Registry No.—**1a**, 53-41-8; **1b**, 481-29-8; **2a**, 67010-38-2; **2b**, 67010-39-3; **3a**, 66966-84-5; **3b**, 52401-33-9; *D*-homo-5α-androstane-3β,11α-diol, 62193-45-7; *D*-homo-5α-androstane-3,7,11-trione, 62193-82-2; *D*-homo-5α-androstane-3,11,17a-trione, 66966-85-6; *D*-homo-5α-androstan-11α-ol, 35649-44-6; *D*-homo-5α-androstane-3,11,17-trione, 62193-85-5; 11α-acetoxy-*D*-homo-5α-androstane-3,17-dione, 62193-69-5; *D*-homo-5α-androstane-2,11,17a-trione, 66966-86-7; *D*-homoandrost-5-ene-3β,11α-diol, 62193-46-8; *D*-homoandrost-4-ene-3,11-dione, 62193-55-9; 3β-hydroxy-D-homoandrost-5-en-11-one, 62193-41-3; trimethyloxosulfonium iodide, 1774-47-6; sodium azide, 26628-22-8; acetic anhydride, 108-24-7.

References and Notes

(1a) We thank the Consejo de Desarrollo, U.C.V., and the Consejo Nacional de Investigaciones Cientificas y Tecnologicas (projects 305 and DF-S1-0121, respectively) for financial support. This work has been partly presented at the Asovac Conference, Puerto La Cruz, 1976. (b) Escuela de Ingenieria.

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Trianions from α-Hydroxy Carboxylic Acids

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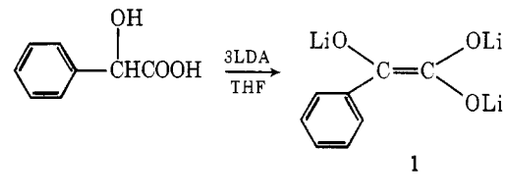
Received April 18, 1978

Polymetalated organic compounds are of both practical interest as synthetic reagents and of theoretical interest as models for charge distribution and stabilization.[1-3] The recent development and use of hindered amide bases has made many diverse types of mono- and dianions available by simple deprotonation reactions.[4-6] In this note, we wish to report the first preparation of a trianion from a substituted α-hydroxy acid (eq 1). The limitations of this procedure for forming such

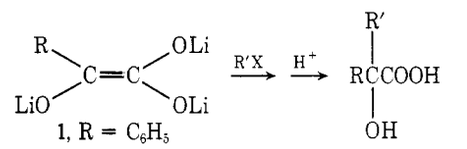


(1)

1

enetriolates have been evaluated and possible synthetic applications of these reactive intermediates have been explored. In addition, we have qualitatively compared the kinetic acidity of dilithio mandelic acid with other weak acids in an attempt to estimate the effect of an adjacent negatively charged electronegative atom on the acidity of a proton attached to the carbon.

Enetriolates like 1 are ambident nucleophiles which could react with electrophiles at either a nucleophilic carbon or oxygen. Based on the known reactions of alkoxyenediolates, geminal enediolates, or enamidolates,[4] alkylation at carbon to give a substituted α-hydroxy acid was expected. This was shown to be the case (see Table I) for enetriolate 1. However, alkylation of 1 or other enetriolates (eq 2) gives only modest



(2)

1, R = C_6H_5
2, R = CH_3
3, R = H

yields of product α-hydroxy acids and would not be synthetically useful when compared to existing procedures. Apparently deprotonation of alkyl halides by the enetriolates results in elimination reactions which compete with the desired substitution reaction. Efforts to increase the yield of desired alkylation product by addition of hexamethylphosphoramide (HMPA) failed, although a higher yield was obtained when an alkyl chloride was used instead of an alkyl bromide or iodide. Deprotonation of mandelic acid with *n*-BuLi (6 eq) and potassium *tert*-butoxide (3 eq) in pentane for 24 h at 25 °C followed by methylation with methyl iodide also failed to yield an alkylated product.[7]

Attempts to generate enetriolates **2** and **3** by deprotonation of glycolic and lactic acid were less successful as is noted in Table I. This failure could be ascribed to the expected de-

Table I. Products Formed in Reactions of Enetriolates with Various Electrophiles

α-hydroxy acid precursor	registry no.	electrophile	product	registry no.	% yield[a] product	% yield[a] (precursor)
mandelic acid	90-64-2	*n*-C_4H_9Cl	$C_6H_5C(n\text{-}C_4H_9)OHCO_2H$	4445-12-9	55	(8)
		n-C_4H_9Br			37	(56)
		n-C_4H_9Br[b]			18	(81)
		n-C_4H_9I			13	(71)
		c-$C_6H_{11}I$	none		0	
		D_2O	$C_6H_5CDOHCO_2H$	67315-76-8	58[c]	
		CH_3I	$C_6H_5C(CH_3)OHCO_2H$	515-30-0	40[d]	(60)
glycolic acid	79-14-1	*n*-$C_{10}H_{21}Br$	$(n\text{-}C_{10}H_{21})CHOHCO_2H$	2984-55-6	10[e]	
		n-$C_{10}H_{21}I$	*f*			
		CH_3I	$(CH_3)_2COHCO_2H$	594-61-6	~10[g]	
lactic acid	50-21-5	CH_3I	$(CH_3)_2COHCO_2H$		<10	

[a] Yields determined by GC after esterification (see text). [b] HMPA was added before the butyl bromide. [c] The crude acid before esterification was 41% d_1 by NMR. [d] The atrolactic acid yield was determined by NMR of the crude reaction mixture. [e] This is an isolated yield. [f] While no alkylation product was isolated, significant amounts of $C_{20}H_{42}$ from reductive dimerization of the *n*-$C_{10}H_{21}I$ were formed. [g] In addition, a trace of lactic acid was formed.

0022-3263/78/1943-3963$01.00/0

crease in acidity of the dilithium derivatives of glycolic and lactic acids relative to that of mandelic acid. Alternatively, solubility problems in reactions leading to **2** and **3** may have interfered with the reactions.

The alkylation results imply at least a transitory existence for enetriolate **1**. Less ambiguous evidence for **1** includes the observation of 41% deuterium incorporation into mandelic acid when the reaction mixture was treated with 20% DCl in D_2O. Since low deuterium incorporation has been observed in deuterations of similar anions solvated by amines,[8] we believe that the alkylation results of **1** are best explained by assuming that nearly complete deprotonation of lithio mandelic acid to give **1** has occurred as shown in eq 1. This interpretation is also consistent with the results of the competition experiments discussed below.

We attempted to characterize enetriolate **1** by both UV–visible spectroscopy and ^{13}C NMR spectroscopy. In the UV–visible spectrum **1** exhibits only end absorption even in dilute solution (ca. 1×10^{-3} M). Absorption by other species in the base solution precluded measurement of either λ_{max} or an extinction coefficient. Solubility problems frustrated our attempts to measure the ^{13}C NMR spectrum of **1**.

We have qualitatively measured the kinetic pK_a of the dilithium derivative of mandelic acid using competitive deprotonation reactions. When a solution containing 1 equiv each of mandelic acid and phenylacetic acid was treated with 4 equiv of LDA, exclusive C–H deprotonation of the phenylacetic acid occurred as measured by the observation of deuterium incorporation only into the phenylacetic acid upon deuteration. Accordingly, we estimate that the kinetic pK_a of the dilithium derivative of mandelic acid is at least 2 units greater than that of the lithium salt of phenylacetic acid. In a similar experiment, an equal molar solution of mandelic acid and triphenylmethane was treated with 3 equiv of LDA under conditions which normally gave **1**. In this case deuteration with DCl in D_2O gave triphenylmethane which contained 5–15% deuterium at the methyl carbon; recovered mandelic acid again contained ca. 40% deuterium at C-2. Finally, treatment of an equal molar mixture of mandelic acid and decanoic acid with 4 equiv of LDA followed by a DCl/D_2O quench yielded a mixture of partially deuterated mandelic and decanoic acids. Thus, the α-C–H of the dilithium derivative of mandelic acid has kinetic acidity at least comparable (within 2 units) to triphenylmethane and lithium decanoate.

Unfortunately, the lack of thermodynamic pK_a values for lithium salts of carboxylic acids precludes us from making a quantitative statement concerning the effect of an adjacent negatively charged heteroatom on C–H pK_a. Qualitatively the α-O–Li group has, as expected, lowered the kinetic acidity of this proton and the α-O–Li has an effect comparable to that of a phenyl substituent[9] but in the opposite direction.

Experimental Section

All preparations involving active organometallic compounds were conducted under nitrogen using conventional inert atmosphere techniques. NMR spectra were recorded on a Varian T-60 NMR spectrometer. Analytical gas chromatography was performed on a 6 ft × ⅛ in. SE-30 column using a Hewlett Packard Model 3830 gas chromatograph. Cyclohexyl iodide was prepared by the method of Stone and Shechter.[10] All other reagents were purchased from commercial sources in reagent quality and used without further purification. Alkylation products were converted to ethyl esters and identified by NMR spectral and gas chromatographic comparison to authentic materials. THF was distilled from sodium–benzophenone, and HMPA was distilled at reduced pressure from sodium. Deuterium incorporation was determined by comparing the integrals of various peaks in the NMR spectra of the deuterated compounds.

General Procedure. A solution of ca. 1 mmol of α-hydroxy acid and an equivalent amount of internal standard in 10 mL of THF was added at −78 °C to a THF solution containing 3.3 equiv of LDA (from diisopropylamine and *n*-BuLi). The resulting mixture was allowed to warm and was stirred for 1 h at 25 °C and then cooled to −78 °C. A THF solution of 2 equiv of the electrophile was added and the mixture was allowed to warm and was stirred at 25 °C for 24 h. Following conventional acidic workup, the product was extracted into ether and the ethereal solution was distilled in vacuo. The residue was esterified in ethanolic HCl and the esterified products were analyzed by gas chromatography.

Deuterations. After preparation of the enetriolate as described above, the reaction mixture was added by syringe to an excess of 20% DCl in D_2O and then worked up immediately and analyzed by NMR for deuterium incorporation.

Acknowledgments. This work was generously supported by the Robert A. Welch Foundation.

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Synthesis of *tert*-Butoxymethyl Ethers: A New Protecting Group for Alcohols

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Received May 4, 1978

A common protecting group for alcohols and phenols is the methoxymethyl ether (I), available in high yield from ei-

$$ROCH_2OCH_3$$

I

ther chloromethyl methyl ether[1] or dimethoxymethane.[2] Unfortunately, removal of this protecting group often requires conditions too vigorous for sensitive functionalities (hot aqueous mineral acid).[1-3] Because of the relative lability of the *tert*-butyl protecting group,[4] we reasoned that the corresponding *tert*-butoxymethyl ether (II) would decompose

$$ROCH_2OC(CH_3)_3$$

II

readily under mild conditions and thus extend the utility of acetals as an alcohol protecting group.[5] Consequently, we set out to prepare chloromethyl *tert*-butyl ether, a hitherto unknown compound.

This task proved to be more difficult than had been anticipated. The reaction of an alcohol with formaldehyde or trioxane and hydrogen chloride gives the corresponding chloromethyl ether[6] but all attempts to generate the desired compound in this way failed. The reaction of *tert*-butyl alcohol with paraformaldehyde or trioxane in the presence of aqueous or gaseous hydrogen chloride or hydrogen bromide

0022-3263/78/1943-3964$01.00/0