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α-HYDROXYBENZYL ANION EQUIVALENT: A CONVENIENT METHOD FOR THE SYNTHESIS OF α-HYDROXY KETONES UTILIZING α-TRIMETHYLSILYLOXYBENZYLPHOSPHONATE

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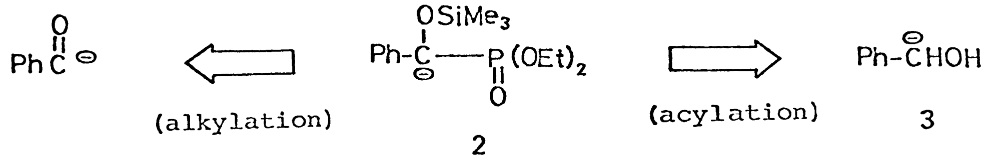
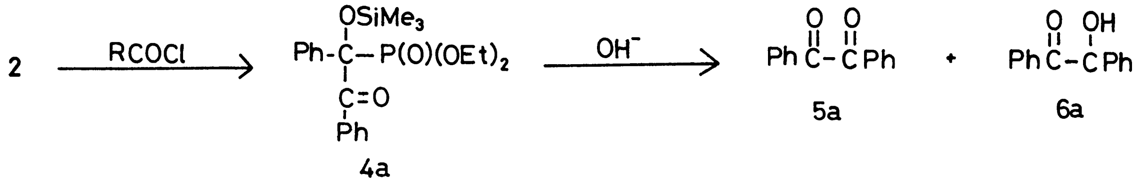
Diethyl α-trimethylsilyloxybenzylphosphonate was treated with lithium diisopropylamide in THF followed by acyl chloride or acyl anhydrides to give the acylated products in good yields. The acylated products were converted easily by mild alkaline treatment to acyloins predominantly along with α-diketones.

In a preceding paper,[1] we have reported the synthesis of unsymmetrical ketones utilizing the 1:1 carbonyl adduct (1) of diethyl trimethylsilyl phosphite and benzaldehyde. The lithio derivative (2) of 1 has proved to be a useful synthon of benzoyl anion, since 2 was easily alkylated and unsymmetrical ketones were obtained in high yields by treatment of the alkylated products with 0.2 N NaOH-EtOH (1:1, v/v). There have been a number of reports on the synthesis of α-hydroxy ketones utilizing benzoyl anion equivalents such as dithioacetals and trimethylsilyl cyanides.[2,3] These methods involve the reaction of masked benzoyl anion equivalents with carbonyl compounds followed by the successive deprotection of the carbonyl groups.

In this paper, we wish to describe a new type of synthon of α-hydroxybenzyl anion (3), i.e., α-trimethylsilyloxybenzylphosphonate anion (2).



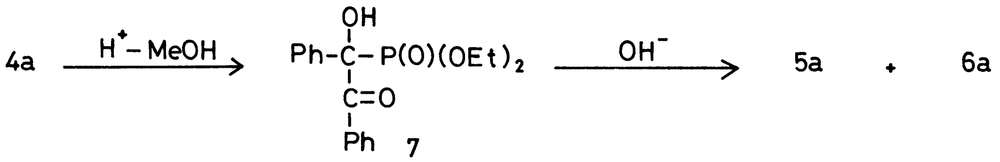
The compound 1 was treated with $[(CH_3)_2CH]_2NLi$ (1.1 equiv.) in dry THF at -78°C for 30 min, whereupon a lithio derivative 2 precipitated, and then benzoyl chloride (1.0 equiv.) was added dropwise to the solution. The mixture was kept at -78°C for 30 min and the reaction was quenched with dilute ammonium chloride solution. The solution was extracted with methylene chloride and the extracts were concentrated. The residue was subjected to a column on silica gel. Thus, a benzoylated product (4a) was obtained in 81% yield. In a similar manner, several acylated products were obtained as shown in Table I. In the acetylation, acetic anhydride gave a better yield than acetyl chloride.



In an attempt to convert 4a to benzil (5a) according to the procedure used in the unsymmetrical ketone synthesis, 4a was treated with 0.2 N NaOH-EtOH (1:1, v/v) at r. t. for 15 min.[1] The alkaline treatment, however, gave 5a only in 14% yield. The major product was found to be benzoin (6a) formed in 59% yield. Since benzil is known to be gradually autooxidized by air under mild alkaline conditions to decompose to benzoic acid, alkaline treatment was carried out under a degassed condition. Under the atmosphere of argon gas, 5a and 6a were obtained in 14% and 77% yields, respectively.

In a similar fashion to that described above, the acylated products, 4b and 4c, were treated with 1 N NaOH-EtOH (1:1, v/v) at r.t. to give thermodynamically stable α-hydroxy ketones of two isomers in 72 and 88% yields, respectively. In the case of alkaline treatment of 4d, 4e, or 4f, two kinds of α-hydroxy ketones were obtained as shown in Table I, but no α-diketones were detected.

In connection with our mechanistical interest, the trimethylsilyl group of 4a was removed by treatment with methanol in the presence of a catalytic amount of p-toluenesulfonic acid at 60°C for 2 h to afford the corresponding hydroxyphosphonate (7). When 7 was further treated with 1 N NaOH-EtOH (1:1, v/v) at r.t. for 1 min, 5a and 6a were obtained in 11 and 67% yields, respectively. This result strongly implies that the reaction giving 5a and 6a from 4a proceeds *via* compound 7. Therefore, it seems that the trimethylsilyl group is initially removed from 4a by the neighboring phosphoryl participation as described in a previous paper[1] (see Scheme I).



As to the predominant formation of 6a, there might be proposed some plausible mechanisms involving the C→O rearrangement of the phosphoryl group and/or involving the simultaneous cleavage of the P-C bond with the attack of hydroxyl ion on the phosphorus atom.[4]

Further study on the reaction mechanism is now in progress.

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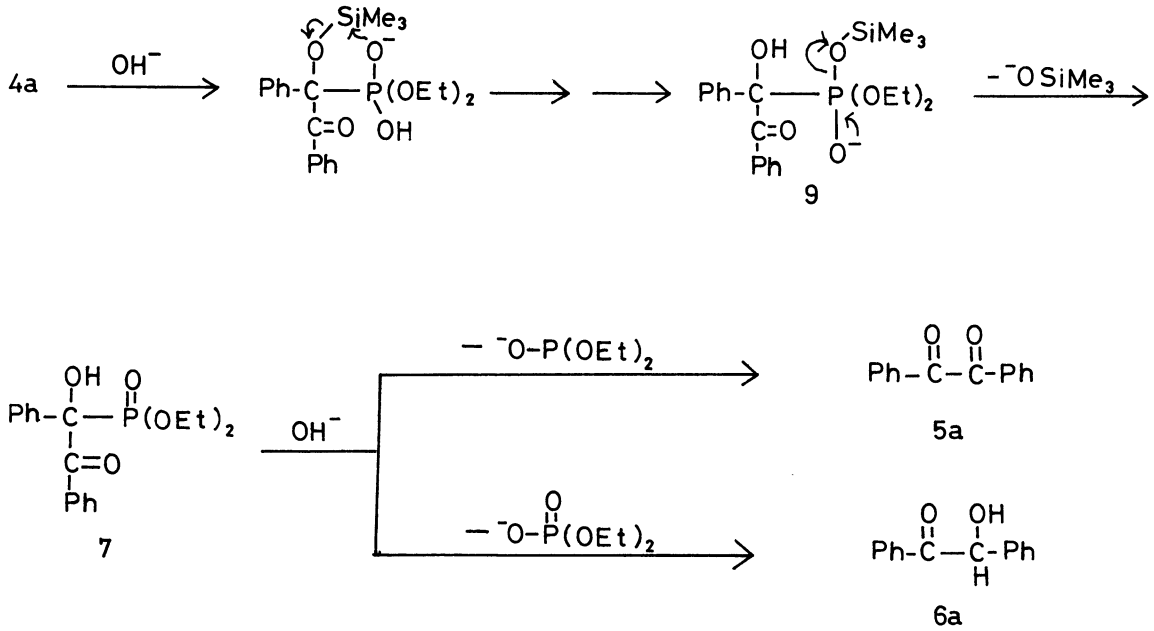
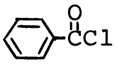
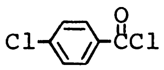
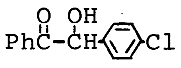
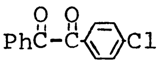
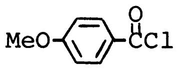
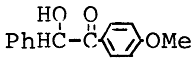
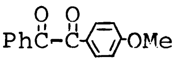


Scheme I

Table I. Acylation of diethyl 1-trimethylsilyloxybenzylphosphonate (1) and alkaline treatment of the acylated products (4)

Acylation			Alkaline Treatment of 4		
Acylating Agent	Product	Yield (%)	Time (min)	Products Yields	
	4a	81	5	$\mathrm{Ph\overset{O}{C}\text{-}\overset{OH}{C}HPh}$ 77%	$\mathrm{Ph\overset{O}{C}\text{-}\overset{O}{C}Ph}$ 8%
	4b	88	5	 72%	 10%
	4c	83	30	 88%	 4%
$\mathrm{CH_3\overset{O}{C}Cl}$	4d	44	10	$\mathrm{Ph\overset{O}{C}\text{-}\overset{OH}{C}HMe}$ 56% (1:2)	$\mathrm{PhH\overset{HO}{C}\text{-}\overset{O}{C}Me}$
$\mathrm{(CH_3\overset{O}{C})_2O}$	4d	78			
$\mathrm{[(Me)_2CH\overset{O}{C}]_2O}$	4e	74	10	$\mathrm{Ph\overset{O}{C}\text{-}\overset{OH}{C}HCH(Me)_2}$ 81% (1:1.3)	$\mathrm{PhH\overset{HO}{C}\text{-}\overset{O}{C}CH(Me)_2}$
$\mathrm{(Pr\overset{O}{C})_2O}$	4f	71	10	$\mathrm{Ph\overset{O}{C}\text{-}\overset{OH}{C}HPr}$ 66% (1:2)	$\mathrm{PhH\overset{HO}{C}\text{-}\overset{O}{C}Pr}$

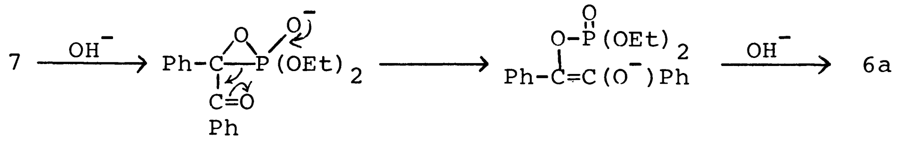
References and Notes

1) T. Hata, A. Hashizume, M. Nakajima, and M. Sekine, Tetrahedron Lett., 363 (1978).

2) For a comprehensive review, see D. Seyferth, "New Application of Organometallic Reagents in Organic Synthesis," Elsevier Scientific Pub. Co. Amsterdam, 1976.

3) O. W. Lever, Jr. Tetrahedron, 32, 1943 (1976).

4) The former is closely related to the mechanism for the Ramirez-type reaction[5] of trialkyl phosphites with α-diketones in which a similar C→O rearrangement of the phosphoryl groups has been postulated.[6]



On the other hand, only a few reactions on the P-C bond cleavage involving the later mechanism have been already reported.[7,8] Rather drastic conditions were required in the case of diethyl β-oxopropylphosphonate,[7] although the conditions depended on the α-substituents and systematic studies on the easiness of the P-C bond cleavage of such β-oxophosphonates must be done.

5) F. Ramirez, Pure and Appl. Chem., 9, 337 (1964); F. Ramirez, Bull. Soc. Chim. France, 2443 (1966); F. Ramirez, Accounts Chem. Res., 1, 168 (1968); F. Ramirez, A. V. Patwardhan, H. J. Kugler, and C. P. Smith, Tetrahedron Lett., 3053 (1966); F. Ramirez, A. V. Patwardhan, H. J. Kugler, and C. P. Smith, J. Am. Chem. Soc., 89, 6276 (1967); F. Ramirez, J. F. Pilot, O. P. Madan, and C. P. Smith, ibid., 90, 1275 (1968); F. Ramirez, Bull. Soc. Chim. France, 3491 (1970); F. Ramirez, Synthesis, 90 (1974).

6) Y. Ogata and M. Yamashita, J. Am. Chem. Soc., 92, 4670 (1970).

7) N. Kreutzkamp and H. Kayser, Chem. Ber., 89, 1614 (1956).

8) P. Nylén, ibid., 57, 1023 (1924).

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