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REACTION OF PHOSPHONODITHIOFORMATES WITH NUCLEOPHILIC REAGENTS; POTENTIAL SYNTHETIC USES.

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Abstract: The reactivity of phosphonodithioformates with trialkylphosphites, organometallics and thiols is studied. The thiophilic addition of these nucleophilic reagents makes the aforementioned dithioesters, suitable precursors of substituted methylene bis-phosphonates and Wittig-Horner reagents.

Phosphodithioformates 1 are readily available compounds from dialkyl-phosphites and carbon disulfide 1 . For these non-enethiolisable dithioesters, the thiophilic addition of nucleophiles to the thiocarbonyl group was expected to be enhanced by its conjugation with the α -phosphonyl substituent 2 . This communication concerns the reactions of these functionalised dithioesters with some nucleophilic reagents. Stabilised ylids, precursors of substituted methylene bis-phosphonates (compounds of biological interest), are prepared with trialkylphosphites and Wittig-Horner reagents are obtained via the thiophilic addition of organometallics and thiols.

O S

$$(R^1O)_2P-C-SR^2$$
 $R^1 = Et$, iPr ; $R^2 = Me$, Et , $MeOCH_2OCH_2$, $C_{12}H_{25}$, Allyl, Crotyl

REACTION WITH TRIALKYLPHOSPHITES

The reactions of trialkylphosphites with thiocarbonyl compounds are quite varied. Products of coupling reactions ³, alkenes ⁴ or phosphonium ylids ⁵ are obtained via thiophilic addition and desulfurisation. Carbophilic addition ⁶ and enethiolisation ⁷ are also observed. From phosphonodithioformates 1, which react (via an assumed thiophilic addition and desulfurisation) with two equivalents of trialkylphosphite, stabilized phosphonium ylids 2 were isolated.

Protonation of the central carbon with Arbuzov-type dealkylation of the phosphonium moiety was observed by reaction of 2 with hydrochloric acid. Alkylthiomethylene bis-phosphonates 3 were obtained quantitatively.

With methyl iodide, S-methylation with alkoxyphosphonium-dealkylation led quantitatively to very stable sulfonium ylids 4.

Addition of allylic or propargylic bromide to ylides 2 led to the respective allylic or allenic bis-phosphonates (5 and 6). This C-alkylation with inversion of the unsaturated chain is rationalized by a [2,3] sigmatropic rearrangement of an initially formed allylic or propargylic sulfonium ylid.

REACTION WITH ORGANOMETALLICS

Dithioacetals of formylphosphonates 8,9 are known to be useful Wittig-Horner reagents for the synthetis of ketene dithioacetals. The thiophilic addition of organolithium com-

pounds to phosphonodithioformates 1 led readily to metallated dithioacetals of formylphosphonates 7 which can be protonated (8), alkylated (9) or used "in situ" as Wittig-Horner reagents (10).

$$R^{1} = \text{Et, iPr}$$

$$R^{2} = \text{Me, Allyl}$$

$$R^{3} = \text{Me, Bu, Ph}$$

$$R^{4} = \text{Me, Crotyl}$$

$$R^{3} = \text{Me, Crotyl}$$

$$R^{4} = \text{Me, Crotyl}$$

$$R^{3} = \text{Me, Re}$$

$$R^{1} = \text{Me, Crotyl}$$

$$R^{4} = \text{Me, Crotyl}$$

$$R^{5} = \text{Me$$

Oxidation of 1 with metachloroperbenzoic acid gave the sulfine 11, equally siutable for thiophilic addition of organometallics ¹⁰.

An excess of Grignard reagent is necessary in order to obtain the magnesium analogue of 7 to avoid its thiophilic addition to the starting phosphonodithioformate which leads to 13.

$$\begin{array}{cccc} O & SR^3 & SR^2O \\ (R^1O)_2P - C - S - C - P(OR^1)_2 & \mathbf{13} \\ & & SR^2 & H \end{array}$$

REACTION WITH THIOLS

Although the addition of amines to phosphonodithioformates 1 was exclusively carbophilic (and was used to prepare the corresponding thioamides), the base catalyzed addition of thiols to phophonodithioformates 1 led nearly quantitatively to the dithioacetal-disulfides 14. This regioselectivity demonstrates again the tendency of these α -phosphonodithioesters to undergo thiophilic addition.

The reactivity of metallated dithioacetal-disulfides was examined:

O SMe
$$(R^{1}O)_{2}^{1}P - C - SR^{3}$$

$$R^{1} = \text{Et, iPr}$$

$$R^{2} = \text{Me, Et}$$

$$R^{3} = \text{Me, n-Pr, t-Bu, Ph, Dodecyl}$$

$$R^{3} = \text{Me, in-Pr, t-Bu, Ph, Dodecyl}$$

$$R^{1} = \text{Et, iPr}$$

$$R^{2} = \text{Me, Et, iPr}$$

$$R^{2} = \text{Me, in-Pr, t-Bu, Ph, Dodecyl}$$

$$R^{3} = \text{Me, in-Pr, t-Bu, Ph, Dodecyl}$$

$$R^{2} = R^{3} = \text{Me}$$

$$R^{2} = R^{3} = \text{Me}$$

$$R^{3} = R^{3} = R$$

Metallation of the dithioacetals 14 followed by methylation led to (tris-alkylthio)-methylphosphonates 15. The formation and rearrangement of an intermediate ylid is assumed to explain this reaction. When benzaldehyde was added to the metallated dithioacetal 14 ($R^2 = Me$; $R^3 = Me$) dithioester 16 (40%, non-optimised yield) was isolated after work up.

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