

A NOVEL METHOD OF PREPARING ALPHA-SUBSTITUTED
HYDRACRYLATE AND ACRYLATE ESTERS

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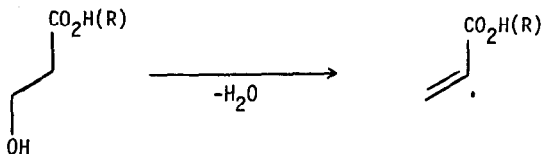
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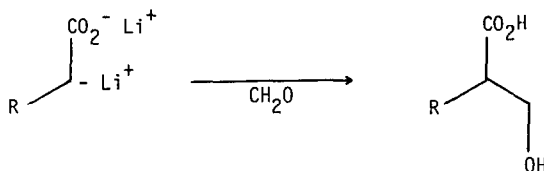
An efficient and simple preparation of α -substituted acrylic acids or their derivatives portends considerable chemical interest in that systems of this type are often found in natural products of chemotherapeutic value.¹ In addition, acrylates have been widely applied to such versatile synthetic operations as the Michael reaction and the Diels-Alder reaction.

Acrylates have been successfully prepared by β -elimination of the elements of water from their corresponding hydracrylate analogues.² The dehydration sequence has seen only limited application, however, because of the relative inaccessibility of hydracrylate species.

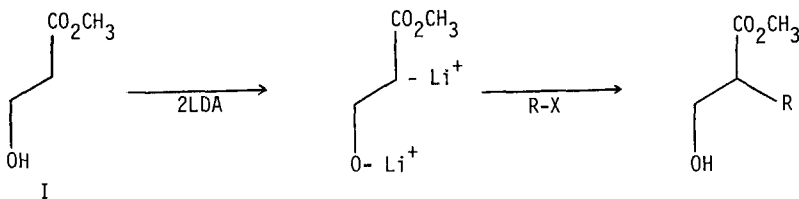


Recently, one approach to the synthesis of α -substituted hydracrylates has been reported.³ This procedure uses the dilithium salt of an acid in combination with anhydrous formaldehyde to give the corresponding substituted hydracrylic acid. While successfully applied to simple acids,

it seemed to us that acids bearing additional functional groups might not be amenable to the formylation method. Furthermore, the formylation procedure is experimentally difficult to carry out, especially with respect to the generation of anhydrous formaldehyde. We felt the preparation of α -substituted hydracrylates, and hence acrylates, might be approached from a strategically different, experimentally simple, and potentially more flexible viewpoint, *i.e.*, alkylation of the readily available ester methyl hydracrylate (I).⁴



We have now found that the lithium enolate of I undergoes high yield reaction with a variety of alkylating agents. Furthermore, these alkylations are not complicated by ester self-condensation, a known propensity of simple ester enolates.⁵



A typical alkylation reaction with I is carried out by adding the ester (0.5 equivalents) at -78° to a THF solution of lithium diisopropylamide (LDA) (1 equivalent, 1 molar). After enolate formation is complete (40 minutes at -78°) the alkylating agent (1.0 to 1.3 equivalents) is added either neat or in THF solution. The reaction mixture is then brought to 4° and held at this temperature for 5 hours. A representative summary of some of our results is given in the table.

TABLE

Ester	Alkylating Agent	R	Product	#	Yield,% ⁶
Methyl Hydracrylate	CH ₃ I	CH ₃ -	HOCH ₂ CH(R)CO ₂ CH ₃	II	94%
Methyl Hydracrylate	CH ₃ CH ₂ CH ₂ I	CH ₃ CH ₂ CH ₂ -	HOCH ₂ CH(R)CO ₂ CH ₃	III	90%
Methyl Hydracrylate	(CH ₃) ₂ CHI	(CH ₃) ₂ CH-	HOCH ₂ CH(R)CO ₂ CH ₃	IV	89%
Methyl Hydracrylate	Br(CH ₂) ₃ Br	Br(CH ₂) ₃ -	HOCH ₂ CH(R)CO ₂ CH ₃	V	93%
Methyl Hydracrylate	CH ₂ =CHCH ₂ Br	CH ₂ =CHCH ₂ -	HOCH ₂ CH(R)CO ₂ CH ₃	VI	92%
Methyl Hydracrylate	HC≡CCH ₂ Br	HC≡CCH ₂ -	HOCH ₂ CH(R)CO ₂ CH ₃	VII	86%
Methyl Hydracrylate	CH ₃ OCH ₂ Cl	CH ₃ OCH ₂ -	HOCH ₂ CH(R)CO ₂ CH ₃	VIII	95% ⁷
Methyl Hydracrylate	(CH ₃ S) ₂	CH ₃ S-	HOCH ₂ CH(R)CO ₂ CH ₃	IX	88% ⁷

It is worthy of note that compounds such as V, VII, VIII, and IX probably could not be prepared *via* the formylation procedure.³ Hence, the alkylation method described herein should allow the construction of a variety of otherwise inaccessible hydracrylate and acrylate systems

We have successfully dehydrated the hydracrylates III, IV, VIII, and IX into their corresponding acrylate analogues. In addition, we are studying the possibility of converting some of these alkylation products into 5- and 6-membered α -methylene lactones.

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REFERENCES

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2. Dehydration of β -hydroxy acids and lactones have been carried out under both acidic and basic conditions. For examples, see reference 3.
3. P. E. Pfeffer, E. Kinsel, and L. S. Silbert, *J. Org. Chem.*, **37**, 1256 (1972). The reaction has also been applied to lactone systems by P. A. Grieco and K. Hiroi, *Chem. Comm.*, 1317 (1972).
4. Methyl hydracrylate can be prepared from β -propiolactone in one step (92% yield) using the method described by P. D. Bartlett and P. N. Rylander, *J. Amer. Chem. Soc.*, **73**, 4273 (1951).
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6. The yields given are for isolated products and are based on the amount of ester used. All compounds exhibited satisfactory spectral and physical properties.
7. This reaction was carried out at -40° for optimum results.