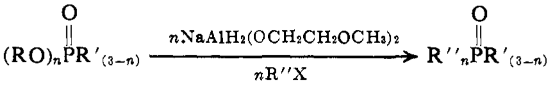
A Convenient Procedure for the Synthesis of Phosphorus–Carbon Bonds Using Sodium Bis(2-methoxyethoxy)aluminum Hydride

Sir:

While attempting to improve yields in the previously reported hydride reduction of phosphinates[1] by using sodium bis(2-methoxyethoxy)aluminum hydride[2] instead of $LiAlH_4$, we have discovered a useful, general method for forming carbon–phosphorus bonds. This method involves initial reaction of a phosphorus ester (phosphate, phosphonate, or phosphinate) with the hydride reagent to form an intermediate which subsequently reacts with an alkyl halide to form new carbon–phosphorus bonds. In the scheme below, R′ may be alkyl or aryl, and R′′ may be a primary or secondary alkyl halide.

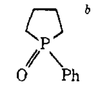
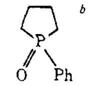
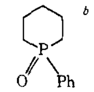


$$(RO)_n\overset{\overset{\displaystyle O}{\|}}{P}R'_{(3-n)} \xrightarrow[nR''X]{nNaAlH_2(OCH_2CH_2OCH_3)_2} R''_n\overset{\overset{\displaystyle O}{\|}}{P}R'_{(3-n)}$$

The examples listed in Table I illustrate the generality of the method. The yields are comparable to those obtained in syntheses involving attack on phosphates, phosphonates, and phosphinates by Grignard reagents.[3] The new reaction has several advantages over the Grignard synthesis, the chief one of which is its experimental simplicity. All the solutions involved in the reaction are homogeneous and easily handled. The reducing agent is available commercially at reasonable cost.[2] The work-up is simple and fast, and the conditions are very mild. In contrast to the Grignard synthesis, the new hydride–halide reactions generally proceed smoothly with 1 : 1 molar ratios of reactants. Since some workers have encountered difficulties in attempting to carry out reactions with particular Grignard reagents or particular leaving groups on phosphorus, the new reaction offers a promising complement to the procedure using Grignard reagent.

The procedure used to prepare benzylmethylphenylphosphine oxide is illustrative of the method. To a stirred solution of 1.60 g (9.4 mmol) of methyl methylphenylphosphinate in 150 ml of dry tetrahydrofuran (THF) at 65°, under nitrogen, was added dropwise over a period of 25 min a solution of 11.3 mmol of $NaAlH_2(OCH_2CH_2OCH_3)_2$[4] in 50 ml of dry THF. Vigorous bubbling due to the evolution of hydrogen occurred throughout the addition. When all the hydride solution had been added, stirring was continued several minutes until bubbling stopped; then a solution of 1.42 g (11.3 mmol) of benzyl chloride in 15 ml of THF was added. The solution, which became cloudy with NaCl after several minutes, was stirred at 65° for 3 hr. Hydrolysis of the stirring reaction mixture at 25° with a minimum amount of water (1–2 ml), followed by filtration (and a wash of the aluminum salts with 50 ml of $CHCl_3$, which was added to the filtrate) and removal of solvent, gave an impure white solid which, upon crystallization from hexane–benzene, gave 1.13 g (52% yield based on phosphinate) of benzylmethylphenylphosphine oxide.

Table I

Reactants	Product	% yield[a]
$PhCH_3P(O)OCH_3$, $PhCH_2Cl$	$PhCH_3P(O)CH_2Ph$[b]	52
$PhCH_3P(O)OCH_3$, CH_3CH_2Br	$PhCH_3P(O)CH_2CH_3$[c]	41
$PhCH_3(O)OCH_3$, $(CH_3)_2CHBr$	$PhCH_3P(O)CH(CH_3)_2$[c,d]	17
$PhCH_2(O)P(OCH_2CH_3)_2$, $CH_3(CH_2)_3Br$	$PhCH_2(O)P(CH_2CH_2CH_2CH_3)_2$[c,e]	23
$(CH_3CH_2O)_3PO$, $PhCH_2Cl$	$(PhCH_2)_3PO$[b]	16
$Ph(CH_3CH_2O)P(=O)$-$(CH_2)_4Br$[c,f]	 [b]	27
$PhP(=O)(OCH_2CH_3)_2$, $Br(CH_2)_4Br$	 [b]	11
$Ph(CH_3CH_2O)P(=O)$-$(CH_2)_5Br$[c,f]	 [b]	28
$PhCH_3P(O)OCH_3$, H_2O	$PhCH_3P(O)H$[c,g]	52
$PhCH_3P(O)H$, $PhCH_2Cl$	$PhCH_3P(O)CH_2Ph$[b]	51

[a] All yields are based on isolated product. [b] Consistent with spectral data plus previously reported melting point and/or boiling point. [c] Consistent with spectral data, plus elemental analysis or accurately measured parent ion in mass spectrum. [d] Bp 88–91° (0.1 mm). [e] Mp 57–60°. [f] Prepared by Arbuzov reaction of the appropriate dibromide with diethyl phenylphosphonite; products were at least 90% pure but decomposed on attempted distillation. [g] Bp 104° (0.6 mm).

This procedure is readily modified at little cost either to yield or procedural simplicity. Benzene, toluene, and glyme were found to give comparable yields, although the use of the lower boiling THF is advantageous in the work-up. Temperatures as low as 0° and as high as 80° have been used to effect the initial hydride reaction. Because sodium bis(2-methoxyethoxy)aluminum hydride attacks phosphorus esters preferentially to alkyl halides, the latter may be present in solution during hydride addition. This was made use of in effecting the cyclization reactions of the phosphinates. The presence of alkyl halide during hydride addition was in fact essential to the conversion of triethyl phosphate to tribenzylphosphine oxide.

It seems likely that the reaction is proceeding by way of an intermediate sodium salt of a phosphorus anion, similar to the sodium dialkylphosphates used in the Michaelis-Becker reaction.[5] After displacement of

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(1) L. Horner and H. Hoffmann, *Chem. Ber.*, **91**, 1583 (1958); several hours' reflux of an ether solution of phosphinate or phosphonate with excess $LiAlH_4$ gave about a 50% yield of the corresponding phosphine.

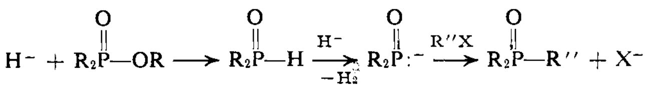
(2) Sodium bis(2-methoxyethoxy)aluminum hydride is available commercially under the names Vitride (Eastman Organic Chemicals Co.) and Red-Al (Aldrich Chemical Co.). For a discussion of the many applications of this new reagent, see the Eastman Organic Chemical Bulletin, Vol. 42, No. 3, Kodak Publication No. JJ60-703, Rochester, N. Y., 1970, p 1.

(3) For a review, see K. D. Berlin, T. Austin, M. Peterson, and M. Nagabhushanam, *Top. Phosphorus Chem.*, 1, 17 (1965). For a recent application in the preparation of optically active phosphine oxides, see O. Korpium, A. Lewis, J. Chickos, and K. Mislow, *J. Amer. Chem. Soc.*, 90, 4842 (1968).

(4) The reducing agent is sold commercially as a 70% solution in benzene. We have found it advisable to use a slight excess (1.1 or 1.2 to 1.0 molar ratio) of the hydride reagent. Although solutions of the reagent are easily standardized, we found it sufficient to weigh the reagent, assuming it to be a 70% solution.

(5) Reactions with alkyl halides by $R(R'O)P(O)Na$ [G. M. Kosolapoff, *J. Amer. Chem. Soc.*, **72**, 4292 (1950)] to give phosphinates, and by $RR'P(O)Na$ [A. K. Hoffmann and A. G. Tesch, *ibid.*, **81**, 5519 (1959)] to give phosphine oxides, have been reported.

alkoxide with hydride, a second hydride, acting as a base, presumably pulls off the new, relatively acidic proton on phosphorus, forming the sodium dialkylphosphine oxide.[6,7] This would then react with



$$H^- + R_2\overset{O}{\overset{\|}{P}}-OR \longrightarrow R_2\overset{O}{\overset{\|}{P}}-H \xrightarrow[-H_2]{H^-} R_2\overset{O}{\overset{\|}{P}}:^- \xrightarrow{R''X} R_2\overset{O}{\overset{\|}{P}}-R'' + X^-$$

the alkyl halide in a nucleophilic substitution to give phosphine oxide and sodium halide.[5] The last two entries in Table I support this mechanism.

Some attempts have been made at improving the yields of certain of the reactions reported; further work in this area is now in progress. We are also attempting to extend the reaction to other phosphorus systems[8] and are investigating the reaction mechanism in greater detail.

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(6) It has been shown that the reaction of R(R′O)P(O)H with R′′X and sodium hydride in dimethylformamide gives R(R′O)P(O)R′′ [W. B. Farnham, R. K. Murray, Jr., and K. Mislow, *J. Amer. Chem. Soc.*, **92**, 5809 (1970)].

(7) It appears that the situation may be somewhat more complex in the reactions of phosphonates and phosphates.

(8) For example, it may be possible, by starting with the appropriate dialkyl dibromoalkylphosphonates, to prepare the elusive bicyclics, 1-phosphabicyclo[2.2.1]heptane and 1-phosphabicyclo[2.2.2]octane.

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The Thermal Gas-Phase Partitioning of 1-Methyl- and 2-Methylbicyclo[2.1.0]pent-2-ene

Sir:

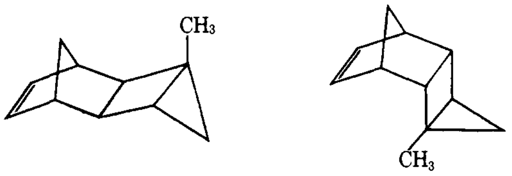
The facile thermal isomerization of bicyclo[2.1.0]-pent-2-ene to cyclopentadiene[1-5] was originally thought to occur through a disrotatory and orbital symmetry disallowed diradical mediated process.

Consideration of alternative mechanisms led us to deuterium labeling experiments, demonstrating that the C-5 methylene group remained intact during the isomerization,[6] and to the discovery that 2-methylbicyclo[2.1.0]pent-2-ene rearranges directly to 1-methylcyclopentadiene.[7] This result, wholly inexplicable by diradical mechanisms, was interpreted through a $[{}_\sigma 2_s + {}_\sigma 2_a]$ symmetry-allowed mechanistic formulation.

The latter finding has been challenged by McLean and Findlay,[8] and the rearrangement course has thus been left open to question.[9]

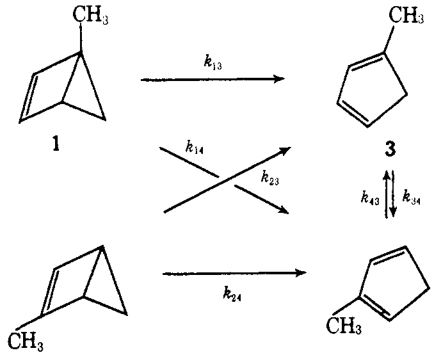
We now report the first isolation of 1-methylbicyclo-[2.1.0]pent-2-ene and gas-phase kinetic work on both 1- and 2-methylbicyclopentene. The results provide grounds for delimiting the mechanistic controversy.

Photolysis of the isomeric methylcyclopentadienes and isolation of the bicyclic products[10] gave a mixture of 2-methylbicyclo[2.1.0]pent-2-ene and the previously undetected 1-methyl isomer, having nmr absorptions in $CDCl_3$ at δ 6.2 (2 H, J_{AB} = 2 Hz), 2.2 (1 H, m), 1.8 (1 H, m), 1.5–1.4 (1 H, m), and 1.47 (3 H, s). The 1-methyl isomer was thermally convertible to methylcyclopentadienes, and reacted with cyclopentadiene to give both exo,anti and endo,anti isomers of 3-methyltetracyclo[5.2.1.0^{2,6}.0^{3,5}]dec-8-ene.[11]



The 1-methyl isomer is much more prone to isomerization during glpc collection than 2-methylbicyclopentene but, with adequate care, it may be obtained uncontaminated by isomeric materials.

Kinetic data for the gas-phase thermal equilibration of bicyclics **1** and **2**, and of dienes **3** and **4**, were obtained at 50°, using glpc on a 0.3 × 600 cm aluminum column packed with β,β'-oxydipropionitrile on non-acid-washed Chromosorb P as the analytical method. Three or more runs with each of the four starting materials and with various reaction flasks gave results sufficiently reproducible to discount vagrant catalytic effects. Three runs with bicyclo[2.1.0]pent-2-ene gave $k = (1.39 \pm 0.02) \times 10^{-4}$ sec^{-1}, which may be compared with 1.1×10^{-4} sec^{-1} interpolated from data obtained by others[3,4] using an ultraviolet method. All kinetic data could be fit to a scheme involving partitioning of both methyl-labeled bicyclics to both methylcyclopentadienes; the numerical values for the rate constants are given in Table I.



The interconversion of 1-methyl- and 2-methylcyclopentadiene is so slow relative to the isomerizations of **1** and **2** that accurate measurements of the kinetically controlled product distribution may be readily obtained. The partitioning ratios $k_{13}/k_{14} = 1.6$ and $k_{24}/k_{23} = 1.3$ are remarkably similar. The total spread in rate constants for isomerizations from the bicyclics is only a factor of 5.4; unlabeled bicyclopentene falls within

(1) J. I. Brauman, L. E. Ellis, and E. E. van Tamelen, *J. Amer. Chem. Soc.*, **88**, 846 (1966).

(2) E. E. van Tamelen, L. E. Ellis, and J. I. Brauman, *ibid.*, **89**, 5073 (1967).

(3) J. I. Brauman and D. M. Golden, *ibid.*, **90**, 1920 (1968).

(4) D. M. Golden and J. I. Brauman, *Trans. Faraday Soc.*, **65**, 464 (1969).

(5) E. E. van Tamelen, J. I. Brauman, and L. E. Ellis, *J. Amer. Chem. Soc.*, **93**, 6145 (1971).

(6) J. E. Baldwin, R. K. Pinschmidt, Jr., and A. H. Andrist, *ibid.*, **92**, 5249 (1970).

(7) J. E. Baldwin and A. H. Andrist, *Chem. Commun.*, 1561 (1970).

(8) Private communication.

(9) Reference 5, footnote 15.

(10) A. H. Andrist, J. E. Baldwin, and R. K. Pinschmidt, Jr., *Org. Syn.*, in press.

(11) *Cf.* J. E. Baldwin and R. K. Pinschmidt, Jr., *J. Amer. Chem. Soc.*, **92**, 5247 (1970).