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On the Reduction of *S*-Alkyl-thionocarbonates (Xanthates) with Phosphorus Compounds

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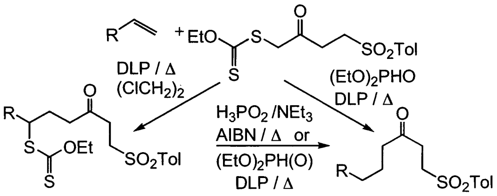
ABSTRACT



Reductive cleavage of the carbon–sulfur bond present in *S*-alkyl-thionocarbonates (xanthates) was achieved by high-yielding, tin-free radical reactions based on phosphorus reagents. The combination hypophosphorous acid/triethylamine/AIBN led to fast, efficient, and smooth formation of the alkane. Reduction with diethyl phosphite was sufficiently slow to permit sequential intermolecular addition of a 2-oxoalkyl xanthate onto an olefin followed by cleavage of the newly formed carbon–sulfur bond.

The last two decades have witnessed a tremendous development of new radical reactions designed for organic synthesis. In this field, Barton has been a pioneer, discovering or sowing the seeds of countless original and useful reactions.[1,2] In particular, xanthates have been found to be not only convenient precursors for transforming an alcohol into the corresponding alkane[3] but also extremely efficient and versatile sources of radicals. The concept of "degenerate reaction" brought to light by Zard et al. has permitted radical processes that would be otherwise difficult to realize by "conventional methods" because of severe, unavoidable, and useless competitive reactions.[4,5] Special mention must be made of intermolecular addition of 2-oxoalkyl radicals to olefins that produces xanthate adducts in generally good yields and tolerates many functional groups. On certain occasions, the rich sulfur chemistry underlying the xanthate moiety in the adduct has been exploited.[6] However, in most cases, reductive cleavage of the newly formed *carbon−sulfur* bond is needed. Essentially two methods are utilized. The first one relies on the tin hydride chemistry with all its stringent drawbacks in terms of toxicity, difficulties encountered in purification, and cost.[7,8] The second one is much more convenient. It requires 2-propanol (or similar compounds) as a hydrogen atom donor and dilauroyl peroxide (DLP) as a radical initiator[9] but is also subject to limitations (vide infra).

We were also faced with the recurrent problem of removing a xanthate located on a molecule sensitive to either acidic or basic conditions. Thus, standard reduction of compounds **1a** and **1b**[10] with tributyltin hydride/AIBN in refluxing toluene led to erratic results strongly depending on the purity of the commercial reagent used. On the other hand, removal of the xanthate group in compound **1a** with

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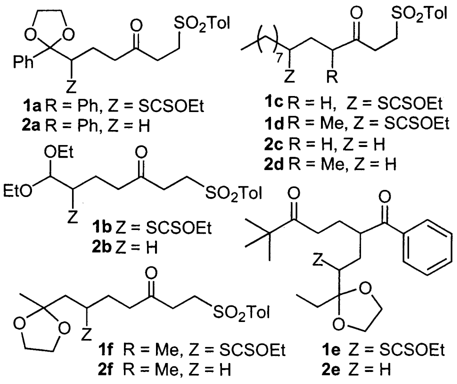

Figure 1.

stoichiometric amounts of dilauroyl peroxide in 2-propanol furnished **2a** with only 33% yield together with a compound resulting from cleavage of the acetal group because of the acidity of the medium reaction in the process. Addition of a base such as 2,6-lutidine to the reaction mixture only led to the formation of a complex mixture due to β-elimination of the sulfonyl moiety that produced a very reactive enone. Some years ago, Barton and, more recently, other groups have developed an efficient, low-cost, and environmentally safe approach based on phosphorus derivatives.[11−14] These methods were originally designed for deoxygenation of alcohols to alkanes through their *O*-alkylxanthate derivatives, by cleavage of the *carbon−oxygen* bond, and were also successfully applied to reduce other compounds such as halides. However, there is no report that phosphorus compounds have been used in radical reduction of an *S*-alkylxanthate group. We wish to report herein the use of hypophosphorous acid and diethyl phosphite to cleave the *carbon−sulfur* bond in order to remove the xanthate function in sensitive compounds such as **1a**.

We were delighted to observe that when a solution of **1a** was heated at reflux under an inert atmosphere for 0.3 h in dioxane in the presence of hypophosphorous acid (5 equiv), triethylamine (5.5 equiv), and catalytic amounts of AIBN (0.2 equiv), the corresponding alkane **2a** was obtained in a gratifying 69% isolated yield (Table 1, entry 1).[15] When compound **1a** was refluxed for 9 h in 1,2-dichloroethane in the presence of diethyl phosphite (15 equiv) and catalytic amounts of DLP (0.3 equiv), the corresponding alkane **2a** was obtained in a slightly lower yield 66% (entry 2). Dibenzoyl peroxide was also used as an initiator, but the reaction remained very slow (12 h, entry 3). Ketals **1b**, **1e**, and **1f**, when treated with hypophosphorous acid (method A), afforded the corresponding saturated compounds **2b**, **2e**, and **2f** in high yields (Table 1, entries 4, 5, and 11). Similarly, adducts **1c** and **1d**, upon reduction with hypophosphorous acid, furnished high yields of saturated compounds **2c** and **2d**, respectively (entries 6 and 7). It is worthy of note that dioxane can be replaced by cheaper and less toxic 1-propanol (Table 1, entries 8 and 9). Sodium hydrogen carbonate has also been used in conjunction with hypophosphorous acid in refluxing ethanol to reduce ketal **1b** with 54% yield (entry 10). Thus, it appears that cleavage of the *carbon−sulfur* bond with the aid of hypophosphorous acid/triethylamine or diethyl phosphite can be achieved under very mild conditions with good to excellent yields.

Table 1. Reduction of Xanthates with Hypophosphorous Acid/Triethylamine/AIBN under Reflux (Method A)[16] and Diethyl Phosphite/DLP [Method B, Dilauroyl Peroxide as Initiator (Method B′, Dibenzoyl Peroxide as Initiator)][a]

entry	xanthate (concn)	method	solvent	reaction time (h)	alkane (% yield)
1	**1a (0.1 M)**	A	dioxane	0.3	**2a** (69)
2	**1a (0.4 M)**	B	1,2-dichloroethane	9	**2a** (66)
3	**1a (0.4 M)**	B′	1,2-dichloroethane	12	**2a** (70)
4	**1b (0.1 M)**	A	dioxane	0.5	**2b** (69)
5	**1e (0.1 M)**	A	dioxane	0.3	**2e** (89)
6	**1c (0.2 M)**	A	dioxane	0.5	**2c** (79)
7	**1d (0.04 M)**	A	dioxane	0.5	**2d** (75)
8	**1c (0.2 M)**	A	*n*-propanol[c]	0.75	**2c** (60)
9	**1d (0.2 M)**	A	*n*-propanol[c]	1.5	**2d** (49)
10	**1b (0.1 M)**	A[b]	ethanol	10	**2b** (54)
11	**1f (0.1 M)**	A	dioxane	0.3	**2f** (75)

[a] Same reaction conditions as those described in ref 17. [b] Triethylamine was replaced with $NaHCO_3$. [c] One portion of 10% AIBN (mmol/mmol of xanthate) was added every 0.75 h.

As reported in Table 1, diethyl phosphite seems to be as efficient as hypophosphorous acid but requires much longer reaction times. What appears as a drawback can in fact be turned into a benefit. Thus, when xanthate **3** was refluxed in 1,2-dichloroethane for 9 h in the presence of 1-decene (2 equiv), diethyl phosphite (15 equiv), and catalytic amounts of DLP (0.4 equiv), the corresponding reduced adduct **1c** was isolated in an encouraging 70% yield (Table 2, entry 1). This means that the reduction process is sufficiently slow to permit the intermolecular addition of the transient 2-oxoalkyl radical onto the olefin to occur. This gives rise to an intermediate xanthate adduct that is progressively reduced, as shown by a careful TLC monitoring. It is noteworthy that addition of diethyl phosphite to olefin, which could be feared on the basis of literature data,[16] does not interfere, at least to a large extent, with the reduction of the xanthate group. Moreover, we showed by a competition

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(10) Full experimental details concerning the preparation of the starting materials mentioned in this Letter will be given in due course.

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(15) **Typical Procedure for Reduction with Hypophosphorous Acid and NEt_3.** A solution of xanthate (1.25 mmol), hypophosphorous acid (50% solution in water, 0.64 mL, 6.2 mmol), and triethylamine (0.69 mL, 6.82 mmol) in dioxane (15 mL) was degassed by refluxing under an argon atmosphere for 0.25 h. The reaction mixture was cooled to room temperature. A 0.4 M solution of AIBN in dioxane (0.44 mL) was then added, and the reaction mixture was refluxed under argon for 0.3−0.5 h. The reaction mixture was cooled and poured into water. Extraction with ether and subsequent flash chromatography afforded the reduced compound.

Table 2. Concomitant Addition/Reduction of Xanthates to Olefins in the Presence of Diethyl Phosphite[17] [a]

entry	xanthate	olefin	initiator (equiv vs xanthate)	reaction time (h)	product (% yield)
1	**3**	**5**	DLP (0.4)	12	**2c** (71)
2	**3**	**6**	DLP (0.4)	12	**2a** (58)
3	**3**	**11**	BPO (0.6)	18	**12** (44)
4	**3**	**9**	DLP (0.3)	9	**14** (76)
5	**4**	**6**	DLP (0.4)	12	**13** (49)
6	**1d**	**10**	AIBN (0.1)	2	**15** (15)

[a] Solvent: 1,2-dichloroethane. DLP = dilauroyl peroxide; BPO = dibenzoyl peroxide; AIBN = azo-bis-isobutyronitrile.

reaction that the xanthate adduct was reduced faster than the starting 2-oxoalkyl xanthate.

When the same methodology was applied to addition of xanthate **3** to the more sensitive vinylic ketal **6**, a satisfactory yield of compound **2a** was obtained (58%, Table 2, entry 2). Addition/reduction of derivative **3** to allyl acetate **11**, initiated with benzoyl peroxide, also proceeded smoothly and gave compound **12** in 44% yield (Table 2, entry 3). In a similar manner, xanthate **4** afforded derivative **13** in 49% yield (entry 7). Addition of xanthate **3** to (−)-β-pinene furnished compound **14** in a fair 76% isolated yield, through an addition/fragmentation/reduction cascade (entry 6).[17]

Some limitations were observed when the addition/reduction sequence was attempted between xanthate **3** and olefins **7** and **8**. Compounds **7** and acrolein diethyl acetal **8** did not produce the desired reduced adducts. For example, in the case of the reaction between xanthate **3** and olefin **7** in the presence of DLP (0.3 equiv), only 30% starting material **3** and 13% 4-*p*-toluenesulfonyl-2-butanone could be isolated even after prolonged heating (9 h). The removal of the stabilizer present in the commercial reagent **8** did not change this situation. It is worthy of note that reduction of adduct **1b** with $(EtO)_2PHO$ also failed, whereas reduction with H_3PO_2 proceeded smoothly (Table 1, entry 4). Obviously, further investigations are needed to clarify these points.

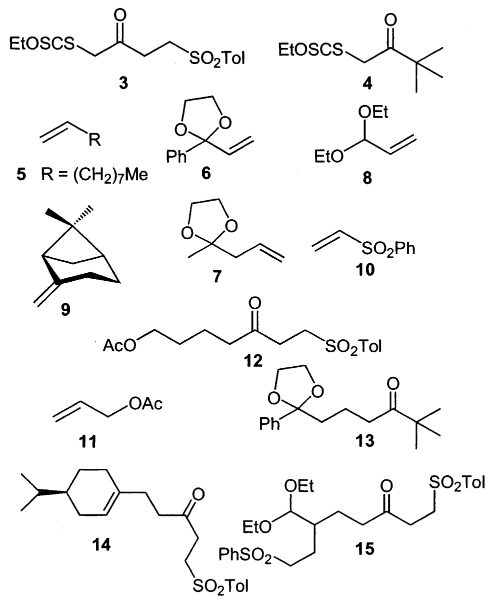
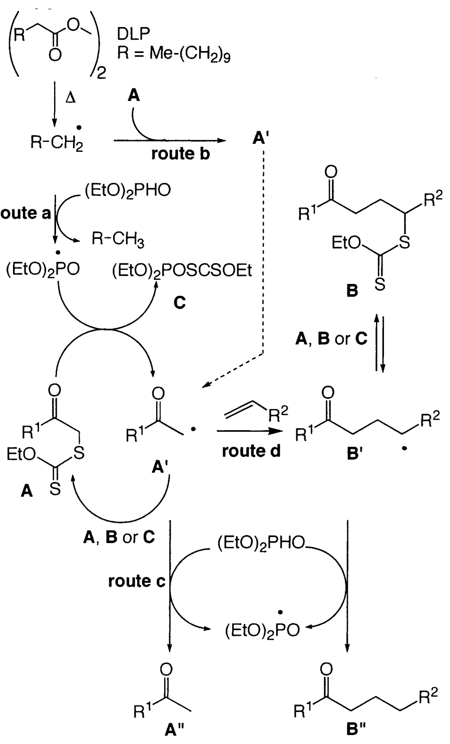


Figure 2.

Scheme 1. Postulated Mechanism for the Reaction of 2-Oxoalkyl Xanthates with Olefins in the Presence of $(EtO)_2PHO$



From a mechanistic viewpoint, one can follow Barton's proposal[11] in which the radical initiator first abstracts an hydrogen from $(EtO)_2PHO$ to produce a phosphorus centered radical. The latter in turn reacts with the thiocarbonyl group (Scheme, route a). In our case, this results in the breaking of the *carbon−sulfur* bond to give rise to radical **A′**. The same radical **A′** can also be generated by reaction between $RCH_2\cdot$ and **A** (route b). The transient radical **A′**, besides the degenerate reactions with thiocarbonyl compounds **A**, **B**, or **C**, can either be reduced very slowly to **A″** (route c) or add to an olefin (route d) to furnish radical **B′**. The latter either reacts with **A**, **B**, or **C** to give **B** or abstracts a hydrogen atom from $(EtO)_2PHO$ to produce the reduced product **B″** and the chain carrier $(EtO)_2P\cdot O$. That we can observe the

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(16) See ref 11a.

(17) **Typical Procedure for Addition/Reduction.** A stirred solution of xanthate (0.5 mmol), olefin (2 equiv), and diethyl phosphite (15 equiv) in degassed 1,2-dichloroethane (2 mL) was refluxed under an argon atmosphere for 15 min. Initiator (0.1 equiv) was added every 3 h until the TLC showed completion of the reaction. The solvent was evaporated under reduced pressure, and saturated aqueous potassium carbonate (20 mL) was added to the resulting residue. The latter was extracted with diethyl ether. The ethereal extract was washed with brine and dried (Na_2SO_4) and the solvent removed by evaporation. Purification by flash chromatography over silica gel afforded the reduced adduct.

formation of the xanthate adduct as an intermediate in the reaction means that transfer of a xanthate moiety onto a carbon radical such as **B′** is probably faster than hydrogen abstraction from $(EtO)_2PHO$. This could indicate that initiation of the process through route b cannot be neglected.

Finally, we showed that even the relatively unfavorable addition/reduction of xanthate **1b** onto phenyl vinyl sulfone occurred, albeit in low yield (15%, entry 6). However, Jang's findings on iodo-derivatives suggest that this process could be improved.[14b]

The preliminary results reported herein demonstrate that the impediment often encountered in the removal of an *S*-alkyl thionocarbonate can by circumvented. A more accurate understanding of the mechanisms and kinetics of the reactions involved should lead to further improvements. We are currently working along these lines.

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Supporting Information Available: Detailed procedures for preparation of new compounds and their spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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