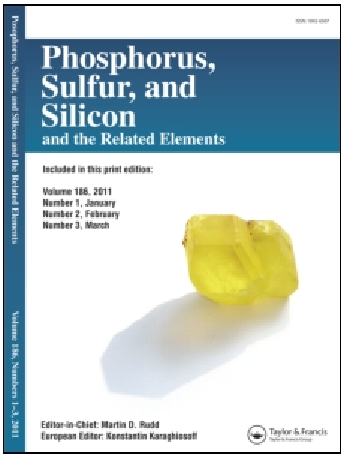

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A DIRECT SYNTHESIS OF 1-CYCLOALKENYLPHOSPHONATES

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A series of 1-cycloalkenylphosphonate diesters has been synthesized starting with the corresponding vinylic chlorides. This has been accomplished using the Cu(I) complexes of triethyl phosphite in a direct reaction with the vinylic chlorides. This represents a convenient method for the synthesis of this class of compounds previously requiring multi-step routes.

INTRODUCTION

In the course of our efforts toward the generation of organophosphorus compounds bearing potential as metabolic regulators, it has been of interest to develop new methods for the direct formation of carbon-phosphorus bonds. It has been of particular interest to develop methods for the direct generation under mild conditions of bonds between phosphorus and unsaturated carbon. To this end we recently reported[1,2] on the synthesis of alpha- and beta-phenyl substituted vinylphosphonates by a replacement reaction of vinylic halogen with copper(I) complexes of trialkyl phosphites. A similar route to these compounds was reported by Hirao, *et al.*[3] through the use of palladium(0) complexes of dialkyl phosphites.

It was also recognized that this reaction system might be a reasonable one for the generation of 1-cycloalkenylphosphonates. Generalized approaches to the synthesis of compounds in this category involved both (1) multi-step procedures of phosphorus incorporation and alkene generation, and (2) the use of starting materials obtained only with relative difficulty. Reaction of a copper(I) complex of a trialkyl phosphite with a 1-halocycloalkene might be anticipated to yield the desired material in a single step using readily available starting materials.

We herein report on our investigations of the feasibility of this reaction system.

RESULTS AND DISCUSSION

A series of 1-chlorocycloalkenes has been investigated in reaction with the copper(I) bromide complex of triethyl phosphite for the generation of 1-cycloalkenylphosphonates, as illustrated in Equation 1. The chlorides used contain rings of six, seven, eight or twelve carbons, several with ring substitution or further unsaturation in the ring. All of the 1-chlorocycloalkenes are readily available from

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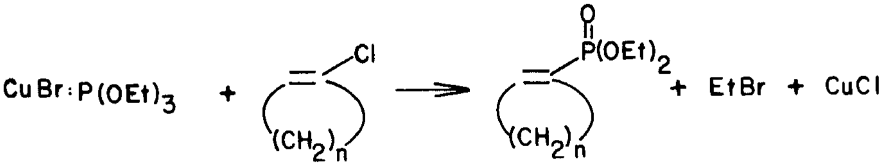

Eq. I

the corresponding ketones in reasonable yield by reaction with phosphorus pentachloride and phosphorus oxychloride. The yields for the preparations of these chlorides are summarized in Table I.

The phosphonate formation reactions were all performed by heating the vinylic chloride with the triethyl phosphite complex of copper(I) bromide. The yields for each reaction system are summarized in Table II.

Several notes should be made regarding the reaction conditions and course of the reactions. Only the vinylic chlorides were used in this study. It is likely that higher yields could be obtained by the use of the vinylic bromides rather than the vinylic chlorides. However, for general utility, the chlorides are of greater significance due to the relative difficulty encountered in obtaining the vinylic bromides. As observed previously in the studies with phenyl-substituted vinylic halides, no halogen exchange is observed in the use of the vinylic chloride in reaction with the copper(I) bromide complex.[1] Nor has any reaction been observed by the use of the copper(I) chloride complex of the phosphite.

With all except one of the reaction systems involved in this study stereochemistry poses no difficulties. For rings of eight members or less the starting chlorides and vinylphosphonate products are all clearly of the *E*-configuration. Only with the twelve membered ring does the possibility exist of both *E*- and *Z*-isomers being present. For this system the spectra clearly indicate the presence of only a single isomer for each of the chloride and the phosphonate and that isomer is of the *E*-configuration.

Work-up of the reactions is facilitated by treatment with ethylenediamine. The purpose of this is to remove copper from the reaction system allowing purification by column chromatography. The yields reported for all systems are of isolated material purified by distillation and chromatography on a silica column.

Overall, the method presented here for the synthesis of 1-cycloalkenylphosphonates represents a facile and efficient method for the preparation of these materials which were hitherto available only with great difficulty.

TABLE I

Yields and TLC R_F values for 1-cycloalkenyl chlorides generated by reaction of the corresponding ketones with phosphorus pentachloride and phosphorus oxychloride

Compound	% Yield	R_F
(1) 1-cyclododecenyl chloride	94	0.57
(2) 1-cyclohexenyl chloride	48	0.60
(3) 2-chloro-1,3-cyclohexadiene	98	0.54
(4) 1-cycloheptenyl chloride	78	0.61
(5) 4-methyl-1-cyclohexenyl chloride	79	0.46
(6) 4-*t*-butyl-1-cyclohexenyl chloride	97	0.64
(7) 1-cyclooctenyl chloride	64	0.48

TABLE II

Yields and TLC R_F values for diethyl 1-cycloalkenylphosphonates from Cu(I)Br-triethyl phosphite complex reactions with 1-cycloalkenyl chlorides

Compound	% Yield	R_F
(8) diethyl 1-cyclododecenylphosphonate	50.0	0.39
(9) diethyl 1-cyclohexenylphosphonate	55.2	0.39
(10) diethyl 2-(1,3-cyclohexadienyl)phosphonate	51.4	0.42
(11) diethyl 1-cycloheptenylphosphonate	64.5	0.28
(12) diethyl 4-methyl-1-cyclohexenylphosphonate	60.0	0.26
(13) diethyl 4-*t*-butyl-1-cyclohexenylphosphonate	55.0	0.42
(14) diethyl 1-cyclooctenylphosphonate	71.4	0.28

TABLE III

Spectral and analytical data for new compounds

Compound	NMR (δ)	IR (cm^{-1})	CH Analysis (%)
(6)	0.87 (s, 9H); 1.08–2.65 (m, 7H); 5.78 (m, 1H)	1652 (olefin)	$C_{10}H_{17}Cl$ Calc.: C, 69.55; H, 9.92 Found: C, 69.60; H, 9.97
(7)	0.72–2.86 (b, 12H); 5.68 (t, 9 Hz, 1H)	1643 (olefin)	$C_8H_{13}Cl$ Cal.: C, 66.43; H, 9.06 Found: C, 66.05; H, 9.18
(8)	1.15–2.68 (b, 26H); 4.02 (dq, J = 10 Hz, J = 7 Hz, 4H); 6.50 (dt, J = 26 Hz, J = 8 Hz, 1H);	1620 (olefin); 1248 (P=O)	$C_{16}H_{31}O_3P$ Calc.: C, 63.55; H, 10.33 Found: C, 63.24; H, 10.69
(9)	1.31 (t, J = 7 Hz, 6H); 1.40–2.51 (m, 8H); 4.10 (dq, J = 8 Hz, J = 7 Hz, 4H); 6.72 (dm, J = 22 Hz, 1H)	1627 (olefin); 1241 (P=O)	$C_{10}H_{19}O_3P$ Calc.: C, 55.03; H, 8.78 Found: C, 55.21; H, 9.04
(10)	1.32 (t, J = 8 Hz, 6H); 1.75–3.00 (m, 4H); 4.03 (dq, J = 8 Hz, J = 8 Hz, 4H); 5.55–6.14 (m, 2H); 6.74 (dm, J = 22 Hz, 1H)	1711 (olefin); 1249 (P=O)	$C_{10}H_{17}O_3P$ Calc.: C, 55.55; H, 7.92 Found: C, 55.24; H, 8.28
(11)	1.27 (t, J = 7 Hz, 6H); 1.35–2.90 (m, 10H); 4.00 (dq, J = 8 Hz, J = 7 Hz, 4H); 6.93 (dt, J = 24 Hz, J = 6 Hz, 1H)	1625 (olefin); 1240 (P=O)	$C_{11}H_{21}O_3P$ Calc.: C, 56.88; H, 9.11 Found: C, 56.86; H, 9.17
(12)	1.00 (d, J = 5 Hz, 3H); 1.32 (t, J = 7 Hz, 6H); 1.18–2.72 (m, 7H); 4.05 (dq, J = 7 Hz, J = 7 Hz, 4H); 6.74 (dm, J = 23 Hz, 1H)	1630 (olefin); 1240 (P=O)	$C_{11}H_{21}O_3P$ Calc.: C, 56.88; H, 9.11 Found: C, 56.53; H, 9.37
(13)	0.88 (s, 9H); 1.32 (t, J = 7 Hz, 6H); 1.25–2.76 (m, 7H); 4.03 (dq, J = 7 Hz, J = 7 Hz, 4H); 6.78 (dm, J = 22 Hz, 1H)	1632 (olefin); 1240 (P=O)	$C_{14}H_{27}O_3P$ Calc.: C, 61.29; H, 9.92 Found: C, 61.31; H, 9.98
(14)	1.28 (t, J = 7 Hz, 6H); 1.35–2.62 (m, 12H); 3.97 (dq, J = 7 Hz, J = 7 Hz, 4H); 6.68 (dt, J = 23 Hz, J = 9 Hz, 1H)	1628 (olefin); 1253 (P=O)	$C_{12}H_{23}O_3P$ Calc.: C, 58.52; H, 9.41 Found: C, 58.15; H, 9.73

EXPERIMENTAL

Reagents

All solvents and liquid reagents used in the preparation of the vinylic chlorides and copper(I) bromide–triethyl phosphite complex, and in the performance and work-up of the reactions, were distilled prior to use, with the exception of anhydrous ethyl ether.

Cuprous bromide was prepared fresh prior to use by a standard method.[4] The triethyl phosphite complex was also prepared fresh prior to use following the method of Wulfman, *et al.*[5]

All new compounds (6–14) gave satisfactory elemental analyses (Schwarzkopf Microanalytical Laboratories, Woodside, NY) and exhibited spectra in accord with the assigned structures. IR spectra were measured using a Perkin-Elmer model 598 spectrophotometer and NMR spectra were measured using a Varian EM-360 instrument. Spectral and analytical data for the new compounds are indicated in Table III. Thin-layer chromatography was performed on Brinkmann Sil N-HR pre-coated sheets eluting with 1 : 1 hexane : ethyl acetate. Care in the handling of the product phosphonates is recommended as they appear to be significantly hygroscopic.

Preparation of 1-chlorocycloalkenes

To an equimolar mixture of phosphorus pentachloride and phosphorus oxychloride at 0°C is added dropwise a molar amount of the ketone. The mixture is stirred for 20 hr at 0°C. After this time the reaction mixture is heated under reduced pressure to remove any phosphorus oxychloride and is then poured into ice-water with vigorous stirring. The resultant mixture is extracted with ether and the extracts washed with 2% sodium bicarbonate and water. The extracts are then dried over magnesium sulfate and evaporated to give the crude vinylic chloride. The product is purified by chromatography on a silica gel column followed by distillation.

Preparation of 1-cycloalkenylphosphonates

In a flask equipped with a short Vigreaux column topped by a Dean-Stark trap and a nitrogen inlet tube is placed the 1-chlorocycloalkene with a 1.5 molar excess of the copper(I) bromide-triethyl phosphite complex. This mixture is heated at 200–205°C while volatile materials are collected in the Dean-Stark trap. The heating was performed until no more volaties were distilled. After cooling to room temperature the reaction mixture was poured into a four-fold volume of toluene and an equivalent of ethylenediamine was added dropwise with stirring. After filtration, the filtrate was acidified with 10% hydrochloric acid and extracted with ether. The organic phase was dried over magnesium sulfate and the solvent evaporated under reduced pressure. The crude product thus isolated was chromatographed on silica gel eluting with hexane-ethyl acetate mixtures, followed by distillation, to give the pure 1-cycloalkenylphosphonates.

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REFERENCES

1. G. Axelrad, S. Laosooksathit and R. Engel, *Synth. Commun.*, **10**, 933 (1980).
2. G. Axelrad, S. Laosooksathit and R. Engel, *J. Org. Chem.*, **46**, 5200 (1981).
3. T. Hirao, T. Masunaga, Y. Oshiro and T. Agawa, *Tetrahedron Lett.*, 3595 (1980).
4. A. I. Vogel, "A Text-Book of Practical Organic Chemistry," 3rd ed., Longmans, Green and Co., New York, 1957, p 190.
5. D. S. Wulfman, N. van Thinh, R. S. McDaniel, B. W. Pierce, C. W. Heitsch and M. T. Jones, *J. Chem. Soc., Dalton Trans.*, 522 (1975).