

ACTIVATION OF METHYLENETRIPHENYLPHOSPHORANE
BY REACTION WITH t-BUTYL- OR sec-BUTYL LITHIUM

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Summary: Experimental details are provided to support a previous report that α -methylene triphenylphosphorane (1) may be activated for reaction with unreactive substrates such as epoxides and hindered ketones by α -metallation to 2.

It has recently been discovered in this laboratory¹ that methylene triphenylphosphorane (1) reacts with t-butyllithium or sec-butyllithium to form a more reactive reagent which is capable of transforming certain substances which do not react with methylene triphenylphosphorane to products that could be explained by the formulation of the reagent as α -lithio methylene triphenylphosphorane (2). Thus fenchone (3) was methylenated to form 4 (87% yield) by the lithiated ylide reagent whereas there was no appreciable conversion of 3 to 4 under the same conditions using methylene triphenylphosphorane as the reagent. Cyclopentene oxide was attacked by the reagent to generate a new ylide (5) which underwent further coupling with benzaldehyde to form the E homoallylic alcohol 6 in 65% yield. Control experiments showed that cyclopentene oxide was unreactive to methylene triphenylphosphorane (1) under the same conditions.

The conversion of fenchone to 4 and cyclopentene oxide to 6 can easily be understood on the basis that the reactive (i.e., activated) reagent is the α -lithio ylide 2.

The same reactions have been observed by the use of a reagent generated from bromomethyltriphenylphosphonium bromide (7) by successive reaction with (a) potassium t-butoxide in tetrahydrofuran (to form bromomethylene triphenylphosphorane (8)²) and (b) t-butyllithium. The essentially similar behavior of the reagent generated from 1 and 8 is also most simply interpreted in terms of structure 2 for the effective reagent.

Recently Schlosser et al.³ have reported that "despite all attempts to repeat the work of Corey and Kang, we were unable to confirm the yields claimed by these authors." They also report the occurrence of some α -metallation upon reaction of 1 with organolithium reagents.

The experimental results reported by Corey and Kang have been reproduced without difficulty in these laboratories, most recently by one of us (K.K.). In this note we provide experimental detail on the crucial results of the earlier publication.^{1, 4, 5}

Synthesis of 4 from 1: To 535 mg (1.5 mmol) of finely powdered methyltriphenylphosphonium bromide (azeotropically dried with 3 x 5 ml portions of toluene) in 6 ml of anhydrous ether at 0° under a nitrogen atmosphere was added dropwise over a 15 min period 0.89 ml (1.5 mmol) of 1.69 M n-butyl-lithium. After stirring for 10 min at 0° and 40 min at 23° the yellow solution was cooled to -78° and treated with 0.73 ml (1.5 mmol) of 2.05 M t-butyl-lithium. The heterogeneous orange reaction mixture was stirred for 2.5 h at 23° and cooled to -20°. (-)-Fenchone (3) (152 mg, 1.0 mmol) was then added followed by 3.4 ml of hexamethylphosphorictriamide (HMPA). The deep red mixture was maintained at -20° for 2 h, then treated with 9.4 ml of t-butyl alcohol and stirred for an additional 10 h at 23°. The reaction mixture was quenched by the addition of 5 ml of water. Extractive workup followed by silica gel chromatography (pentane) afforded 126.6 mg (84.4%) of the methylenated product 4, shown to be homogeneous by pmr, infrared and tlc analysis.

Synthesis of 4 from 8: To 654 mg (1.5 mmol) of bromomethyltriphenylphosphonium bromide (azeotropically dried with 3 x 5 ml of toluene) in 3 ml of anhydrous tetrahydrofuran (THF) at -78° under a nitrogen atmosphere was added 4.9 ml (1.5 mmol) of a 0.307 M solution of potassium t-butoxide (sublimed and powdered) in THF. After stirring for 1.5 h at -78°, 2.5 ml (4.5 mmol) of 1.80 M t-butyl-lithium was added dropwise over a 10 min period. The resulting orange suspension was maintained at -78° for 5 h. The mixture was warmed to -20° then 152 mg (1.0 mmol) of (-)-fenchone (3) was added followed by 3.4 ml of hexamethylphosphorictriamide. The dark red-brown mixture was maintained at -20° for 2 h, then treated with 9.4 ml of t-butyl alcohol and stirred for an additional 10 h at 23°. The reaction mixture was quenched by the addition of 5 ml of water. Extractive workup followed by silica gel chromatography (pentane) afforded 117 mg (78%) of the olefinic product 4 which was identical with 4 as described above from 1 as shown by tlc, pmr and infrared comparison.

Synthesis of 6 from 1: To 393 mg (1.10 mmol) of methyltriphenylphosphonium bromide (azeotropically dried with 3 x 5 ml portions of toluene) in 3 ml of anhydrous ether at -78° under a nitrogen atmosphere was added dropwise over a 15 min period 1.60 ml (2.30 mmol) of 1.45 M sec-butyl-lithium to furnish a yellow solution. After stirring for 10 min at -78°, 1 h at -40° and 2.5 h at 23°, the resulting orange-red suspension was cooled to 0° and a solution of 100 mg (1.20 mmol) of cyclopentene oxide in 1 ml of tetrahydrofuran (THF) was added. Stirring for 17 h at 23° furnished a yellow suspension which was cooled to -78° and treated with a solution of 106 mg (1.0 mmol) of benzaldehyde in 1 ml of THF. After stirring for 6 h at 23°, the reaction mixture was quenched by the addition of water (5 ml) and the product was isolated by extractive workup followed by silica gel chromatography (1 : 5 ether-hexane) to furnish 114.5 mg (60%) of E-homoallylic alcohol 6: ¹H-NMR (270 MHz, CDCl₃); δ 2.45 (m, 1H, allylic H), 3.92 (q, J=6.59 Hz, 1H, CH-OH), 6.10 (dd, J=8.57, 15.82 Hz, 1H, vinylic H), 6.42 (d, J=15.82 Hz, 1H, vinylic H), 7.10-7.34 (m, 5H, C₆H₅).

Synthesis of 6 from 8: To 480 mg (1.1 mmol) of bromomethyltriphenylphosphonium bromide (azeotropically dried with 3 x 5 ml portions of toluene) in 6 ml of anhydrous THF at -78° under a nitrogen atmosphere was added 1.43 ml (1.1 mmol) of a 0.77 M solution of potassium t-butoxide (sublimed and

possible that 2 and the ortho lithio ylide of 1 may interconvert in the reaction mixture. Nonetheless, it would seem that the simplest interpretation of the transformations described herein, especially in view of the essentially identical results obtained with reagents prepared from either ylide 1 or 8, involves the intermediacy of 2 as indicated previously.^{1,6}

References and Notes

1. E. J. Corey and J. Kang, J. Am. Chem. Soc., 104, 4724 (1982).
2. M. Matsumoto and K. Kuroda, Tetrahedron Letters, 21, 4021 (1980).
3. B. Schaub, T. Jenny, and M. Schlosser, Tetrahedron Letters, 25, 4097 (1984).
4. These experiments were conducted by K. Kyler following the procedures used in the earlier work¹ by J. Kang.
5. Satisfactory infrared, pmr and mass spectroscopic data were obtained for each reaction product using chromatographically purified and homogeneous samples.
6. This research was assisted financially by the National Institutes of Health and the National Science Foundation.

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