less oily bromide (**5** and **9**), too unstable to purify and therefore used directly in the next step, was 671 mg (92%): $\nu_{max}$ (film) 1655 (C=C), 1245, 1200, 1150, 1110, 1070, 950 cm$^{-1}$; $\delta_{Me_4Si}$ ($CCl_4$), 5.49 (t, $J$ = 8.5 Hz, C=CH), 3.93 (d, $J$ = 8.5 Hz, $CH_2Br$), 3.30 (quartet, $J$ = 7 Hz, $OCH_2CH_3$), 1.78 ("$Z$" vinyl $CH_3$), 1.73 ("$E$" vinyl $CH_3$), 1.11 (s, 6 H, geminal $CH_3$'s), 1.10 ppm (t, $J$ = 7 Hz, $OCH_2CH_3$). NMR analysis indicated that approximately 30% of the bromide mixture consisted of tertiary vinyl bromide **9**, characterized by peaks at 6.33, 6.17, 6.05, and 5.88 ppm ($CH=CH_2$) as well as a singlet ($W_{1/2}$ = 1.4 Hz) at 1.83 ppm ($BrCCH_3$).

**7-Ethoxy-1-(*p*-ethylphenoxy)-3,7-dimethyl-2-octene (6).** A mixture of 666 mg (2.53 mmol) of crude bromide **5**, 3.5 ml of acetone, 350 mg (2.86 mmol) of 4-ethylphenol, and 1.36 g of anhydrous $K_2CO_3$ was stirred vigorously at room temperature for 15 h. Isolation of the product by extraction[8] with pentane, followed by fractional distillation, afforded 506 mg (66%) of JH-25 (**6**): bp 120–140 °C (bath temperature, 0.05 mm); >97% pure by VPC analysis,[9] oven temperature 225 °C, $E/Z$ ratio 75/25, retention times 8.2 ($Z$), 9.4 min ($E$); $\nu_{max}$ (film) 1665 (C=C), 1610, 1578, 1505, 1240, 1225, 1167, 1105, 1065, 1000, 950, 817 cm$^{-1}$; $\delta_{Me_4Si}$ ($CCl_4$) 6.81 (AB quartet, 4 aryl H, peaks at 7.05, 6.91, 6.74, 6.59), 5.43 (t, $J$ = 6 Hz, C=CH), 4.43 (doublet, $J$ = 6 Hz, $CH_2OAr$), 3.27 (quartet, $J$ = 7 Hz, $OCH_2CH_3$), 2.56 (quartet, $J$ = 7 Hz, $ArCH_2CH_3$), 1.77 ("$Z$" vinyl $CH_3$), 1.71 (s, "$E$" vinyl $CH_3$), 1.09 (s, 6 H, geminal $CH_3$'s), 1.08 ppm (t, $J$ = 7 Hz, 2 $CH_3$).

**Registry No.—1,** 110-93-0; **2,** 51079-72-2; **3,** 57762-04-6; **4,** 123-07-9; **5,** 51079-70-0; ($E$)-**6,** 52730-76-4; ($Z$)-**6,** 57762-05-7; **9,** 57762-06-8; PBr, 7789-60-8.

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(7) The *E/Z* ratio was determined by integration of the signals for the vinyl methyl group. Chemical shift data for vinyl methyls in similar functionalized trisubstituted olefins have been previously reported. See R. B. Bates and D. M. Gale, *J. Am. Chem. Soc.*, **82**, 5749 (1960); K. Ogura, T. Nishino, T. Koyama, and S. Seto, *ibid.*, **92**, 6036 (1970).

(8) Reactions were carried out under a nitrogen atmosphere. Unless indicated otherwise, the isolation of reaction products was accomplished by pouring the mixture into water or saturated brine and extracting thoroughly with the specified solvent. The combined extracts were washed with 1 M aqueous NaOH and saturated brine, and dried over anhydrous magnesium sulfate. The solvent was removed from the dried extracts by using a rotary evaporator under reduced pressure. Evaporative distillation refers to bulb-to-bulb (Kugelrohr) short-path distillation. The NMR spectra were recorded with a Varian A-60 NMR spectrometer and infrared spectra were obtained using a Beckman Acculab 1 spectrophotometer. Microanalyses were performed by Micro-Tech Laboratories, Inc., Skokie, Ill.

(9) A 6 ft × 0.125 in. SE-30 column was used for this analysis.

(10) Resolution of the signal peaks between $\delta$ 5.29 and 4.85 was not sufficient to allow a simple determination of $J_{AB}$ and the chemical shifts for these two protons.

(11) When the reaction was run at −5 °C, the yield of crude bromide **5** was 79%, and none of the tertiary vinyl bromide **9** could be detected in the product.

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## Substitution at Phosphorus. The Unusual Effect of the Lithium Ion

W. S. Wadsworth, Jr.,* and R. L. Wilde

*Department of Chemistry, South Dakota State University, Brookings, South Dakota 57006*

*Received September 23, 1975*

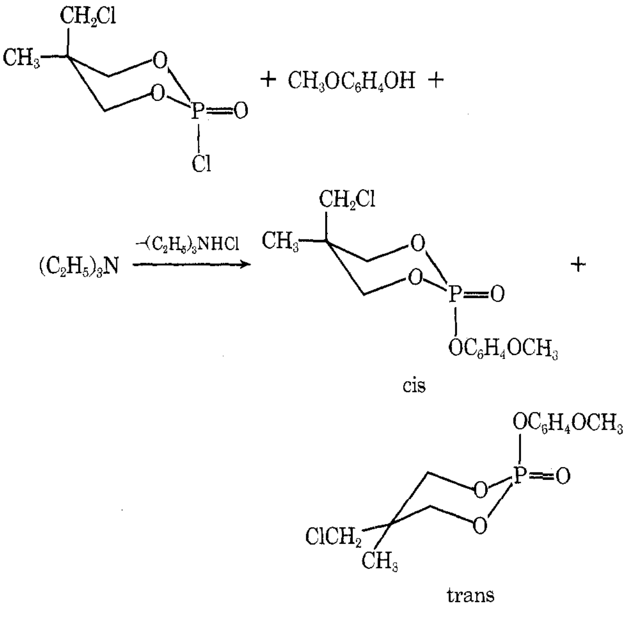
In previous papers we have shown that nucleophilic substitution at phosphorus in phosphates is strongly influenced by added cations.[1,2] We wish to report additional observations in this area and present a possible rationalization for them. As before, the conformationally immobile 2-substituted 5-chloromethyl-5-methyl-2-oxo- or 2-thio-1,3,2-dioxaphosphorinan systems were employed as substrates.[3] Inversion or retention at phosphorus upon substitution can conveniently be determined by NMR spectroscopy. Hydrogens on groups at the 5 position have different chemical shifts depending upon whether they are axial or equatorial.[4]

Table I

| | Solvent | Added salt | Retention, % | Inversion, % |
|---|---|---|---|---|
| a | $CH_3CN$ | O | 8.8 | 91.2 |
| b | $CH_3CN$ | $LiClO_4$ (1 equiv) | 96.1 | 3.9 |
| c | $CH_3CN$ | $Mg(ClO_4)_2$ (1 equiv) | 0 | 100 |
| d | $CH_3CN$ | $KClO_4$ (1 equiv) | 0 | 100 |
| e | Benzene | O | 40.8 | 59.2 |
| f | $CH_3CN$ | $LiClO_4$ (½ equiv) | 88.3 | 11.7 |
| g | Tetrahydrofuran | $LiClO_4$ (1 equiv) | 78.6 | 21.4 |
| h | $CH_3CN$ | $(C_2H_5)_3N^+CH_2$-$C_6H_5Cl^-$ (1 equiv) | 38.4 | 61.6 |
| i | $CH_3CN$ | $(C_2H_5)_3N^+CH_2$-$C_6H_5Cl^-$ (1 equiv) + $LiClO_4$ (1 equiv) | 94.5 | 5.5 |
| j | $CH_3CN$ | LiCl (1 equiv) | 87.5 | 12.5 |

We have found that we can control the stereochemical pathway in at least one system (Scheme I) by the judicious selection of the cation, Table I.

Scheme I



The combined product yields are greater than 90% with the product ratio unaffected by work-up procedures. The small yield of minor isomer in those cases where it is obtained may be due to prior isomerization of starting material by chloride ion formed as by-product. Thus, under identical reaction conditions the phosphorochloridate is slowly isomerized by slightly soluble triethylammonium chloride with 3 days required to establish equilibrium. In contrast substitutions are over in a matter of minutes. Prior isomerization would be expected in h where a soluble quaternary chloride is employed.

Strangely, the starting phosphorochloridate does not isomerize when triethylamine is added to acetonitrile or chloroform solutions. This behavior contrasts with the action of pyridine, which promotes almost istantaneous isomerization and heat evolution. The products are stable under reaction conditions. The ratios are unaffected upon addition of product to acetonitrile–triethylamine–salt mixtures, evidence that product formation is kinetically controlled.

Without added salt, inversion predominates and is apparently aided by the ammonium salt formed as a by-product. Indeed, in the case of a less polar solvent, benzene, in which the by-product is less soluble and effective than in acetonitrile, retention competes. The ability of cations, other than lithium ion, to promote the inversion route is apparent from c and d. As pointed out in a previous publication,[1] tetramethylammonium and sodium salts have an effect on the mode of substitution which is similar to that of the soluble potassium and magnesium salts included in Table I.

Surprisingly, added lithium ion in the form of its soluble salts effects substitution in a manner directly opposite to that of other cations tested; retention is nearly 100%, b. The unusual effect of the lithium ion is further demonstrated by its ability to overcome any possible effect exerted by an added soluble salt, i. It is effective in less than equivalent concentrations, f, and although diminished, its ability to divert the reaction to retention prevails in a solvent in which it would be expected to be at least partially solvated, g, or sparingly soluble, j. From spectral data, ir and NMR, we can find no evidence of bonding between substrate and cation. Spectra taken in acetonitrile are essentially identical irrespective of the salt added. Thus added cations listed in Table I most likely exert their influence during the course of the substitution and do not alter the structure of the reactant.

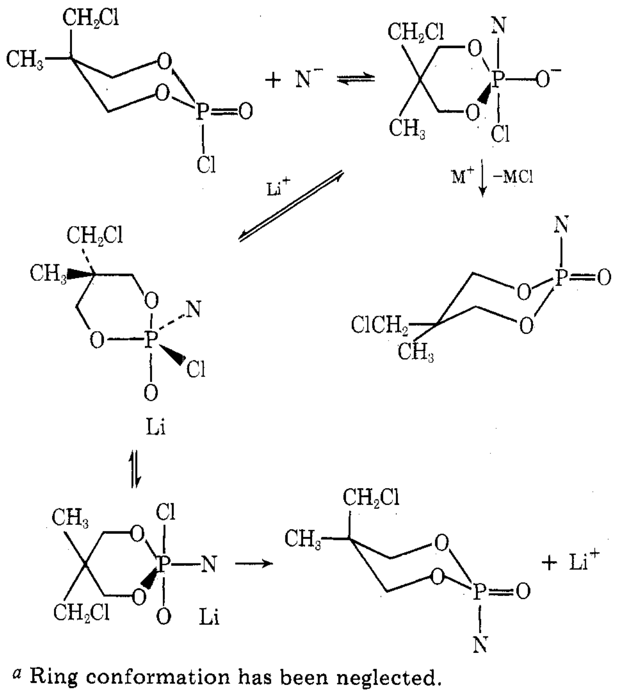
To explain our observations we propose a scheme which is a modification of our original and similar to that recently put forth by others (Scheme II).[5] We assume two competing pathways. Cations, other than lithium, act as electrophiles toward the chloride ion aiding its departure and inversion. It is not unlikely that the catalyzed inversion process entails partial bond breakage prior to complete bond formation and that a formal trigonal bipyramid intermediate may not form.

In the absence of cation effects, the retention pathway via pseudorotational permutations of the initially formed intermediate is of lower energy. Singly bonded oxygen has a preference for an equatorial position, a condition met for all three alkoxy groups by the retention pathway.[6] Lithium ion, with its affinity toward oxygen and small ionic radius, may bond with negatively charged oxygen thereby enhancing the preference for an axial position by the original phosphoryl oxygen. Further, as a consequence of bonding with lithium, the P–O bond may be lengthened and P–Cl bond strengthened[7] thereby reducing the effectiveness of extraneous cations and rendering the inversion pathway less favorable.

We have observed that the influence of lithium ion is independent of the leaving group. Either pure cis or trans 2-*p*-nitrophenyl esters in the presence of lithium ion undergo substitution predominantly by retention whereas in the presence of other salts, both geometric isomers of the product are produced with that from inversion in excess. In those cases where inversion is the only pathway, i.e., methanolysis of the starting phosphorochloridate, the lithium ion is unique in its ability to effect a sharp decrease in the substitution rate.[8] The fact that inversion is the only pathway for solvolysis may reflect the ability of a protic solvent to aid in the removal, by means of hydrogen bonding, of the chloride ion.

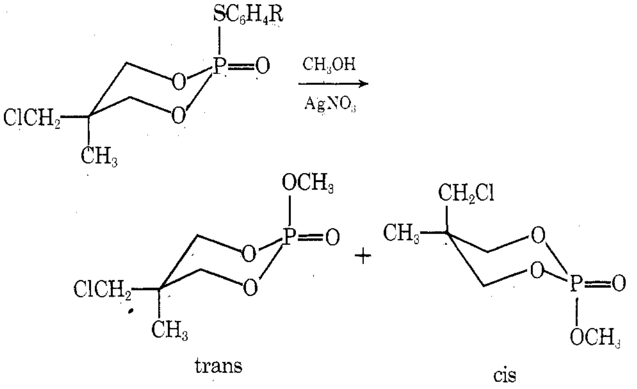
Of further possible bearing is our observation that *trans*-2-thiophenyl-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan undergoes substitution completely via retention, a situation which prevails in the absence of salts or in the presence of those cations which are not expected to coordinate strongly to sulfur.[9] Only the trans methyl ester[10] is produced (Scheme III) with its rate of formation dependent upon the substituent, R, in a predictable manner. In the presence of silver or mercury salts, however, where coordination between cation and leaving group is a possibility, the cis methyl ester, produced via inversion, predominates.[8] Thus, as we propose, there is a distinct possibility that coordination of cations with leaving groups promotes inversion whereas in the absence of such effects, retention is favored.

Scheme II[a]



[a] Ring conformation has been neglected.

Scheme III



## Experimental Section

**General.** NMR spectra were recorded on a Varian A-60A spectrometer with deuteriochloroform as solvent and tetramethylsilane as an external standard. Isomer ratios were obtained by interpretation of peaks due to hydrogens on either axial or equatorial 5-methyl groups; axial $CH_3$ 1.29 ppm, equatorial $CH_3$ 0.97 ppm.

**Starting Materials.** The phosphorochloridate was prepared as previously described[4] and recrystallized ($CCl_4$) just prior to use. Before their employment, salts were thoroughly dried and stored under anhydrous conditions. *p*-Methoxyphenol was the reactant of choice owing to the ease of product work-up. Other nucleophiles including phenol gave similar results under the various conditions.

**2-*p*-Methoxyphenoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan.** A solution of phosphorochloridate (2.18 g, 0.01 mol) and lithium perchlorate (1.06 g, 0.01 mol) in 10 ml of dried, freshly distilled acetonitrile was added to a solution of *p*-methoxyphenol (1.24 g, 0.01 mol) and triethylamine (1.01 g, 0.01 mol) in 10 ml of the same solvent. The solution was stirred at room temperature for 2 h and added to 200 ml of $H_2O$. The crystalline solid was removed by suction filtration, washed well with water, and dried. The product was recrystallized from carbon tetrachloride without undergoing a change in isomers ratio, 2.65 g (92.7%), 96.1% cis, 3.9% trans.

Anal. Calcd for $C_{12}H_{16}ClO_5P$:[11] C, 50.35; H, 5.59; Cl, 12.24. Found: C, 50.46; H, 5.52; Cl, 12.38.

This procedure is typical of those used to obtain the ratios of Table I.

**Registry No.**—*cis*-2-*p*-Methoxyphenoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 36912-31-9; *trans*-2-*p*-methoxyphenoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan 36912-32-0; *trans*-2-chloro-5-(chloromethyl)-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 28097-07-6; *p*-methoxyphenol, 150-76-5; $LiClO_4$, 7791-03-9; $Mg(ClO_4)_2$, 13770-16-6; $KClO_4$, 7778-74-7; $(C_2H_5)_3N^+CH_2C_6H_5Cl^-$, 56-37-1; *trans*-2-thiophenyl-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 36912-44-4; *trans*-2-methoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 36912-27-3; *cis*-2-methoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 28097-12-3.

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(2) W. S. Wadsworth, Jr., and Y. Tsay, *J. Org. Chem.*, **39**, 984 (1974).

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(7) The fact that $Mg^{2+}$ does not parallel the lithium ion in its effect may be due to its higher coordination number. No attempt was made to remove waters of coordination from the salt.

(8) Unpublished results.

(9) Our original observation, ref 4, of substitution with 100% retention in the case of *S*-phenyl phosphorothioates has recently been extended to a similar *S*-alkyl system: T. D. Inch, G. J. Lewis, R. G. Wilkenson, and P. Watts, *J. Chem. Soc., Chem. Commun.*, 500 (1975).

(10) The NMR spectra of the methyl esters and their preparation by another route has been reported, ref 4.

(11) Analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

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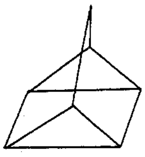
# Addition of Lithium Iodide to a Strained Carbon–Carbon $\sigma$ Bond. In Situ Protonation, Methylation, and Benzylation of the Adduct

Gerald F. Koser* and Attila G. Relenyi

*Department of Chemistry, The University of Akron, Akron, Ohio 44325*

*Received September 22, 1975*

Tetracyclo[3.2.0.0$^{2,7}$.0$^{4,6}$]heptane (1) has emerged as a useful substrate for the study of nucleophilic additions to strained carbon–carbon $\sigma$ bonds. When electrophilic substituents are attached at C-1, the 1–7 bond becomes vulnerable to nucleophilic cleavage, under mild reaction conditions.[1a,b,2,3] It seems likely that such reactions proceed through nortricyclyl anions of general structure 2, their ease of formation being determined by the ability of the attached group X to stabilize adjacent negative charge.[2] However, until now those anions have been intercepted only by protonation, even when acetonitrile was the sole proton source.[3] This research was initiated with the objective of trapping 2 with alkylating agents, and, to that end, the iodide opening of 1-carbomethoxyquadricyclene (3) was chosen as a model reaction.



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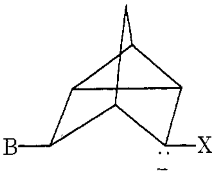

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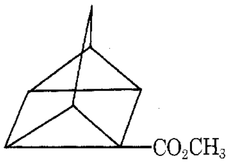

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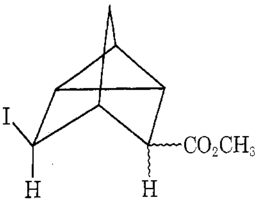

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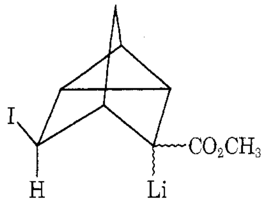

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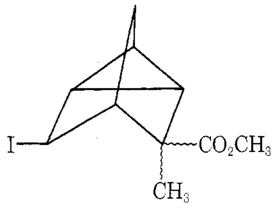
Our first task, then, was to demonstrate the feasibility of 1–7 bond cleavage in 3 by iodide ion, and, accordingly, 3 was allowed to react with lithium iodide in acetonitrile. Following work-up, a 43% yield of crude 3-carbomethoxy-5-iodonortricyclene (4), epimeric at C-3, was obtained.[4] The structure of 4 was inferred from its elemental composition and spectra (ir, near ir, NMR). Specifically, the 60-MHz $^1$H NMR spectrum of 4 displays a complex 7 H multiplet at high field, a carbomethoxy singlet at $\delta$ 3.67, and a pair of broad singlets at $\delta$ 3.92 and 4.10 which we assign to H-5 of the individual epimers.

It seems likely that 3-lithio-3-carbomethoxy-5-iodonortricyclene (5) is an *intermediate* in the above reaction. Indeed, a successful in situ methylation of 5 has been achieved. When a solution of 3 in THF was added dropwise to a solution of lithium iodide in iodomethane–THF, a mild, exothermic reaction ensued. Following work-up, a 74% yield of *crude* 3-methyl-3-carbomethoxy-5-iodonortricyclene (6) was obtained as a yellow oil. Unfortunately, while 4 is stable in air, 6 rapidly turns green, and the precipitation of a black, amorphous solid follows. The 60-MHz $^1$H NMR spectrum of 6 is similar to that of 4 except that it exhibits a carbon-bound methyl singlet at $\delta$ 1.23. However, we have been unable to obtain a *completely* satisfactory $^1$H NMR spectrum of 6. The carbomethoxy singlet invariably



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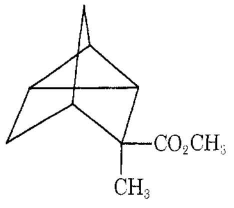

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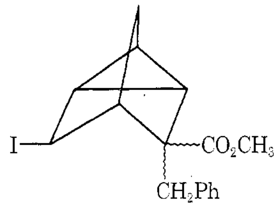

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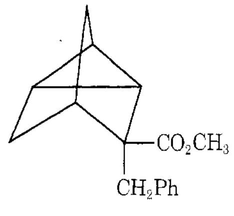

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