2880, 1718, 1648, 1309, 1242, 1152, 1107 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.73 (6, J = 7.5 Hz, 1 H, HC=C), 3.77 (s, 3 H, CO_2CH_3), 2.6–2.0 (m, 4 H, 2 CH_3CH_2), 1.07 (t, J = 7.0 Hz, 3 H, CH_3CH_2), 1.02 (t, J = 7.0 Hz, 3 H, CH_3CH_2); MS (70 eV), m/e (rel intensity) 142 (46.1, M^+), 127 (28.9), 113 (35.5), 111 (30.3), 95 (23.7), 83 (42.1), 67 (47.4), 59 (28.9), 55 (100).

(*E*,*E*)-Hepta-2,5-dien-4-one (52).[24] In a separatory funnel were placed 53.8 g (0.349 mol) of distilled diene ketal **49**, 100 mL of diethyl ether, and 50 mL of cold 3% aqueous sulfuric acid. The mixture was shaken for several minutes and then worked up in the usual manner to provide 29.2 g (90%) of **52** as a pale yellow liquid: IR 3040, 1670, 1618, 1449, 1308, 1300, 1210, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.93 (d of q, J = 16 and 6 Hz, 2 H, CH_3CH=CH), 6.33 (d, J = 16 Hz, 2 H, CH_3CH=CH), 1.95 (d of d, J = 6 and 1 Hz, CH_3CH=CH); MS (70 eV), m/e (rel intensity) 110 (21.4, M^+), 95 (20.7), 69 (100).

(23) For data on the corresponding ethyl esters see: (a) Kinstle, T. H.; Mandanas, B. Y. *J. Chem. Soc., Chem. Commun.* **1968**, 1699. (b) Savitsky, G. B.; Ellis, P. D.; Namilkawa, K.; Maciel, G. E. *J. Chem. Phys.* **1968**, *49*, 2395.

(24) Braude, E. A.; Coles, J. A. *J. Chem. Soc.* **1951**, 2078.

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Registry No. 1, 183-03-9; **2a**, 68434-69-5; **2b**, 71718-31-5; **3**, 1728-35-4; **4**, 1073-76-3; **5**, 68434-73-1; **6**, 68434-74-2; **7**, 71718-32-6; **8**, 1460-16-8; **9**, 32777-26-7; **10a**, 68434-75-3; **11a**, 64187-85-5; **12**, 65844-65-7; **13**, 21448-77-1; **14a**, 36744-59-9; **14b**, 4729-30-0; **15**, 68434-70-8; **16**, 71718-33-7; **17**, 68434-72-0; **18**, 68434-76-4; **23**, 4321-25-9; **24**, 56745-53-0; **27**, 184-26-9; **28a**, 71718-34-8; **29**, 71718-35-9; **30**, 1192-93-4; **31**, 71718-36-0; **32**, 71718-37-1; **36b**, 18448-47-0; **37**, 177-10-6; **38**, 71718-38-2; **39**, 71718-39-3; **40**, 122-99-6; **41**, 49783-32-6; **42**, 1728-28-5; **43**, 71718-40-6; **44**, 71718-41-7; **45**, 1073-14-9; **46**, 41329-93-5; **47**, 71718-42-8; **48**, 71718-43-9; **49**, 71718-44-0; **50**, 71718-45-1; **52**, 71718-46-2; **53a**, 71718-47-3; **53b**, 71718-48-4.

Acyclic Stereoselection. 4. Assignment of Stereostructure to β-Hydroxycarbonyl Compounds by Carbon-13 Nuclear Magnetic Resonance

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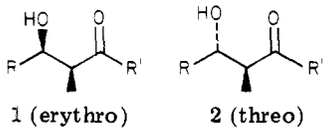
^{13}C NMR spectra for over 40 sets of β-hydroxycarbonyl compounds possessing diastereoisomerism were recorded. Empirical observations were made which allow the assignment of stereostructure to these compounds. A model for the preferred conformations of these molecules was developed which accounts for the observed chemical shift trends.

We have recently been interested in the use of the aldol condensation as a means for establishing chiral centers in acyclic systems in a controlled fashion.[1,2] Consequently, we desired a method to reliably ascertain the stereochemical outcome of any particular aldol condensation. We have found that ^{13}C NMR is an excellent tool for this determination. Diastereomeric β-hydroxycarbonyl compounds exhibit consistent ^{13}C NMR chemical shifts on the basis of which stereostructure may be assigned.

Results

α-Methyl-β-hydroxycarbonyl Compounds. When aldol condensations between ethyl carbonyl compounds and aldehydes are carried out as previously described,[1,2] erythro and threo diastereomeric products **1** and **2** may be produced. For these model studies, the R groups (incorporated from the aldehyde portion) include Ph, *p*-NO_2Ph, *p*-MeOPh, Et, *i*-Pr, *t*-Bu, $(Ph)_2CH$, and $PhCH(CH_3)$. The R′ groups (incorporated from the ethyl carbonyl compound) include H, OH, O-alkyl, *i*-Pr, *t*-Bu, Et, Ph, $C(CH_3)_2OMe_3Si$, and mesityl. The resonances that are of the greatest interest to us are those present in all compounds **1** and **2**, namely, the methyl, carbinol, and methine carbons. Table I lists the resonances observed for these three carbons in a number of diastereomeric pairs, along with resonances for some compounds for which we have only a single isomer.



1 (erythro) 2 (threo)

We take as a typical case from this table the adduct produced from reaction of methyl propionate with benzaldehyde (R′ = OMe, R = Ph). The erythro carbinol absorption is found at 73.6 ppm, while that in the threo isomer occurs at 76.3 ppm. Similar upfield shifts are observed for the other two resonances in the erythro isomer. In fact, in all the compounds listed in Table I, we note an upfield shift of the carbons in the erythro isomer compared with those in the threo isomer. This shift is smaller for methine carbons than for the other two.

In Table II the chemical shift ranges for each carbon in each isomer are given. In the carbinol and methyl signals, we note a slight overlap between the ranges for a given isomer in all compounds studied. However, Table I shows a minimum separation of 1.1 ppm in carbinol and methyl resonances of diastereomeric pairs. The maximum separation observed is 5 ppm. The methine carbons, being more directly affected by R′, show a much wider chemical

(1) W. A. Kleschick, C. T. Buse, and C. H. Heathcock, *J. Am. Chem. Soc.*, **99**, 247 (1977).

(2) C. T. Buse and C. H. Heathcock, *J. Am. Chem. Soc.*, **99**, 8109 (1977).

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Table I. Chemical Shift Values for β-Hydroxycarbonyl Compounds 1 and 2 (in ppm)

			erythro			threo		
entry	R	R′	carbinol	methyl	methine	carbinol	methyl	methine
1	Ph	OMe	73.6	10.8	46.6	76.3	14.4	47.1
2	Ph	Et	73.5	10.9	52.5	76.2	16.1	52.5
3	Ph	mesityl	71.6	8.4	53.8	76.4	14.0	54.5
4	Ph	$C(CH_3)_2OMe_3Si$	73.8	11.6	46.1	77.0	15.5	46.4
5	Ph	*t*-Bu	74.0	12.2	46.5	77.5	16.5	46.8
6	Ph	*i*-Pr	75.1	12.7	*a*	76.8	14.8	*a*
7	$PhCH(CH_3)$	$C(CH_3)_2OMe_3Si$	76.1	9.9	42.7			
8	*p*-MeOPh	mesityl				76.0	14.1	55.2
9	$PhCH(CH_3)$[b]	OH	74.9	8.6	42.5			
10	*p*-NO_2Ph	*t*-Bu	73.1	11.6	45.6			
11	*p*-MeOPh	*t*-Bu				77.0	16.3	46.9
12	$PhCH(CH_3)$	OEt	75.7	10.0	42.8			
13	$PhCH(CH_3)$	*t*-Bu	75.7	9.9	42.9			
14	*i*-Pr	$C(CH_3)_2OMe_3Si$	76.4	10.1	40.2			
15	*p*-MeOPh	OMe	73.5	11.2	46.7	75.9	14.2	47.2
16	$PhCH(CH_3)$	mesityl				77.6	14.0	*a*
17	$(Ph)_2CH$	OMe	73.0	9.2	41.6	75.8	14.7	42.4
18	$PhCH(CH_3)$	$C(Ph)_2OMe_3Si$	75.2	9.7	40.1			
19	Ph	H	72.6	7.6	*a*	75.4	10.9	*a*
20	*i*-Pr	OMe	76.7	10.3	42.0	78.0	14.4	42.6
21	Et	OMe	73.2	10.6	44.1	74.4	13.7	44.9
22	*i*-Pr	Et	76.2	9.5	47.5	78.2	14.1	48.1
23	Et	Et	72.8	10.2	49.7	74.9	13.9	50.7
24	*i*-Pr	mesityl	71.7	10.3	50.9	74.0	13.0	52.9
25	*t*-Bu	OMe	78.1	12.8	38.6	82.5	17.9	41.1
26	*t*-Bu[b]	OH	78.1	12.4	40.1			
27	*i*-Pr	*i*-Pr	76.2	9.7	39.7	78.3	14.4	40.8

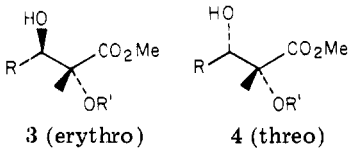
[a] Resonance could not be assigned. [b] $(CD_3)_2CO$ solution.

Table II. Chemical Shift Ranges for Diastereomeric β-Hydroxycarbonyl Compounds 1 and 2 (in ppm)

	carbinol	methine	methyl
erythro	71.6-78.1	38.6-53.8	7.6-12.9
threo	74.0-82.5	40.8-55.2	10.9-17.9

shift range, in addition to smaller separations within a diastereomeric pair. This separation sometimes vanishes. In no case, however, does any crossing over of erythro and threo resonances occur.

α-Alkoxy-α-methyl-β-hydroxycarbonyl Compounds. When alkoxypropionates are condensed with aldehydes, erythro and threo diastereomers **3** and **4** may be produced.

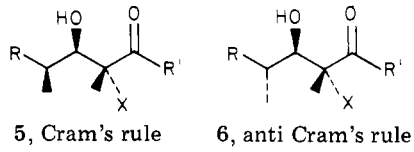


3 (erythro) 4 (threo)

The preparations of these compounds will be described elsewhere.[3] For these studies, the R groups include Et, *i*-Pr, *t*-Bu, Ph, and $PhCH(CH_3)$. The R′ groups include H, Me, CH_2Ph, and $CH_2O(CH_2)_2OCH_3$ (MEM). The resonances in which we are interested are the carbonyl, carbinol, and methyl signals. The resonances observed in a number of diastereomeric pairs for these three carbons are listed in Table III (in some cases, only isomer **3** was available for study).

Although these are the signals of interest for determining the stereostructure of α-alkoxy aldol adducts, we do observe diastereomeric shifts for other carbons (in R and R′ as well as in the ester methyl). The data in Table III show that coincidence of resonances occurs for **3** and **4** much more often than for **1** and **2**. This is not unusual with carbonyl carbons and happens occasionally with carbinol carbons. If they are resolved, threo carbonyl resonances and erythro carbinol resonances generally appear downfield of the corresponding resonances in their diastereomers. In all compounds we have investigated, the methyl resonances are resolved, with the resonance of the erythro diastereomer being downfield of the comparable resonance for the threo diastereomer. As is readily evident from Table III, the chemical shift ranges for corresponding carbons in erythro and threo diastereomers are virtually identical. Clearly, both isomers must be available for examination before reliable assignments may be made for α-alkoxy aldol adducts.

α,γ-Dimethyl-β-hydroxycarbonyl Compounds. When an aldol condensation is performed on an aldehyde bearing an α-asymmetric center, two diastereomeric erythro products **5** and **6** may result. The isomer which



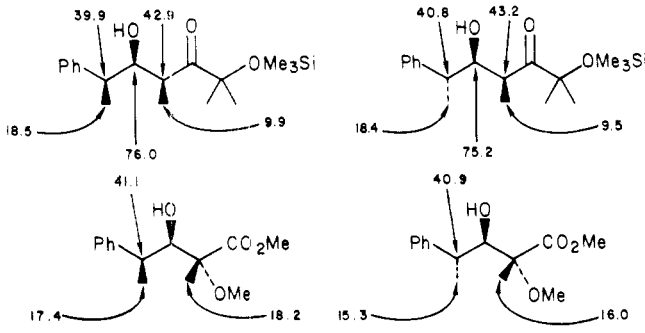
5, Cram's rule 6, anti Cram's rule

X = H, OR″

predominates may be predicted by the application of Cram's Rule.[4] Our efforts to correlate the ^{13}C NMR spectra of **5** and **6** with their stereostructures were not as fruitful as for compounds **1**–**4**. We have examined 16 such pairs, including some derived from alkoxypropionates, and although we have yet to discover any **5**, **6** pair which does not exhibit shifts in at least some carbons, there is no pronounced trend which allows us to assign stereostructure. Two representative pairs are illustrated as follows.

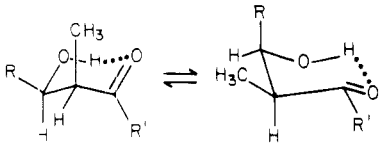
(3) M. C. Pirrung and C. H. Heathcock, to be submitted for publication.

(4) D. J. Cram and F. A. Abd Elhafez, *J. Am. Chem. Soc.*, **74**, 5828 (1952).

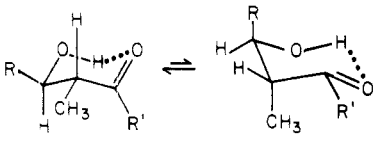


Discussion

Our initial goal in undertaking ^{13}C NMR correlations for compounds of types **1** and **2** was to supplement our more usual method of assigning stereostructure by ^{1}H NMR. It has been demonstrated[5,6] that β-hydroxycarbonyl compounds **1** and **2** exist in an intramolecularly hydrogen-bonded form. Two possible chairlike conformers for such structures are illustrated by structures **7** and **8**. The



7a **7b**



8a **8b**

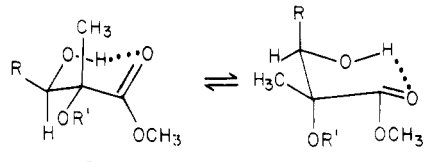
observed vicinal coupling constants for the C_α–C_β protons in **1** and **2** are easily rationalized in terms of these structures. The conformational equilibrium for **8** generally favors **8a**, in which these protons are held in an anti relationship. Consequently, the observed coupling constant is large (J_{vic} = 7–12 Hz). Conversely, in either conformer of **7**, these protons are held in a gauche relationship, resulting in a small coupling constant (J_{vic} = 0–4 Hz). This is a satisfying argument, and we routinely use this method to assign stereostructure to aldol products when the C_β resonance can be clearly resolved. Naturally, when R contains one or more protons coupled to the C_β (carbinol) proton, this analysis is less straightforward. In the more complex molecules which we expect to encounter during the course of our synthetic efforts, pertinent proton resonances could be obscured or difficult to assign. Furthermore, there exist some notable examples in which the threo coupling constant is smaller than the erythro.[7] Therefore, the fact that we were able to observe consistent shifts in the ^{13}C NMR spectra for diastereomers **1** and **2** was quite gratifying.

In an attempt to rationalize the observed shifts in the ^{13}C NMR spectra of **1** and **2**, we return to the hydrogen-bonded structures **7** and **8**. Comparing the number of gauche interactions in these conformers, we can readily account for the upfield shifts of methyl groups in erythro diastereomers **7**. The source of this shielding is the additional gauche interaction between the methyl and the C–O bond in **7a** and between R and the C_α—C=O bond in **7b**. We have not considered **8b** since (in all but a few cases) the ^{1}H NMR evidence indicates that this conformer is highly unfavored. Nevertheless, an evaluation of its gauche effects still allows us to predict that methyl groups in threo isomers will resonate downfield. This certainly demonstrates the reliability of ^{13}C NMR as a tool for stereochemical assignment. It should be mentioned that, when considering the gauche effects in **7** and **8**, we have ignored any interaction between methyl and R′, since our evidence (for R′ = H) indicates this effect is small.

An intriguing comparison may be made between the chemical shift trends observed for our six-membered ring, hydrogen-bonded structures **7** and **8** and those for 1,3-dioxanes[8a–c] and cyclohexanes.[8d] In the latter two systems, carbons within the ring which bear "axial" groups consistently resonate upfield of the carbons which bear "equatorial" groups. This differential-shift effect is reduced in the 1,3-dioxanes as compared to the cyclohexanes. Typical values for the former case are 0–2 ppm, while for the latter they are 3–5 ppm. We have seen differential-shift effects for carbinol and methine carbons throughout these ranges, so it seems unclear which system provides the better analogue to **7** and **8**. Even more confusing is the shift of the methyl groups. Axial methyl groups in cyclohexane systems absorb upfield of their equatorial methyl isomers by ca. 5 ppm, while in simple 1,3-dioxane systems, the axial methyls at C-5 absorb *downfield* by ca. 2 ppm.[8a,b] This unusual effect has been attributed to the lack of hydrogens in a 1,3-diaxial relationship to the methyl group. However, in a recent ^{13}C NMR study[8c] of 1,3-dioxanes which are *very* closely analogous to our molecules, the opposite trend was noted; that is, an equatorial methyl at C-5 absorbed at 14 ppm, while an axial methyl at C-5 absorbed at 10 ppm. The discrepancy between the 1,3-dioxane model for **7** and **8** (which seems to be more strictly analogous) and the cyclohexane model (which more accurately accounts for the chemical shift trends) is not easily resolved.

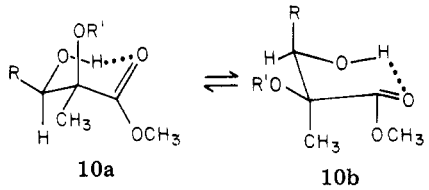
Attempts to fit the α-alkoxy aldol adducts into the above framework as six-membered ring derivatives **9** and **10** have

erythro



9a **9b**

threo



10a **10b**

been much less successful. In these cases, the conformational preferences are not nearly so well-defined, and it is difficult to estimate the weighting for each conformer. Nonetheless, the larger effect is likely to be that of the R group, and we will make an assumption (which is probably inadequate, at least for **9a** and **9b**) that the conformer having R "equatorial" is favored. Applying cyclohexane-type substituent effects[8d] to the carbinol and carbonyl carbons predicts that both will lie upfield in the threo isomer by about 1 ppm. The actual results are that threo

(5) M. Stiles, R. Winkler, Y. Chang, and L. Traynor, *J. Am. Chem. Soc.*, **86**, 3337 (1964).
(6) H. O. House, D. S. Crumrine, A. Y. Teranishi, and H. P. Olmstead, *J. Am. Chem. Soc.*, **95**, 3310 (1973).
(7) J. E. Dubois and P. Fellmann, *Tetrahedron Lett.*, 1225 (1975).
(8) (a) A. Jones, E. Eliel, D. Grant, M. Knoeber, and W. Bailey, *J. Am. Chem. Soc.*, **93**, 4772 (1971); (b) G. Kellie and F. Riddell, *J. Chem. Soc. B*, 1030 (1971); (c) L. Cazaux, J.-P. Gorrichon, and P. Maroni, *Can. J. Chem.*, **56**, 3017 (1978); (d) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, 1972.

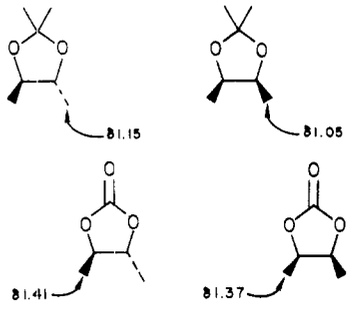
Table III. Chemical Shift Values for β-Hydroxycarbonyl Compounds 3 and 4 (in ppm)

			erythro			threo		
entry	R	R′	carbinol	methyl	carbonyl	carbinol	methyl	carbonyl
1	Et	H	77.8	22.3	175.8	77.7	21.3	176.7
2	*i*-Pr	H	79.2	24.0	176.3	78.3	22.0	177.9
3	*t*-Bu	H	81.6	26.3	177.2	77.0	24.6	177.2
4	Ph	H	77.9	22.4	175.0	77.6	21.9	176.2
5	Et	CH_2Ph	77.2	17.0	173.4	77.6	16.2	173.4
6	*i*-Pr	CH_2Ph	79.8	21.3	173.6	79.8	20.8	173.6
7	*t*-Bu	CH_2Ph	82.5	20.8	174.1	82.1	17.1	173.9
8	Ph	CH_2Ph	77.8	16.5	172.6	78.4	16.0	173.0
9	Et	Me	77.2	16.1	173.4	77.4	15.0	173.4
10	*i*-Pr	Me	79.7	21.2	173.5	79.7	20.7	173.5
11	*t*-Bu	Me	82.4	19.6	174.1			
12	Ph	Me	77.7	15.6	172.5	78.2	14.9	172.5
13	$PhCH(CH_3)$	Me	79.3	18.2	173.0			
14	Et	MEM[a]	77.1	16.4	173.4	77.1	16.2	173.4
15	*i*-Pr	MEM	79.5	20.9	173.6	79.0	19.7	173.6
16	*t*-Bu	MEM	81.9	21.0	174.6	*b*	17.8	174.6
17	Ph	MEM	77.4	16.5	173.0	77.8	16.3	173.0
18	$PhCH(CH_3)$	MEM	79.2	19.4	*b*			

[a] MEM = $CH_2O(CH_2)_2OCH_3$. [b] Resonance could not be assigned.

carbinols appear upfield, while threo carbonyls appear downfield of the corresponding carbons in their diastereomers. Much more disturbing is the fact that comparison with isomeric substituted 1-methylcyclohexanols[9,10] leads to the prediction that threo diastereomer **10a** should possess a methyl resonance downfield of that in **9a** by 2–6 ppm.[11] That these signals are consistently resolved and found in the same pattern (erythro downfield), a pattern which is the reverse of that predicted, speaks very poorly for this model.

An alternative representation to the hydrogen-bonded structures **9** and **10** was first suggested to us by our attempts to rationalize the chemical shift of the methyl groups of **3** and **4** in ^1H NMR spectra. As a typical example, the methyl group in the erythro adduct **3** (R = Et, R′ = H) absorbs at 1.47 ppm, while that in the threo adduct **4** (R = Et, R′ = H) absorbs at 1.33 ppm. This may be compared with the observed methyl resonances for the dioxolanes illustrated.[12] In both pairs, the more sterically

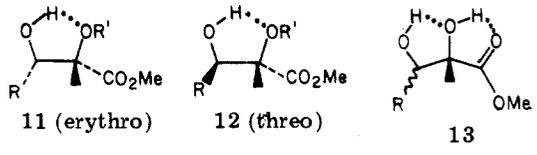


congested isomer with cis-oriented methyl groups has the upfield methyl absorption. If analogous five-membered ring structures are constructed for **3** and **4**, this upfield shift in the ^1H NMR spectrum of threo isomer **4** is readily explained by the shielding effect of the cis alkyl group in **12**.[13] Application of ^{13}C NMR shifts to these hypothetical

Table IV. ^{13}C NMR Resonances for β-Hydroxycarbonyl Portions of Isomers 15, 16, and 17 (in ppm)

	carbinol	methine	methyl
15	71.5	49.4	8.0
16	71.9	49.1	8.1
17	76.5	50.1	13.6

structures would indicate that, for the methyl groups, the more sterically congested isomer **12** would resonate upfield,



11 (erythro) **12** (threo) **13**

as is indeed the case. Furthermore, in the carbonyl resonances, the more sterically congested isomer **11** would be expected to appear upfield, again as is observed. It is not at all clear, however, what these representations predict for the carbinol carbon. For the hydroxy compounds (R′ = H), an additional hydrogen bond may be formed to result in a bicyclo[3.3.0] system (**13**), a ^{13}C NMR study of which has recently appeared.[14] However, the trends observed by these workers are not demonstrated in our system. While they observe carbons bearing endo groups to resonate upfield, the carbinol carbons in our erythro isomers resonate downfield. We are nonetheless able to draw an analogy between the methyl group in our system **12** and the sterically compressed methyl groups in *o*-xylene. These methyl groups resonante ca. 2 ppm upfield of those in the meta and para isomers.[8d] It thus seems that a similar, if slightly less dramatic, "steric shielding" effect is operating in structures **11** and **12**.

We have encountered ample opportunity to apply our findings to a number of aldol products whose stereostructure was in question. An example involved characterization of the products resulting from condensation of ethyl ketone **14** with benzaldehyde.[15] The isomers **15**, **16**, and **17** were separated and their ^1H NMR and ^{13}C NMR spectra recorded. While the proton spectra proved inconclusive

(9) Y. Senda, J. Ishiyama, and S. Imaizumi, *Tetrahedron*, **31**, 1601 (1975).

(10) M. Miljkovic, M. Gligorijevic, T. Satoh, and O. Miljkovic, *J. Org. Chem.*, **39**, 1379 (1974).

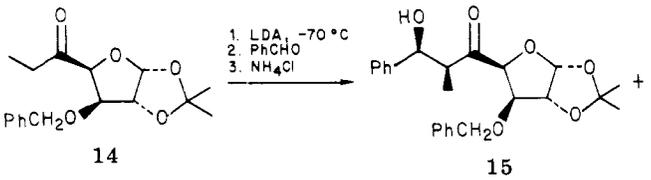
(11) It is unclear how the substituent effects discussed in ref 8d should be applied to these molecules. For instance, it is not stated whether the β-axial alkoxy group effect of −2 ppm applies to methyl groups on cyclohexanes as well as to ring carbons. For that reason we chose to make our comparisons with materials which should be more closely analogous. In isomeric 4-*tert*-butyl-1-methylcyclohexanols, the axial methyl appears at 25.4 ppm, while the equatorial one appears at 31.4 ppm.[9,10]

(12) F. A. L. Anet, *J. Am. Chem. Soc.*, **84**, 747 (1962).

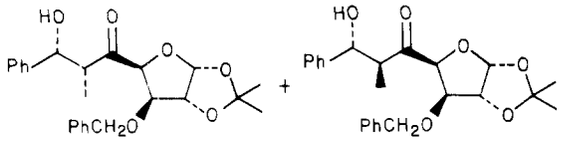
(13) A discussion of the shielding effects of alkyl groups is found in L. M. Jackman and S. Sternhell, "Application of Nuclear Magnetic Resonance Spectroscopy to Organic Chemistry", Pergamon Press, New York, 1969.

(14) J. K. Whitesell and R. S. Matthews, *J. Org. Chem.*, **42**, 3878 (1977).

(15) C. T. White and C. H. Heathcock, unpublished results.



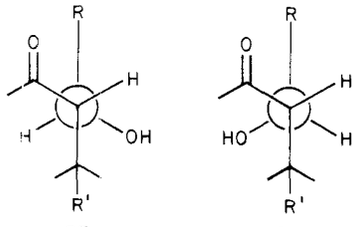
14 15



16 17

(J_{vic} = 2, 2, and 4 Hz, respectively), the resonances of the methyl, carbinol, and methine carbons (summarized in Table IV) showed both **15** and **16** to be erythro isomers, while **17** was a threo isomer.[16]

Smith and Hewg have recently examined the ^1H NMR and ^{13}C NMR spectra of β-hydroxy ketones **18–26**, which are obtained by conjugate addition of a cuprate reagent to mesityl oxide, followed by reaction of the resulting enolate with an aldehyde.[17] NMR data for some compounds prepared in this manner are summarized in Table V. In each pair, the diastereomer having the smaller vicinal coupling constant also has its methine and carbinol resonances downfield. Professor Smith has determined the stereostructure of compounds **20** and **21** by single-crystal X-ray analysis of the benzoate ester of one of the diastereomers. He finds that, for this pair of aldols, the erythro diastereomer has the larger vicinal coupling constant. Thus, for this pair of isomers, both the conventional ^1H NMR and the currently described ^{13}C NMR criteria for stereostructure are reversed. Consideration of the probable conformational preferences for these compounds leads to an understanding of this reversal. The observed 10-Hz coupling constant for the erythro isomer **20** suggests that this compound exists in the conformation (**27**) in which the vicinal hydrogens are anti. Although the hydroxy group cannot hydrogen bond to the carbonyl group in this conformation, a gauche interaction of the phenyl and tertiary alkyl groups is avoided. It is interesting to note that conformation **27** is the conformation adopted by the benzoate of aldol **20** in the crystal. It is likely that the threo diastereomer **21** also exists in a conformation having the phenyl and tertiary alkyl groups anti (**28**), resulting in a gauche arrangement of the two hydrogens and a small vicinal coupling constant. The assumption that conformations **27** and **28** are the preferred conformations for erythro and threo diastereomers **20** and **21** accounts for the ^{13}C NMR chemical shifts quite well. Conformation **27** has one



27 28

less guache interaction than **21**, which explains why the methine and carbinol carbons resonate at lower field. Although structures for stereoisomeric pairs **18,19** and **22,23** have not been rigorously established, it is likely that these compounds have structures analogous to those of **20** and **21**, as indicated in Table V.

Table V. NMR Data for β-Hydroxycarbonyl Compounds 18–26

18, R = Et; R′ = Me
20, R = Ph; R′ = Me
22, R = Ph; R′ = Bu

19, R = Et; R′ = Me
21, R = Ph; R′ = Me
23, R = Ph; R′ = Bu
24, R = Me; R′ = Bu
25, R = Et; R′ = Bu
26, R = Me; R′ = Me

compd	J_{vic}, Hz	methine[a]	carbinol[a]	isomer
18	0	63.4	72.6	threo ?
19	9	66.7	73.2	erythro ?
20	3.5	66.5	72.7	threo
21	10	67.7	75.0	erythro
22	3	64.8	72.4	threo ?
23	10	66.2	74.8	erythro ?
24	7	66.2	67.7	erythro ?
25	8	65.2	73.2	erythro ?
26	7	67.9	67.9	erythro ?

[a] Relative to Me_4Si, in ppm.

For compounds **24–26**, only one diastereomer is available. On the basis of our results, we may conclude that these compounds are erythro stereoisomers. Although we prefer to have data for both isomers in cases which are not clear-cut, modification of the chemical shift values for known molecules by ^{13}C NMR substituent parameters does permit tentative assignments. As an example, consider the aldol **19** (R = Et, R′ = Bu; entry 8). We may compare this compound with the diastereomeric pair **18,19** (R = Et, R′ = Me; entries 1 and 2). The methine carbon in the butyl compound has an additional γ effect, relative to the methyl compound. If we take a value of −2 ppm for a γ effect, then the methine resonance for the butyl compounds should occur at 64.7 ppm in the erythro diastereomer and at 61.4 ppm in the threo diastereomer. The observed value of 65.2 ppm strongly suggests that this aldol has the erythro configuration. In summary, the model developed here for **1** and **2** provides a firm assignment of stereostructure, particularly when considering the chemical shift of the methyl carbons. In the case of **18** and **19**, the trends themselves are different, but the underlying explanations are not: the favored conformations of the compounds are compared and ^{13}C NMR substituent parameters applied to obtain the observed chemical shift trends.

Conclusions

We have demonstrated that stereoisomeric pairs of β-hydroxycarbonyl compounds **1** and **2**, as well as **3** and **4**, exhibit consistent ^{13}C NMR shifts and that comparison of such shifts permits assignment of stereostructure. However, we were not able to make analogous correlations for Cram's rule stereoisomers. We have accounted for the data with a six-membered hydrogen-bonded ring (in the case of **1** and **2**) and with a five-membered hydrogen-bonded ring (in the case of **3** and **4**). This is the first example of which we are aware (excluding some simple disubstituted butanes[18] and some sugar alcohols[19]) in which

(16) It should be noted that the relative stereochemistry between the β-hydroxycarbonyl unit and the sugar moiety is drawn as such only for convenience. The absolute stereostructures of **15**, **16**, and **17** have not been determined.
(17) R. A. J. Smith and K. Hewg, *Tetrahedron*, **35**, 425 (1979).
(18) N. Wilson and J. B. Stothers, *Top. Stereochem.*, **8** (1974).
(19) (a) W. Voelter, E. Breitmaier, G. Jung, T. Keller, and D. Hiss, *Angew. Chem., Int. Ed. Engl.*, **9**, 803 (1970); (b) G. Schwarr, D. Vyas, and W. Szarek, *J. Chem. Soc., Perkin Trans. 1*, 496 (1979).

^{13}C NMR has been utilized to assign stereochemistry in an acyclic system. We anticipate the continued use of ^{13}C NMR for the assignment of stereochemistry to acyclic systems.

Experimental Section

FT ^{13}C NMR spectra were recorded at 25.144 MHz by using a Nicolet Technology Corp. TT-23 spectrometer. The sweep width was 5 or 6 kHz, with a heteronuclear lock on deuterated solvent (deuteriochloroform). Chemical shift values were determined by computer analysis of the spectra and are accurate to ±0.1 ppm. Repetition rates of 2 s with pulse angles of 70° were typical. All spectra were recorded by using ^{1}H-noise decoupling. Chemical shift values are given relative to internal deuteriochloroform signals (77.0 ppm relative to external Me_4Si).

Acknowledgment. This work was supported in part by grants from the United States Public Health Services (NIH Grant No. AI-11607 and AI-15027) and the National Science Foundation (Grant No. CHE 75-23368). M.C.P. gratefully acknowledges the Fannie & John Hertz Foundation for financial support in the form of a fellowship. We are also grateful to the National Science Foundation for providing funds for the purchase of the ^{13}C NMR spectrometer (NSF Departmental Equipment Grant No. CHE 76-05512).

Registry No. *erythro*-I-1, 14366-89-3; *threo*-I-1, 17226-79-8; *erythro*-I-2, 71699-15-5; *threo*-I-2, 71699-16-6; *erythro*-I-3, 61878-66-8; *threo*-I-3, 61878-67-9; *erythro*-I-4, 71699-17-7; *threo*-I-4, 71699-18-8; *erythro*-I-5, 36677-29-9; *threo*-I-5, 36677-30-2; *erythro*-I-6, 71699-19-9; *threo*-I-6, 71699-20-2; Cram's-I-7, 71748-71-5; anti-Cram's-I-7, 71748-75-9; *threo*-I-8, 71699-21-3; Cram's-I-9, 71699-22-4; anti-Cram's-I-9, 71748-76-0; *erythro*-I-10, 71699-23-5; *threo*-I-11, 71699-24-6; I-12, 71699-25-7; I-13, 71748-72-6; *erythro*-I-14, 71699-26-8; *erythro*-I-15, 17226-86-7; *threo*-I-15, 17226-85-6; I-16, 71699-27-9; *erythro*-I-17, 71699-28-0; *threo*-I-17, 71699-29-1; Cram's-I-18, 71699-30-4; anti-Cram's-I-18, 71748-77-1; *erythro*-I-19, 71699-31-5; *threo*-I-19, 71699-32-6; *erythro*-I-20, 67498-18-4; *threo*-I-20, 67498-07-1; *erythro*-I-21, 67498-21-9; *threo*-I-21, 67498-06-0; *erythro*-I-22, 71699-33-7; *threo*-I-22, 71699-34-8; *erythro*-I-23, 71699-35-9; *threo*-I-23, 71699-36-0; *erythro*-I-24, 71699-37-1; *threo*-I-24, 71699-38-2; *erythro*-I-25, 71699-39-3; *threo*-I-25, 71699-40-6; *erythro*-I-26, 71699-41-7; *erythro*-I-27, 71699-42-8; *threo*-I-27, 71699-43-9; *erythro*-III-1, 71699-44-0; *threo*-III-1, 71699-45-1; *erythro*-III-2, 71699-46-2; *threo*-III-2, 71699-47-3; *erythro*-III-3, 71699-48-4; *threo*-III-3, 71699-49-5; *erythro*-III-4, 71699-50-8; *threo*-III-4, 71699-51-9; *erythro*-III-5, 71699-52-0; *threo*-III-5, 71699-53-1; *erythro*-III-6, 71733-84-1; *threo*-III-6, 71699-54-2; *erythro*-III-7, 71699-55-3; *threo*-III-7, 71699-56-4; *erythro*-III-8, 71699-57-5; *threo*-III-8, 71699-58-6; *erythro*-III-9, 71699-59-7; *threo*-III-9, 71699-60-0; *erythro*-III-10, 71699-61-1; *threo*-III-10, 71699-62-2; *erythro*-III-11, 71699-63-3; *erythro*-III-12, 71699-64-4; *threo*-III-12, 71699-65-5; III-13, 71699-66-6; *erythro*-III-14, 71699-67-7; *threo*-III-14, 71699-68-8; *erythro*-III-15, 71699-69-9; *threo*-III-15, 71699-70-2; *erythro*-III-16, 71699-71-3; *threo*-III-16, 71699-72-4; *erythro*-III-17, 71699-73-5; *threo*-III-17, 71699-74-6; III-18, 71699-75-7; **14**, 50693-03-3; **15**, 71699-76-8; **16**, 71748-73-7; **17**, 71748-74-8; **18**, 71686-69-6; **19**, 71686-70-9; **20**, 71686-71-0; **21**, 54008-25-2; **22**, 71686-79-8; **23**, 71686-78-7; **24**, 71699-77-9; **25**, 71686-76-5; **26**, 54008-24-1; benzaldehyde, 100-52-7.

Supplementary Material Available: The complete ^{13}C NMR spectra of the compounds reported herein (4 pages). Ordering information is given on any current masthead page.

Steroid Photochemistry. Photocycloaddition of a Linear Dienone to Diels–Alder 1,3-Dienes[1]

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The photocycloaddition of 3-keto-4,6-dienic steroids to seven *s*-trans, one *s*-cis, and one cis Diels–Alder dienes has been studied. The products obtained do not correlate with either the predominant configuration of the diene nor its triplet energy, but do correlate with the diene ionization potential. The dienes, butadiene, 2-methylbutadiene, 1-acetoxybutadiene, and 2,4-dimethyl-1,3-pentadiene, all undergo two competing cycloadditions. The first is a [2 + 2 + 2 + 2] cycloaddition on the α face of the steroid where both dienone double bonds add across the diene double bonds to form three annulated cyclobutane rings. The structure was confirmed by the isolation of the cyclobutanone derived from 1-acetoxybutadiene. The alternative [2 + 2 + 2 + 2] adduct, yielding a 5:4:5 ring system, was also obtained in a low yield with 2,3-dimethylbutadiene. The adducts with terminally substituted dienes are formed in a tail-to-tail manner. The second type of cycloaddition observed is a photo-Diels–Alder reaction to yield [4 + 2] adducts. The addition across the α,β dienone double bond yields exclusively the symmetry-allowed trans-4α,5β [4 + 2] adduct in a head-to-tail manner. This reaction is ascribed to an excited-state reaction rather than a ground-state trans double bond. Accompanying this product were tail-to-tail cis [4 + 2] cycloadditions across the γ,δ double bond. A transition occurs at approximately 8.4 eV, where the products are best described as being formed through a diradical with initial bonding at C4 of the dienone, followed by ring closure to generate cis and trans [2 + 2] as well as cis-4α,5α [4 + 2] adducts. This transition is characterized by 1-vinylcyclohexene, which gave a mixture of all the observed adducts with the exception of the [2 + 2 + 2 + 2] adduct. Below approximately 8.4 eV, the [2 + 2 + 2 + 2] and γ,δ [4 + 2] adducts were not formed. Thus, *trans,trans*-2,4-hexadiene, 1,1′-bicyclohexenyl, and 1,3-cyclohexadiene, normally a very reactive Diels–Alder diene, gave mainly [2 + 2] adducts across the α,β-dienone double bond, together with lesser amounts of the cis [4 + 2] adduct. The dienone does not phosphoresce but does fluoresce and the fluorescence is quenched by *trans, trans*-2,4-hexadiene. The photocycloadditions are efficiently, and differentially, quenched by 3,3,4,4-tetramethyl-1,2-diazetidine 1,2-dioxide. The reactions are postulated to occur through the $\pi\pi^*$ triplet excited state of the dienone. The cycloadditions are discussed in terms of Epiotis and Shaik's theoretical $\pi\pi^*$ triplet photocycloaddition model.

The study of the photocycloaddition of steroidal enones to olefins succeeded the original discovery of the photocycloaddition of simple cyclohexenones to olefins.[2] Although there are many similarities between these enones,

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