substitution pattern quite different from that of compound **26** could also be obtained from the ketone **18**. Thus, treatment of **18** with LDA (THF, −78 °C), followed by trapping of the resultant enolate anion with C_6H_5SeCl,[16] gave the α-phenylseleno ketone **33** (69%). Subjection of the latter material to an oxidation–elimination procedure (H_2O_2, CH_2Cl_2)[16] afforded, albeit in modest yield (47%),[10] the α,β-unsaturated ketone **34**. Interestingly, thermolysis (mesitylene solution, reflux, 2 h) of **34** produced (73%) 1-(carbomethoxy)bicyclo[3.2.1]octa-2,6-dien-8-one (**35**): IR (film) 1765, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.34–3.02 (m, 2 H, H-4), 2.9–3.1 (m, 1 H, H-5), 3.82 (s, 3 H, CO_2Me), 5.60 (d of t, 1 H, J = 7, 4 Hz, H-3), 6.30 (m, 1 H, H-2), 6.28 (d of d, 1 H, J = 7, 3 Hz, H-6), 6.71 (d, 1 H, J = 7 Hz, H-7).

As an overall method for the preparation of bicyclo[3.2.1]octane systems, the preliminary work summarized above would appear to hold considerable promise. The substrates (**22–25, 34**) employed for the key Cope rearrangements can be obtained via relatively simple and well-known chemical transformations. Furthermore, it is clear that the methodology allows for the convenient preparation of bicyclo[3.2.1]octane compounds with substituents at either bridgehead position (cf. **27, 29**) and with functionality on two of the three bridges (**26–29**) or on all three bridges (**35**). Studies aimed at the synthesis and thermal rearrangement of structurally more complex 6-(1-alkenyl)bicyclo[3.1.0]hex-2-enes are being carried out and the results will be reported in due course.

Acknowledgment. Financial support from the National Sciences and Engineering Research Council of Canada (NSERC) and a NSERC postgraduate scholarship (to E.H.R.) are gratefully acknowledged.

Registry No. 1, 2984-57-8; **2**, 4096-95-1; **3**, 58166-68-0; **4**, 5717-37-3; **5**, 1001-93-0; **6**, 1572-72-1; **7**, 53190-50-4; **8**, 73193-12-1; **9**, 73193-13-2; **10**, 73193-14-3; **11**, 73193-15-4; **12**, 73193-16-5; **13**, 73193-17-6; **14**, 73193-18-7; **15**, 73193-19-8; **16**, 73193-20-1; **17**, 73193-21-2; **18**, 73193-22-3; **19**, 73193-23-4; **20**, 73193-24-5; **21**, 73193-25-6; **22**, 73193-26-7; **23**, 73193-27-8; **24**, 73193-28-9; **25**, 73193-29-0; **26**, 73193-30-3; **27**, 73193-31-4; **28**, 73193-32-5; **29**, 73193-33-6; **30**, 73193-34-7; **31**, 31444-29-8; **33**, 73193-35-8; **34**, 73193-36-9; **35**, 73193-37-0; propenal, 107-02-8; (*E*)-2-butenal, 123-73-9.

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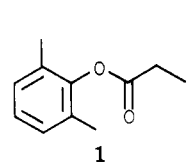
Received December 11, 1979

Acyclic Stereoselection. 8. A New Class of Reagents for the Highly Stereoselective Preparation of *threo*-2-Alkyl-3-hydroxycarboxylic Acids by the Aldol Condensation[1]

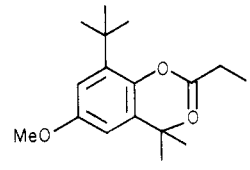
Summary: *threo*-3-Hydroxy-2-methylcarboxylic acids may be prepared in high stereochemical yield by condensing aryl propionates **1** or **2** with aldehydes followed by hydrolytic or oxidative removal of the aryl group.

Sir: The recent flurry of activity on stereoselective aldol condensations has resulted in methods for realizing high stereochemical control (>95%) in the preparation of *erythro*-2-alkyl-3-hydroxycarboxylic acids using the preformed lithium enolate of ethyl ketones in which the carbonyl group also bears a bulky oxygen-containing function,[2] the boron enolate of *S*-*tert*-butyl propanethioate,[3] or the boron enolate of *S*-phenyl propanethioate.[4] Similar high selectivity in the preparation of the threo diastereomers may be achieved by using the preformed lithium enolates of certain alkoxyalkyl propionates[5] or by way of the boron enolate of *S*-*tert*-butyl propanethioate.[3,6] Stereoselectivity, albeit of a lesser magnitude, has also been found in the condensations of zinc and magnesium enolates of ketones,[7] in the titanium tetrachloride promoted condensation of *O*-trimethylsilyl ketene acetals,[8] in the equilibration of the lithium aldoloxides arising from the condensation of carboxylic acid dianions with certain aldehydes,[9a] and in the condensation of potassium carboxylic acid dianions with certain aldehydes.[9b] Finally, erythro and threo diastereomers may be obtained in indirect methods employing either a (*Z*)-2-butenylboronate ester[10] or an (*E*)-2-butenylchromium reagent.[11] We now report a new class of reagents which allows a more convenient preparation of *threo*-2-alkyl-3-hydroxycarboxylic acids.

2,6-Dimethylphenyl propionate (**1**, bp 100 °C (0.7 torr)) is produced in quantitative yield by reaction of propionyl chloride with lithium 2,6-dimethylphenoxide in THF at −78 °C. The analogous propionate ester **2** (mp 45 °C) is prepared in a similar fashion from 2,6-di-*tert*-butyl-4-methoxyphenol ("butylated hydroxyanisole", BHA).[12,13]

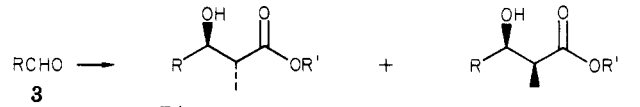


1



2

Ester **1** was converted into its lithium enolate by the normal procedure[2] and allowed to react with various aldehydes (**3**) to obtain aldols **4** and **5** (eq 1). Results are



3

4, R′ = 2,6-$(CH_3)_2C_6H_3$ **5**, R′ = 2,6-$(CH_3)_2C_6H_3$
6, R′ = H

a, R = C_6H_5
b, R = *n*-C_5H_{11}
c, R = *i*-C_3H_7
d, R = *t*-C_4H_9
e, R = $C_6H_5(CH_3)CH$

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(10) R. W. Hoffman and H.-J. Zeiss, *Angew. Chem.*, **91**, 329 (1979).

(11) C. T. Buse and C. H. Heathcock, *Tetrahedron Lett.*, 1685 (1978).

(12) Obtainable from the Gallard-Schlesinger Chemical Mfg. Corp.

(13) We have also prepared aryl propionate esters analogous to **1** and **2** (e.g., with crotonic acid) by treatment of the acid with the phenol and trifluoroacetic anhydride (R. W. Dugger, unpublished results).

0022-3263/80/1945-1727$01.00/0

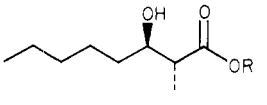
Table I. Reaction of Ester 1 with Various Aldehydes (Eq 1)

aldehyde	aldol yield,[a] %	4/5	mp, °C	acid 6 yield, %	mp, °C
3a	72	88/12	62–63[b]	99	oil[c]
3b	70	86/14	oil[b]	91	oil[c]
3c	78	>98/2	77	90	oil
3d	82	>98/2	70–71	98	74.5–76.5
3e	81	>98/2	oil[d]	85	108–110[b]

[a] Purified by preparative high-pressure LC. [b] Major diastereomer. [c] Mixture of diastereomeric acids. [d] Mixture of Cram's rule and anti-Cram's rule diastereomers: ratio = 4:1.

summarized in Table I. In all cases, the major diastereomer is found to be the *threo*-3-hydroxy-2-methylcarboxylic ester. With the α-branched aldehydes **3c–e** no erythro product can be found. Aldehydes having "smaller" groups give a threo/erythro ratio of about 6:1. With the chiral aldehyde **3e** both possible threo adducts are produced, with the Cram/anti-Cram ratio being 4:1. Treatment of the initial esters with KOH in aqueous methanol at 25 °C effects conversion to the hydroxy acids without detectable epimerization or retroaldolization.

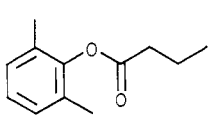
For the aldehydes which show diminished threo selectivity with reagent 1, one may use the more selective BHA propionate **2**. For example, condensation of the lithium enolate of **2** with *n*-hexanal affords the threo adduct **7** (oil) in 72% yield. Although the BHA group cannot be removed hydrolytically, it is conveniently eliminated by oxidation with ceric ammonium nitrate[14] or silver(II) oxide,[15] whereupon acid **8** (oil) is obtained in 67% yield.



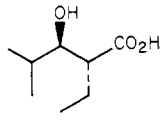
7, R = 2,6-$(CH_3)_2$-4-$CH_3OC_6H_2$
8, R = H

Reagent **2** shows equally high threo selectivity with α-branched aldehydes and benzaldehyde. However, the necessity of oxidative removal of the aryl group renders it less useful than reagent 1 for reaction on α-branched aldehydes. Thus far, we have been unable to oxidatively remove the aryl ester when the aldehyde also contains a benzene ring.

The generality of the current procedure is further demonstrated by condensation of 2,6-dimethylphenyl butyrate (**9**, bp 100 °C (0.6 torr)), prepared in a manner similar to that used to prepare **1** and **2**, with isobutyraldehyde. After hydrolysis, pure *threo*-β-hydroxy acid **10** (oil) is obtained in an overall yield of 69%.



9



10

Reagents **1** and **2** provide convenient, highly stereoselective routes to a variety of *threo*-β-hydroxy acids. Both provide superior stereoselectivity compared to Meyers' reagent[5] and are at least as selective as the Masamune–Evans reagent.[3,6] In addition, the convenience of working with lithium enolates, rather than boron enolates, offers an attractive advantage. For α-branched aldehydes, the reagent of choice is **1** because it combines the features of exceptional stereoselectivity with ease of hydrolysis to the resulting aldol adduct. For α-unbranched aliphatic aldehydes reagent **2** may be used to achieve high stereoselectivity. Although deblocking in this case is not as convenient, good yields of *threo*-β-hydroxy acids are realized. Applications of these threo-selective reagents to the synthesis of natural products is under investigation.

Acknowledgment. This work was supported by a grant from the United States Public Health Service (NIH Grant AI-15027). M.C.P. gratefully acknowledges the Fannie and John Hertz Foundation for financial support in the form of a fellowship.

Registry No. 1, 51233-80-8; 1 lithium enolate, 73198-87-5; **2**, 73198-88-6; **2** lithium enolate, 73198-89-7; **3a**, 100-52-7; **3b**, 66-25-1; **3c**, 78-84-2; **3d**, 630-19-3; **3e**, 93-53-8; **4a**, 73198-90-0; **4b**, 73198-91-1; **4c**, 73198-92-2; **4d**, 73198-93-3; **4e**, isomer 1, 73198-94-4; **4e**, isomer 2, 73245-83-7; **5a**, 73198-95-5; **5b**, 73198-96-6; *erythro*-**6a**, 14366-87-1; *threo*-**6a**, 14366-86-0; *erythro*-**6b**, 73198-97-7; *threo*-**6b**, 73198-98-8; *threo*-**6c**, 73198-99-9; *threo*-**6d**, 73199-00-5; **6e**, isomer 1, 73245-84-8; **6e**, isomer 2, 73245-85-9; **7**, 73210-20-5; **9**, 73199-01-6; **9** lithium enolate, 73199-03-8; **10**, 73199-02-7; propionyl chloride, 79-03-8; lithium 2,6-dimethylphenoxide, 24560-29-0; 2,6-di-*tert*-butyl-4-methoxyphenol, 489-01-0; butanoyl chloride, 141-75-3.

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Received December 17, 1979

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Recent Reviews. 5

Reviews are listed in order of appearance in the sources indicated. In multidisciplinary review journals, only those reviews which fall within the scope of this Journal are included. Sources are listed alphabetically in three categories: regularly issued review journals and series volumes, contributed volumes, and monographs. Titles are numbered serially, and these numbers are used for references in the index.

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This installment of Recent Reviews covers the second half of the 1979 literature. Previous installment: *J. Org. Chem.* **1979**, *44*, 4016. For regularly issued journals and series volumes, the coverage in this installment continues from the last items included in Recent Reviews 4.

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