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α-HETEROSUBSTITUTED PHOSPHONATE CARBANIONS IX(1): DIETHYL 1-PHENYL-1-TRIMETHYLSILOXYMETHANE PHOSPHONATE AS AN ACYL ANION EQUIVALENT; A NOVEL METHOD FOR THE PREPARATION OF α-HYDROXYKETONES.

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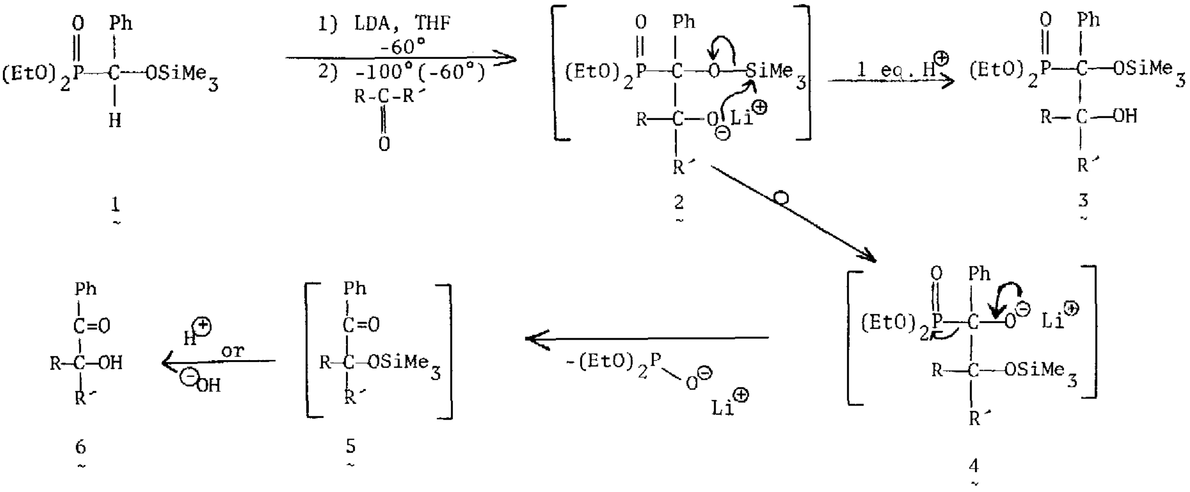
ABSTRACT: Diethyl 1-phenyl-1-trimethylsiloxymethane *phosphonate carbanion was found to react* as an effective acyl anion equivalent in the preparation of α-hydroxy ketones from aliphatic and aromatic aldehydes and ketones. A 1,4-oxygen-oxygen silicon migration was also observed.

Masked acyl anions have become important synthetic tools in organic synthesis. The most popular being the dithio acetals[3] or the O-protected cyanohydrins.[4] Recent reviews[5] on the concept of charge affinity inversion[6] or "Umpolung"[7] have appeared. The practical use of masked acyl anions imposes two general restrictions. First, that the anion precursor be an inexpensive and stable compound. Second, the unmasking of the latent carbonyl function should be easily and mildly accomplished at the end of the desired synthetic transformation in the same reaction vessel without prior isolation of an intermediate. To this end, we have applied the use of diethyl 1-phenyl-1-trimethylsiloxymethane phosphonate (1).

In a series of papers, we have described the utility of α-heterosubstituted phosphonate carbanions for the preparation of a wide variety of different classes of compounds.[8] We now wish to report the synthesis of α-hydroxy ketones utilizing the carbanion of 1 as an acyl anion equivalent. The phosphonate, 1 (B.P. = 95-6°, 0.05 mm) was prepared from triethyl phosphite, benzaldehyde, and chlorotrimethylsilane in excellent yield (94%) by a previous method.[9] In a recent paper, Hata[10] reports on the alkylation of this phosphonate carbanion with activated alkyl halides to synthesize ketones.

The synthesis of the α-hydroxy ketones (6) is outlined in Scheme I. The 1,2-adducts (2) were prepared by adding 1 to a solution of lithium diisopropylamide (LDA)[11] (THF, -60°, Argon) followed by addition of the aldehyde or ketone at -60° or -100°.[12] These 1,2-adducts 2 could only be isolated as the alcohol (3) when the electrophile was an aromatic aldehyde. In all other cases, the 1,2-adduct 2 rearranged too quickly to be seen on TLC of quenched samples drawn from the reaction flask. In agreement with recently reported results[13], it was found that lowering the initial reaction temperature from -60° to -100° led to dramatically increased yields when enolizable aldehydes or ketones were used. Thus with cyclohexanone as electrophile, a 36% yield of the corresponding 6 was obtained at -60°; at -100° the yield increased to 83%. The α-trimethylsiloxy ketones (5) could be isolated as in the case of 5 derived from benzophenone (95% yield, M.P. = 55-6°) but were usually hydrolyzed to 6 in the same reaction flask without prior work-up. The yields of 6 (Table I) are quite good. Total reaction time for the described transformation averaged three hours when base hydrolysis was employed.

Scheme I



Using diethyl 1-ethoxy-1-phenyl methane phosphonate carbanion instead of the carbanion derived of 1, products resulting from a typical Wittig-Horner reaction, namely enol ethers, have been obtained[14]. This result is in striking contrast to the one presented here for the following reason. As shown in Scheme I, 5 if formed by a 1,4-oxygen-oxygen silicon migration resulting in a lithium salt of an α-hydroxy phosphonate (4), a class of compounds which is known to fragment easily[15]. This type of silicon migration has been observed before[16]. An example of such a rearrangement is the recently reported[17] reaction sequence shown in Scheme II. The leaving group in this transformation is the cyanide ion where in this report (Scheme I) it is the lithio diethyl phosphite moiety.

Scheme II

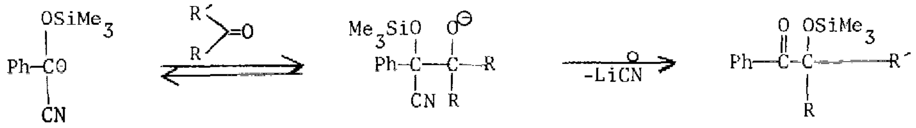
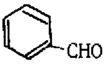
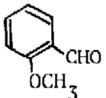
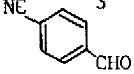
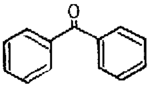
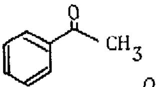
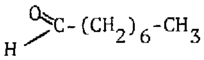
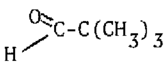


Table I

Electrophile	Alcohol 3			α-Hydroxy Ketone 6		
	%[a]	MP°C[b,c]	Mol. Formula[d]	%[a]	MP°C[c]	Mol. Formula[d]
	86	115-7	$C_{21}H_{31}O_5PSi$	91[f]	134-5.5[j]	$C_{14}H_{12}O_2$
	84	137-8.5	$C_{22}H_{34}O_6PSi$	90[f]	57-8.5[k]	$C_{15}H_{14}O_3$
	82	173-4.5	$C_{22}H_{30}NO_5PSi$	81[f,g]	112-3	$C_{15}H_{11}NO_2$
	87	114-5.5	$C_{20}H_{32}O_5PSSi$	92[f]	142-3.5	$C_{13}H_{12}O_2S$
		n.i.[e]		92[f]	82-4[l]	$C_{20}H_{16}O_2$
		n.i.[e]		91[h]	66-8[l,m]	$C_{15}H_{14}O_2$
		n.i.[e]		83[h]	43-44.5[l,m]	$C_{13}H_{16}O_2$
 $H-C(=O)-(CH_2)_6-CH_3$		n.i.[e]		95[i]	122-3(0.30mm)	$C_{15}H_{22}O_2$
 $H-C(=O)-C(CH_3)_3$		n.i.[e]		80[i]	79-80(0.30mm)[l]	$C_{12}H_{16}O_2$

a) All yields are isolated yields. b) Obtained as a mixture of diastereomers; reported M.P. is for the higher melting one. They can be separated by fractional recrystallization (Et_2O).
c) M.P. and B.P. are uncorrected. d) All C, H, N, S analyses of the compounds agree within 0.45% with the required values. In addition the compounds have been characterized by H^1NMR and IR.
e) Not isolated. f) Hydrolyzed with 2 eq. of 2N NaOH for 20 minutes room temperature. g) 15% of 4-cyanobenzil was also isolated, M.P. = 111.5-113° (T. van Es, O. G. Backeberg, J. Chem. Soc., 1963, 1371, M.P. = 108-9°). h) Hydrolyzed with 4 eq. of 2N HCl for 4 hours reflux. i) Hydrolyzed with excess 0.4N HOAc/NaOAc buffer. j) R. Adams, C. S. Marvel, Org. Synthesis, I, 94 (1941), M.P. = 129°. k) Y. Asahina, M. Terasaka, J. Pharm. Soc. Japan, 494, 219 (1923), M.P. = 58°.
l) See ref. 15, $C_{20}H_{16}O_2$ M.P. = 84°; $C_{15}H_{14}O_2$ M.P. = 66-7°; $C_{13}H_{16}O_2$ B.P.= 140(0.1mm); $C_{12}H_{16}O_2$ M.P. nor B.P. reported. m) $C_{15}H_{14}O_2$ B.P. = 132-4°, 0.30mm; $C_{13}H_{16}O_2$ B.P.= 117-8°, 0.30mm.

In summary, preliminary results on a one pot procedure for the preparation of α-hydroxy ketones via a masked acyl anion which meets both of the initially stated criteria are presented. We are presently exploring the use of α-trimethylsiloxy alkyl phosphonates to prepare α-hydroxy dialkyl ketones as well as other classes of compounds.

References and Notes

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11. Prepared in situ from diisopropylamine and n-BuLi at -60°C.
12. A -100° temperature was conveniently obtained by adding liquid N_2 to a methanol dry ice bath already at -60°C. After addition of electrophile, the solution was allowed to warm up to -60°C.
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