a common aldehyde, benzaldehyde, to minimize the changes in reaction variables, we have found our observations to be general. For example, the (*Z*)-dibutylboron enolate derived from 3-pentanone affords cleanly the *erythro*-aldol adducts with *n*-butyraldehyde, isobutyraldehyde, crotonaldehyde, and methacrolein.[15]

The generality of these reactions and the application of chiral boron enolates to enantioselective aldol condensations will be reported in due course.

Acknowledgment. This work has been supported by the National Science Foundation.

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(1) (a) J.-E. Dubois and M. Dubois, *Tetrahedron Lett.*, 4215 (1967); (b) J.-E. Dubois and P. Fellmann, *C.R. Acad. Sci.*, **274**, 1307 (1972); (c) J.-E. Dubois and P. Fellmann, *Tetrahedron Lett.*, 1225 (1975).

(2) (a) W. A. Kleschick, C. T. Buse, and C. H. Heathcock, *J. Am. Chem. Soc.*, **99**, 247 (1977); (b) C. T. Buse and C. H. Heathcock, *ibid.*, **99**, 8109 (1977).

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(4) H. O. House, D. S. Crumrine, A. Y. Teranishi, and H. D. Olmstead, *J. Am. Chem. Soc.*, **95**, 3310 (1973).

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(6) Preliminary reports indicate that dialkylaluminum enolates might prove useful in some cases; however, bond length considerations[5] render these systems somewhat less attractive: (a) E. A. Jeffery, A. Meisters, and T. Mole, *J. Organomet. Chem.*, **74**, 365 (1974); (b) K. Marnoka, S. Hashimoto, Y. Kitagawa, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **99**, 7705 (1977).

(7) (a) T. Mukaiyama and T. Inoue, *Chem. Lett.*, 559 (1976); (b) W. Fenzl and R. Köster, *Justus Liebigs Ann. Chem.*, 1322 (1975); the (*Z*)- and (*E*)-enolates (R_1 = Ph) were reported to undergo stereoselective condensation with C_2H_5CHO to give **4a** and **5a**, respectively.

(8) (a) For representative B–O bond lengths, see W. H. Zachariasen, *Acta Crystallogr.*, **16**, 385 (1963). (b) For representative B–C bond lengths, see D. Groves, W. Rhine, and G. D. Stucky, *J. Am. Chem. Soc.*, **93**, 1553 (1971); L. S. Bartell and B. L. Carroll, *J. Chem. Phys.*, **42**, 3076 (1965).

(9) (a) G. Schmitt and B. Olbertz, *J. Organomet. Chem.*, **152**, 271 (1978); (b) E. Vedejs, D. A. Engler, and J. E. Telschow, *J. Org. Chem.*, **43**, 188 (1978).

(10) To tricyclopentylborane (H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **81**, 6423 (1959)) (1 equiv) was added with cooling 1 equiv of trifluoromethanesulfonic acid. Short-path distillation afforded **2b** in 90% yield, bp 70–72 °C (1.0 mmHg).

(11) Satisfactory spectral and analytical data were obtained on all new compounds.

(12) Boron trilfate **2c** was generated in situ in the following manner. A mixture of 1 equiv each of thexylborane and cyclopentene in THF (1.0 M) was stirred at −30 °C (1 h), cooled to −78 °C, and quenched with 1 equiv of trifluoromethanesulfonic acid (dropwise).

(13) Treatment of *tert*-butyl thiopropionate with LDA (Et_2O, −78 °C) affords ≥95% enolate corresponding to **3E** in direct analogy to the observation of Ireland.[14]

(14) R. E. Ireland, R. H. Mueller, and A. K. Willard, *J. Am. Chem. Soc.*, **98**, 2868 (1976).

(15) NOTE ADDED IN PROOF. S. Masamune has recently reported qualitatively similar observations with boron enolates: S. Masamune, S. Mori, D. Van Horn, and D. W. Brooks, *Tetrahedron Lett.*, 1665 (1979).

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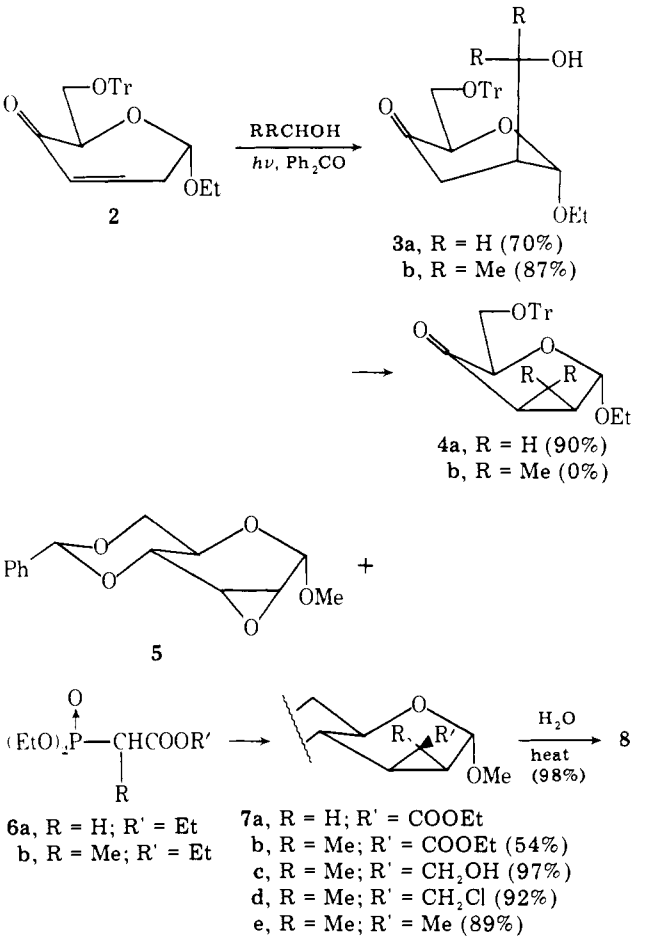
Annulated Pyranosides as Chiral Synthons for Carbocyclic Systems. Enantiospecific Routes to Both (+)- and (−)-Chrysanthemumdicarboxylic Acids from a Single Progenitor

Sir:

There is currently considerable interest in the use of carbohydrate derivatives as chiral synthons as may be judged from the growing number of synthetic accomplishments in recent years.[1] These accomplishments fall largely into two categories

Scheme I



for which we have suggested[2] the terms (a) **acyclic transfer** and (b) **cyclic transfer** to denote the manner in which the carbohydrate moiety has been employed. A third category, (c) **transcription,** may be recognized[1,8] which is particularly applicable to carbocyclic compounds, and, in this context, it is noteworthy that Stork's synthesis of the prostaglandins[9] is the only instance, to our knowledge, where a carbocyclic natural product has been synthesized from a sugar.[10]

In this communication, we introduce the novel concept of annulated pyranosides as chiral synthons for carbocyclic systems, and exemplify the potential of this methodology by outlining the enantiospecific syntheses of (+)- and (−)-chrysanthemumdicarboxylic acids (**1**) from a single precursor, whereby all stereochemical centers of the target are of known, predetermined configuration by *"transcription"* from the carbohydrate template. *A significant aspect of this work is that it makes provision for preparing chrysanthemates with isotopic labels at a variety of specific sites.*

In the context of this project, the key structural feature is the *gem*-dimethylcyclopropane ring, and, of the many routes[12-14] which we and others have developed to *cyclopropano*-pyranosides, the one chosen for initial study is that summarized in Scheme I. Thus, the photoinduced alkylation of enone **2** with methanol gave the ketol **3a** which was converted into **4a** in excellent yield.[13] For the synthesis of **4b,** the tertiary alcohol **3b** was obtained in 87% yield by alkylation of **2** with 2-propanol. However, all attempts[15] to bring about cyclization **3b**[16] → **4b** met with abject failure.

We next turned our attention to the carboethoxy cyclopropane **7a,** first prepared by Meyer zu Reckendorf[14a] and studied further by us.[14b] Attempts to α-methylate **7a** were unsuccessful. We therefore examined the reaction of **5** with the

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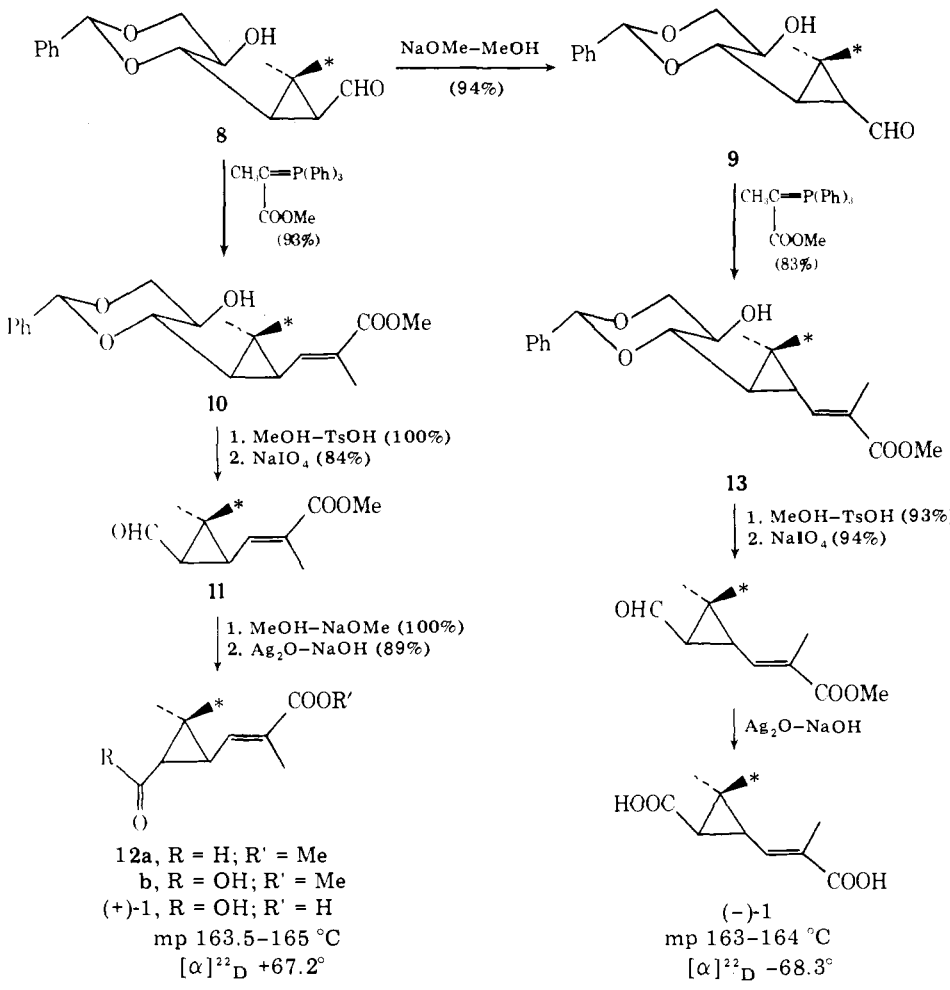
Scheme II



propionate **6b,** but with some reluctance since Denney had reported that, unlike the acetate **6a,** the propionate **6b** did not react with oxiranes to give cyclopropanes. However, unstinting experimentation was rewarded with a procedure[18] which gave 54% **7b**[16] after chromatography. In spite of this comparatively low yield, scrupulous searching failed to reveal any identifiable product in the detritus of the reaction thereby establishing that **7b** *was the only stereoisomer formed.* The endo location of the methyl group was deduced by irradiating the methyl signal at 1.38 ppm whereupon an NOE (10%) was detected for H-1.

The most satisfactory route to the *gem*-dimethyl derivative **7e,** proved to be reduction of **7b** to the alcohol **7c** ($LiAlH_4$, Et_2O, 23 °C, 97%), chlorination[19] to **7d**[16] (DMF, CH_3SO_2Cl, 23 °C, 92%), and again reduction to **7e**[16] ($LiAlH_4$, THF, reflux, 89%).

As was expected, the hydrolysis of the anomeric acetal of **7e** giving the hydroxy aldehyde **8**[16] occurred readily[20,21] under neutral conditions (H_2O–dioxane, reflux, 1.5 h, 98%). That this treatment had not caused concomitant epimerization at C-2 was established by treating **8** with sodium methoxide (23 °C, 12 h) whereupon a new aldehyde was obtained in *quantitative* yield. The latter was assigned as the thermodynamically preferred trans isomer **9,** and, although both **8** and **9** had the same mobility in TLC, the difference was apparent in the doublets for H-1 (9.45 and 9.32 ppm, respectively).

Reaction of **8** with 1.1 equiv of $Ph_3P{=}C(CH_3)CO_2CH_3$ in CH_2Cl_2 (23 °C, 1.5 h) afforded **10**[16] in 93% yield after chromatography. This assignment of structure follows from the known stereochemistry of these reactions,[22] and the failure to detect the other *Z* isomer in the mother liquors. Since the reagent is neutral, epimerization of the aldehyde should not occur—and this is subsequently shown to be true (Scheme II).

Hydrolysis of the benzylidene ring (MeOH, TsOH, 23 °C, 5 h) followed by cleavage with sodium metaperiodate gave **11**[16] in 84% overall yield, and epimerization (NaOMe, MeOH, room temperature, 12 h) gave **12a**[16] quantitatively. The signals for the aldehydic protons (9.60 and 9.50 ppm, respectively) readily differentiated **11** from **12a.**

Oxidation of the aldehyde in alkaline solution (Ag_2O, NaOH, H_2O, dioxane) was complete within 10 min at 23 °C giving pyrethric acid (**12b**). However, the mixture was normally allowed to stand for 4 h, whereupon chrysanthemumdicarboxylic acid ((+)-**1**) was obtained in 89% overall yield. The physical constants (Scheme II) were identical with those of an authentic sample.[23]

The isolation of the dextrorotatory enantiomer of **1** confirmed our earlier assignment of the aldehydes **8** and **9.** However that epimerization had been undertaken for reasons other than structure elucidation. Thus, isomer **9** could be transformed into the other enantiomer (−)-**1** by exactly the same sequence of reactions—with the exception of the epimerization at the penultimate stage. There were only minor differences as, for example, the formation of some of the *Z* isomer corresponding to **13.**

With the exception of the initial cyclopropanation, giving **7b,** all reactions are seen to proceed in excellent yields. Thus, the nine steps from **7b** to (+)-**1** and (−)-**1** occur in 55 and 45% overall yield, respectively.

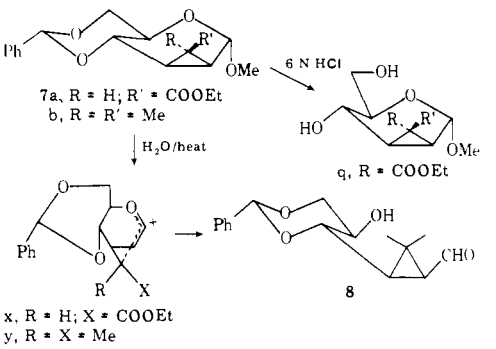
The mode of formation of the *gem*-dimethyl function in **7e** (Scheme I) indicates that the *exo*-methyl group can be specifically tagged with a variety of labels (e.g., CT_3, CD_2T,

CH_2D, CT_2H, etc.) depending on the reagent used ($LiAlH_4$, $LiAlD_4$, or $LiAlT_4$) in the two reduction steps. Thus, the (*pro-S*)-methyl group of (+)-**1** may be specifically identified. Furthermore, reduction of the ester of **10** to a methyl group could yield chrysanthemic acid labeled at that geometric site. Alternatively the "other" methyl groups in **7e** and **10** could be labeled by using the suitably labeled propionates for the reaction with **5**. In addition, the epimerization **11** → **12a** allows for the introduction of hydrogen isotopes at C-2 of (+)-**1**. Thus, multiple labels may be introduced into the chrysanthemate esters, the locations of which are known by "*transcription*" from the original sugar template.

Acknowledgments. We are indebted to the National Research Council of Canada, Bristol Laboratories (Syracuse), and Merck Sharp and Dohme (Rahway) for financial support. We thank Mr. Brian Sayer of McMaster University for NOE measurements on **7b** and Dr. A. Grey of the Canadian 220 MHz NMR Centre for the 220-MHz spectra.

References and Notes

(1) R. C. Anderson and B. Fraser-Reid, *Fortschr. Chem. Org. Naturst.*, in press.
(2) For detailed discussion of these categories, see ref 1. Briefly, in "cyclic transfer" the chiral component of the target molecule is displayed in linear form so as to facilitate stereochemical correlations with Fischer projections of various sugars. The required segment is then fabricated from a suitable sugar template, excised if necessary therefrom, and incorporated into the target molecule. The majority of examples of the use of carbohydrates in asymmetric syntheses falls into this category although the synthetic targets vary widely as to their degree of modesty[3] and complexity.[4] In cyclic transfer, pyranoid or furanoid modules of the target molecule are prepared by attaching the required stereochemical and functional paraphernalia to an appropriate pyranose or furanose substrate, and than transferring the entire assembly as a discrete entity. Examples falling into this category are our syntheses of avenaciolide[5] and its congeners[6] and the various syntheses of thromboxane.[7]
(3) D. R. Hicks and B. Fraser-Reid, *J. Chem. Soc., Chem. Commun.*, 869 (1976).
(4) S. Hanessian and G. Rancourt, *Can. J. Chem.*, **55**, 1111 (1977); S. Hanessian, G. Rancourt, and Y. Guindon, *ibid.*, **56**, 1843 (1978).
(5) R. C. Anderson and B. Fraser-Reid, *J. Am. Chem. Soc.*, **97**, 38-70 (1975).
(6) R. C. Anderson and B. Fraser-Reid, *Tetrahedron Lett.*, 2865 (1977); 3233 (1978).
(7) S. Hanessian and P. Lavalle, *Can. J. Chem.*, **55**, 562 (1977); E. J. Corey, M. Shibasaki, and J. Knolle, *Tetrahedron Lett.*, 1625 (1977); O. Hernandez, *ibid.*, 219 (1978).
(8) The term "transcription" is best appreciated by considering, as a specific example, the elegant synthesis of $PGF_{2\alpha}$ by Stork and co-workers[9a] where, in contrast to the examples in "cyclic" or "acyclic transfer", the structural element derived from the carbohydrate is not immediately identifiable. Nevertheless, all of the stereochemical features, chiral as well as geometric, were "transcribed" from the sugar.
(9) (a) G. Stork, T. Takahashi, I. Kawamoto, T. Suzuki, *J. Am. Chem. Soc.*, **100**, 8272 (1978); (b) G. Stork and T. Takahashi, *ibid.*, **99**, 1275 (1977); (c) G. Stork and S. Raucher, *ibid.*, **98**, 1583 (1976).
(10) 6-Deoxy-6-nitroaldohexoses may be cyclized into deoxynitroinositols,[11] but these may be considered to represent a special case.
(11) J. M. Grosheintz and H. O. L. Fischer, *J. Am. Chem. Soc.*, **70**, 1479 (1948); J. Kovar and H. H. Baer, *Can. J. Chem.*, **51**, 1801 (1973); F. W. Lichtenthaler, *Chem. Ber.*, **94**, 3071 (1961).
(12) See, for example, B. K. Radatus and B. Fraser-Reid, *Can. J. Chem.*, **50**, 2909 (1972); E. L. Albano, D. Horton, and J. H. Lauterbach, *Carbohyd. Res.*, **9**, 149 (1969).
(13) B. Fraser-Reid, N. L. Holder, D. R. Hicks, and D. L. Walker, *Can. J. Chem.*, **55**, 3978 (1977).
(14) (a) W. Meyer zu Reckendorf and U. Kamprath-Scholtz, *Chem. Ber.*, **105**, 673 (1972); (b) B. Fraser-Reid and B. J. Carthy, *Can. J. Chem.*, **50**, 2928 (1972).
(15) These studies will be described in detail in the full paper.
(16) This compound gave satisfactory elemental and/or mass spectral analysis and spectroscopic (220-MHz, NMR, IR, UV) data.
(17) D. B. Denney, J. J. Vill, and M. J. Boskin, *J. Am. Chem. Soc.*, **84**, 3944 (1962).
(18) In a glass-lined monel pressure reactor, the phosphoropropionate **6** (5 equiv) was added dropwise to a suspension of sodium hydride (5 equiv) in dry dioxane and compound **5** (1 equiv) was then added. After 4 days at 160 °C the starting material was all consumed and the product was recovered by standard procedures.
(19) M. E. Evans, L. Long, and F. W. Parrish, *J. Org. Chem.*, **33**, 1074 (1968).
(20) The ease of hydrolysis of the glycosyl acetal in **7e** is readily rationalized by formation of the intermediate ion y which we had previously named "cyclopropylcarbinyl-oxocarbonium" to depict the two primary modes of stabilization operating therein.[21] In keeping with this rationalization, treatment of **7a** with 6 N HCl left the anomeric center completely untouched, removing instead the benzylidene acetal to give the diol q.[14a] Obviously,



the stabilization of the positive charge is not favored in the ion x because of the electron-withdrawing nature of the carboxylate group. On the other hand, the two methyl groups in y give added stabilization to the ion, thereby facilitating the formation of **8**.
(21) B. K. Radatus and B. Fraser-Reid, *J. Chem. Soc., Perkin Trans. 1*, 1872 (1975), and references cited therein.
(22) H. House, "Modern Synthetic Reactions", W. A. Benjamin, Menlo Park, Calif., 1972, p 701 ff.
(23) We are grateful to Professor Leslie Crombie for an authentic sample of (+)-**1**.
(24) Holder of a NRC (Canada) predoctoral studentship, 1978-1979.

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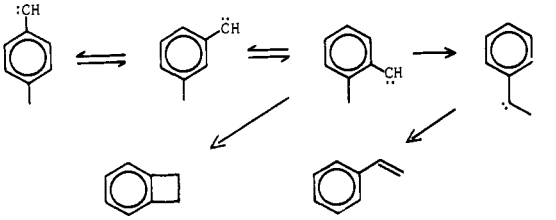
The Carboranylcarbene Rearrangement[1]

Sir:

The interconversion of substituted phenylcarbenes in the gas phase reveals itself through intramolecular trapping.[2] For instance, *p*-tolylcarbene gives benzocyclobutene and styrene through a series of intramolecular rearrangements passing over the meta and ortho isomers.



The analogy between benzene and the icosahedral carboranes (dicarba-*closo*-dodecaborane(12)s) has been often made.[3] It occurred to us that a question worth probing was the extent of stabilization conferred on a divalent carbon by an adjacent carborane polyhedron. To what extent would the reactions of phenylcarbene and diphenylcarbene be mimicked by those of carboranylcarbene and dicarboranylcarbene? How similar would the three-dimensional carborane cage compounds be to their more classically "two-dimensional" aromatic relatives?[4a] Although we are currently investigating intermolecular solution chemistry,[4b] we also conceived of examining the ability of the carborane cage to act as a conduit for the passage of divalent carbon from one position to another, much as does a benzene ring.[2,5] It is this reaction that we report here.

The required diazo compound **3c** was produced most conveniently from 1-vinyl-*o*-carborane (**1**)[6] by a sequence involving methylation to give 1-vinyl-2-methyl-*o*-carborane (**2**) and ozonolysis to give aldehyde **3a** which could be converted in unexceptional steps into the tosylhydrazone salt **3b**. Dry distillation at 60–100 °C (0.05 Torr) yielded diazo compound **3c** (diazo band, 2080; B-H, 2590 cm^{-1}).

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