7.30 (m, 4H) ppm.}\end{align*}
\]

1,2-Benzocyclohepta-1,3-diene (3) and Benzocycloheptene (4):

A suspension of sodium (0.08 g, 0.003 g-atom) in a solution of o-allylstyrene (2, 1.44 g, 0.01 mol) in isopropylamine (10 ml) is stirred for 12 hr at room temperature. Sodium is then removed and the solution added to ethanol and then to water. The resultant mixture is extracted with ether, the organic extract evaporated, and the residue subjected to chromatography on silica gel using cyclohexane/ethyl acetate (97/3) as eluent. Compound 3; yield: 0.8 g (55%); purity (G.L.C.): >99%. U.V. (cyclohexane): \( \lambda_{\text{max}} = 253 \text{ nm (} \epsilon = 12000). \)

1H-N.M.R. (CDCl\(_3\)): \( \delta = 1.95 \text{ (m, 2H), 2.35 (m, 2H), 2.85 (m, 2H), 5.83 (sexet, 1H, J=12.5 Hz and J=4.5 Hz), 6.40 (sexet, 1H, J=12.5 Hz and J=1.6 Hz), 7.05 (s, 4H) ppm. The spectrum is identical with that reported in Ref.}^7 \text{ (except for the misprint in that publication).} \)

Compound 4; yield: 0.1 g (7%); purity (G.L.C.): >99%. The compound was identical with a sample obtained by Wolff-Kishner reduction of 5.

\[
\begin{align*}
\text{1H-N.M.R. (CDCl}_3\text{:} & \quad \delta = 1.70 \text{ (m, 6H), 2.71 (m, 4H), 6.92 (s, 4H) ppm.}
\end{align*}
\]

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A General Procedure for the Conversion of a Carbonyl Group into a Thione Group with Tetraphosphorus Decasulfide

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Although tetraphosphorus decasulfide \( \text{(P}_4\text{S}_{10}) \) has been known as a reagent for the sulfurization of carbonyl groups, it has never achieved general importance for the synthesis of thiophene compounds. \(^1\)–\(^3\) Useful results have only been reported with carboxamides \(^4\) and some cyclic ketones \(^2\). In these synthetic investigations, the carbonyl compound, dissolved in a non-polar solvent such as toluene, was generally refluxed with suspended \( \text{P}_4\text{S}_{10} \). The isolation of the sulfur derivative is simple, since residual phosphorus compounds are insoluble in the solvent. Reactions of carbonyl compounds with silicon disulfide or boron sulfide \(^6\), recently proposed as alternatives for sulfurizations with \( \text{P}_4\text{S}_{10} \), have been carried out in the same solvent.

It is remarkable that the use of more polar solvents in these reactions seems to have never been attempted, although a very polar intermediate has been suggested for the (incompletely understood) sulfurization of amides with \( \text{P}_4\text{S}_{10} \), and the catalytic influence of salts on this reaction has long been recognized \(^8\).

In our investigations on reactions of orthoesters, ketals, and several kinds of carbonyl compounds with \( \text{P}_4\text{S}_{10} \), we found that the conversions were much faster in polar solvents than in toluene. Addition of two molar equivalents of sodium sulfide, carbonate, or hydrogen-carbonate to the reaction mixture further accelerated the transformation and clear solutions were obtained with evolution of heat. Under these conditions, several types of carbonyl compounds \((1); \text{ see Table}) could be converted into the corresponding thiocarbonyl compounds \((3)\), often in higher yields than by known methods.

Little is known about the interaction of \( \text{P}_4\text{S}_{10} \) with inorganic salts in organic solvents, but it may be assumed that such solutions contain the anion \( X_2\text{PS}_2^-(X^0 \text{ is the monovalent anion in the salt used}) \) in monomeric or polymeric form \(^9\), \(^10\).

In solutions prepared from \( \text{P}_4\text{S}_{10} \) and sodium carbonate or hydrogen-carbonate, which evolve carbon dioxide, \( \text{OPS}_2^- \) and \( \text{SPO}_2^- \) \((2)\) should thus be present. For sulfurization reactions, such solutions have to be used when freshly prepared, because they become syrupy on standing or heating, probably due to polymerization.
Table. Conversion of Carbonyl Compounds (1) into Thiono Compounds (3)

<table>
<thead>
<tr>
<th>R₁</th>
<th>R₂</th>
<th>Reaction Conditions²</th>
<th>Molar Equivalents of P₂S₁₀</th>
<th>Molar Equivalents of NaHCO₃</th>
<th>Solvent</th>
<th>Concentration of 1 (%)</th>
<th>Isolation Procedure</th>
<th>Yield (%)</th>
<th>m. p. or b. p. (Lit. value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[环]</td>
<td>[环]</td>
<td>30°, 3 hr 1.5</td>
<td>6</td>
<td>acetonitrile</td>
<td>10</td>
<td>B</td>
<td>65</td>
<td>m. p. 51-53° [m. p. 52-54°; b. p. 129-133°/0.06 torr]¹²</td>
<td></td>
</tr>
<tr>
<td>H₂C-[环]</td>
<td>H₃C-[环]</td>
<td>30°, 3 hr 1.5</td>
<td>6</td>
<td>acetonitrile</td>
<td>10</td>
<td>A</td>
<td>80</td>
<td>m. p. 74-75° [m. p. 76°]¹³</td>
<td></td>
</tr>
<tr>
<td>H₂C-[环]</td>
<td>H₂CO-[环]</td>
<td>30°, 3 hr 1.5</td>
<td>6</td>
<td>acetonitrile</td>
<td>10</td>
<td>A</td>
<td>85</td>
<td>m. p. 105°</td>
<td></td>
</tr>
<tr>
<td>H₂C-[环]</td>
<td>H₂CO-[环]</td>
<td>30°, 3 hr 1.5</td>
<td>6</td>
<td>acetonitrile</td>
<td>10</td>
<td>A</td>
<td>85</td>
<td>m. p. 116-118° [m. p. 116°]¹³</td>
<td></td>
</tr>
<tr>
<td>H₂C₆N-[环]</td>
<td>H₂C₆N-[环]</td>
<td>30°, 3 hr 1.5</td>
<td>6</td>
<td>acetonitrile</td>
<td>10</td>
<td>A</td>
<td>85</td>
<td>m. p. 200-202° (dec) [m. p. 198-205°]⁶</td>
<td></td>
</tr>
<tr>
<td>CH₃</td>
<td>[环]</td>
<td>30°, 4 hr 1.0</td>
<td>4</td>
<td>diglyme</td>
<td>20</td>
<td>B</td>
<td>35</td>
<td>b. p. 78-82°/1 torr [b. p. 97-100°/12 torr]¹⁴</td>
<td></td>
</tr>
<tr>
<td>1-C₆H₅</td>
<td>H₂CO-[环]</td>
<td>30°, 4 hr 1.0</td>
<td>4</td>
<td>diglyme</td>
<td>20</td>
<td>B</td>
<td>55</td>
<td>b. p. 102°/0.6 torr</td>
<td></td>
</tr>
<tr>
<td>[环]</td>
<td>[环]</td>
<td>120°, 5 hr 1.5</td>
<td>6</td>
<td>diglyme</td>
<td>20</td>
<td>A</td>
<td>70</td>
<td>m. p. 143-145° [m. p. 145°]²</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>C₃H₅O⁻</td>
<td>30°, 5 hr 0.15</td>
<td>0.6</td>
<td>diglyme</td>
<td>50</td>
<td>D</td>
<td>(18)b</td>
<td>b. p. 86-87° [b. p. 86.5-87.5°]¹⁵</td>
<td></td>
</tr>
<tr>
<td>CH₃</td>
<td>C₃H₅O⁻</td>
<td>reflux, 24 hr 0.1</td>
<td>0.01</td>
<td>none</td>
<td>C</td>
<td>(14)b</td>
<td>b. p. 105° [b. p. 108-110°]¹⁶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[环]</td>
<td>H₂CO⁻</td>
<td>80°, 24 hr 0.15</td>
<td>0.01</td>
<td>none</td>
<td>C</td>
<td>(25)b</td>
<td>b. p. 107-108°/15 torr [b. p. 112-115°/26 torr]¹⁷</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH₃</td>
<td>C₃H₅S⁻</td>
<td>reflux, 6 hr 1.0</td>
<td>4</td>
<td>diethyl ether (20)</td>
<td>C</td>
<td>50</td>
<td>b. p. 44°/16 torr [b. p. 61°/24 torr]¹⁸</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>H₂C₆N⁻</td>
<td>reflux, 5 hr 0.6</td>
<td>2</td>
<td>diethyl ether (20)</td>
<td>C</td>
<td>85</td>
<td>b. p. 108°/14 torr [b. p. 111-113°/10 torr]¹⁹</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ After recrystallization from methanol.
² Conversion of starting compound (which was used in large excess).
³ The amounts of carbonyl compounds used were 0.02 mol for benzophenones and xanthone and 0.1 mol for other compounds.
Sulfurization may be due to nucleophilic attack of these anions on the carbonyl C-atom followed by elimination of $O_2PS^\ominus$ or $OPS^\ominus$ (4), respectively, e.g.

$$ R^1\text{C}=O \quad + \quad SPS^\ominus \quad \rightarrow \quad R^1\text{C}=S \quad + \quad OPS^\ominus $$

If $R^1$ or $R^2$ is a good leaving group (as in acid chlorides), no thiono compound (3) is obtained, probably as a consequence of substitution of the leaving group. For aromatic ketones, the reaction rate is lower when $R^1$ or $R^2$ is electronegative, suggesting that nucleophilic attack of the negative oxygen on phosphorus in the addition product is rate-determining.

In general, the reaction rates are higher in acetonitrile than in the other solvents used (see Table), but the nitrite is not completely inert towards $P_4S_{10}$. During work-up under hydrolyzing conditions, thioacetamide is formed as a side product. With more reactive compounds such as carboxamides, even diethyl ether can be used as a solvent, although it does not give clear solutions with the sulfurizing agent. With esters, except formates, the best yields of thione derivatives are obtained when no solvent and only a catalytic amount of sulfuric or hydrogen-carbonate is used. We have no explanation for these observations.

**Conversion of Carbonyl Compounds into Thiono Compounds; General Procedure:**

All sulfurization reactions were performed by dissolving the carbonyl compound in a suitable solvent, adding the solution of $P_4S_{10}$ in the same solvent, and adding solid sodium-hydrogen carbonate to the mixture under stirring and at such a rate as allowed by the evolution of carbon dioxide. Stirring was then continued for several hours. Experimental details are given in the Table. Isolation of the products was performed using several, slightly different procedures:

**Isolation Procedure A:** The reaction mixture was poured into water. The solid product which separated was isolated by filtration, washed several times with water, and dried at low pressure (0.5 torr) and $-50\degree$.

**Isolation Procedure B:** Ether was added to the reaction mixture. The ethereal solution was washed several times with aqueous sodium-hydrogen carbonate (5%) and water, dried, and distilled at low pressure.

**Isolation Procedure C:** The reaction mixture was diluted with ether, filtered, and the filtrate distilled at low pressure.

**Isolation Procedure D:** Low-boiling reaction products were distilled from residual phosphorus compounds in the reaction mixture at low pressure and collected in a dry-ice trap. They were purified by redistillation.

Using these procedures, the products contained in some cases small amounts (up to 10%) of the starting compound. Pure samples (> 95%), however, could be obtained by redistillation or recrystallization. O-Ethyl thioacetate contained some S-ethyl thioacetate, which could not be separated by distillation. To obtain a pure sample, the S-ethyl thioacetate was converted into ethyl di-thioacetate via the sulfurization described. Separation of O-ethyl thioacetate and ethyl di-thioacetate was possible by distillation. All products were identified and checked for purity by I.R.-spectrometry. A comparison of the melting and boiling points found with values from the literature is given in the Table.

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**Mixed Acylals; Synthesis of Alkylidene Carboxylic Formates**

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Since excellent synthetic procedures for the preparation of pure mixed anhydrides of formic acid and other carboxylic acids are now available, it appeared worthwhile to investigate the reactivity of these anhydrides towards aldehydes, which might lead to a synthesis of the hitherto unknown mixed alkylidene dicarboxylates of formic acid and other carboxylic acids.
The relevant mixed anhydrides decompose readily at higher temperatures and in the presence of acids and bases. Thus, we performed our first experiments at 0° using iron(III) chloride as a catalyst; formaldehyde was introduced into ethereal solutions of mixed anhydrides. However, the yields of mixed acylals obtained under these conditions were very low due to polymerization of the aldehyde and decomposition (evolution of gas) of the anhydride.

With acetaldehyde, the yields were better (up to 50%), but the reaction mixtures always contained substantial amounts of the ethylidene dicarboxylate with identical acid residues. In some cases, complete separation of this side product from the desired alkylidene carboxylate formate was difficult or even impossible. Ethylene diformate was never found, probably due to its low stability.

Because the use of pure mixed anhydrides did not prevent the formation of acylals with identical acid residues, we modified the procedure, replacing the mixed anhydride by a formic acid-carboxylic acid mixture. It is known that such mixtures contain the mixed anhydride as a consequence of equilibrium (1).

\[
R_2\text{CHO} + R'\text{COOH} \rightleftharpoons R_2\text{CH} = \text{O} - \text{C} - R' + R'\text{COOH}
\]

The best results were obtained when the anhydride and formic acid were used in excess (50% and 500%, respectively). If the molar ratio between aldehyde and anhydride is higher, \(\alpha,\alpha'\)-acyloxyethers, e.g.

\[
\begin{align*}
R_2\text{CHO} & \rightarrow R_2\text{CH} = \text{O} - \text{C} - \text{H} \\
\text{R} - \text{C} - \text{H} & \rightarrow \text{R} - \text{C} - \text{H}
\end{align*}
\]

are found as side products. Among the several possible catalysts tested (FeCl₃, H₂SO₄, P₂O₅, HCOONa, pyridine), phosphorus pentoxide appeared to be the most effective.

The alkylidene carboxylate formates (5) prepared by this procedure are listed in the Table. The compounds were identified and tested for purity by N.M.R. In all compounds, the \(\text{H}_2\) peak of

\[
R_2\text{CHO} + R'\text{COOH} \rightleftharpoons R_2\text{CH} = \text{O} - \text{C} - \text{R}' + R'\text{COOH}
\]

was found between \(\delta = 6.5\) and 6.9 ppm (TMS as internal references).

In view of the strong acylating and preferential formylating ability of the formic acid – acetic anhydride system, a tentative reaction scheme might be represented as follows.

\[
\text{Preparation of Mixed Acylals; General Procedure:}
\]

The carboxylic aphonydrile is mixed with formic acid in a molar ratio of 1:5. After standing for 30 min at room temperature, an aldehyde (2/3 equivalents based on anhydride) and phosphorus pentoxide (0.5 g per mol of aldehyde) are added. The mixture becomes warm and a gas is evolved. After the mixture has been left for 3 hr at room temperature, formic acid is evaporated at reduced pressure (15 torr), ether is added, and the ethereal solution is extracted several times with aqueous sodium-hydrogen carbonate and finally with water. The solution is dried with sodium sulfate, ether is evaporated, and the residue is distilled using a Vigreux column (80 x 1.2 cm). Alkylidene acetate formates free from alkylidene diacetates can only be obtained by distillation of the crude products using a spinning-band column of at least 25 theoretical plates.