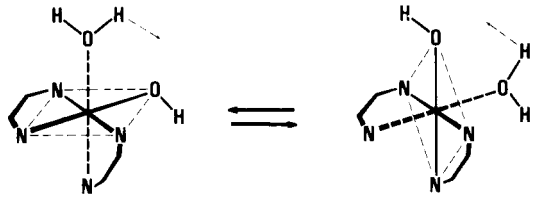

Figure 6. Proposed structure of title complex in basic solution.

^{1}H NMR spectrum of the tris(2,2′-bipyridine)osmium(II) complex[6] in which all of the H-6 hydrogens have δ 7.6 ppm. The ^{13}C NMR spectra of $[Pt(bpy)_2OH]^+$ (Figure 5) and *cis*-$[Rh(bpy)_2Cl_2]^+$ (which was measured because it was readily available to us) are also very similar, and it is especially noteworthy that the four broad bands referred to in Figure 5 also appear in the kinetically inert rhodium complex. Since chemical exchange can presumably be excluded in this latter complex, these bands are probably due to intramolecular distortions in the flexible ligands.

All experimental evidence therefore points toward a configurational change from a distorted square planar structure in neutral solutions to a five- (or six-) coordinated species in alkaline solution. In the latter the two bpy ligands are in the cis position to each other. This is also supported by the ^{1}H-methyl resonance in the platinum(II) complex with 5,5′-dimethyl-substituted bipyridine which splits in basic solution[4] just as do the H-5 and the H-5′ protons of Figure 4, and we see no way to explain our data within the "covalent hydration of the ligand" hypothesis advanced by Gillard.[2]

A more detailed structure of $[Pt(bpy)_2OH]^+$ must necessarily be speculative. This could be a five-coordinate trigonal bipyramid but also could be a distorted six-coordinate complex derived from a normal square planar Pt(II) complex. Thus the structure in Figure 6 is consistent with all the NMR experiments because proton transfer enables OH^- to exchange between the two sites shown as OH and OH_2 in the figure with a rate which is rapid on the NMR time scale.

It is a notable feature of the so-called "Gillard pseudo base mechanism" that phen and bpy and also OH^- and CN^- are assumed to behave analogously. It is therefore relevant to the present work that OH^- and CN^- give analogous changes in the UV-visible spectrum of $[Pt(phen)_2]^{2+}$ and that studies of the $[Pt(phen)_2CN]^+$ cation have shown that the CN^- group is directly coordinated to the platinum both in solution[7] and in the solid state.[8] Neither for this complex nor for $[Pt(bpy)_2OH]^+$ is it necessary to invoke new or "novel" mechanisms or structures.

The present NMR study confirms the suggestion[3] that the hydrolysis of $Pt(bpy)_2^{2+}$ in basic solution occurs via attack on the metal center and therefore by the associative mechanism generally accepted for substitution reactions in Pt(II) complexes.[9]

Acknowledgment. Thanks are due to O. Wernberg and A. Hazell for access to unpublished data and to E. Jonas Pedersen and K. Bock for help with the interpretations of the NMR spectra. The NMR spectrographs are the property of the Danish Natural-Science Research Council.

References and Notes

(1) The following abbreviations are used in this paper: phen, 1,10-phenanthroline; bpy, 2,2′-bipyridine.
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Stereoselective Aldol Condensations via Boron Enolates

Sir:

The aldol condensation is a reaction of fundamental importance in biosynthesis. Consequently, considerable effort has been expended to develop stereoregulated variants of this process in the laboratory. It is now well appreciated that *kinetic* aldol stereoselection is, in part, defined by enolate geometry for those condensations wherein two new stereocenters are created in the condensation step (Scheme I).[1,2] Given the reasonable postulate that the reaction proceeds via a pericyclic process,[1a,2a] the influence of variable steric parameters may be analyzed to determine their effects upon the relative heats of formation of diastereoisomeric transition states from an enolate of defined geometry. For example, for (*E*)-enolates one might anticipate that transition state T_2 might be destabilized relative to T_1 by maximizing *both* $R_2 \leftrightarrow R_1$ and $R_2 \leftrightarrow L$ steric parameters. Heathcock and co-workers have recently dem-

Scheme I

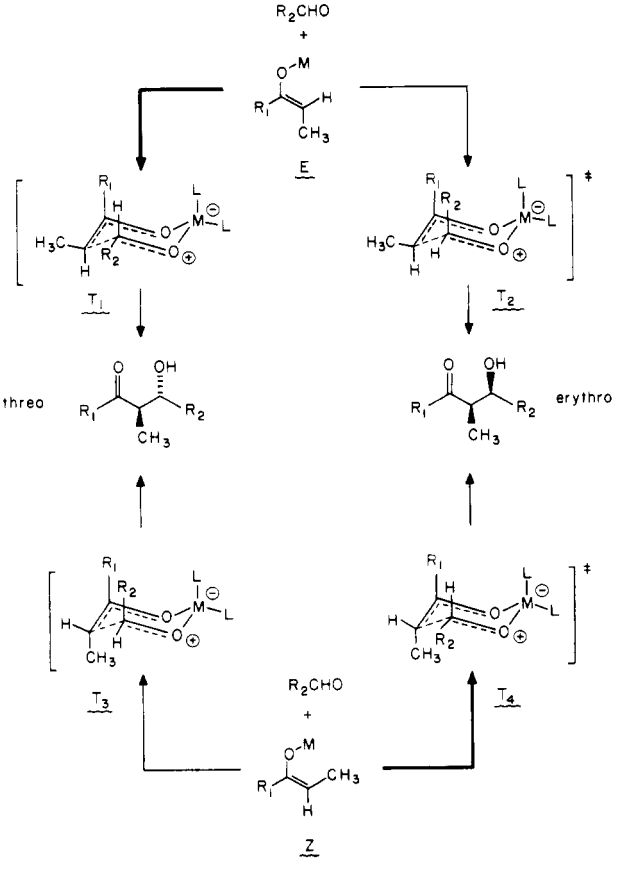
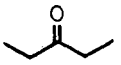
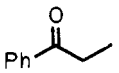
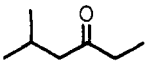
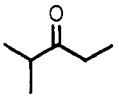
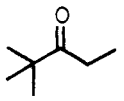
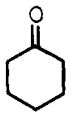
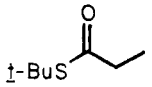


Table I.[11] Aldol Condensation of Dialkylboron Enolates with Benzaldehyde

Entry	$RCOCH_2CH_3$ (1)	L_2BOTf (2)	Conditions[a] Enolate Formation	Enolate Ratio[b] 3Z:3E	Aldol Ratio[c] 4b:5b	Yield, %[d]
A		L = n-C_4H_9 (2a)	-78 °C, 30 min	>99:1	>97:3	77
		L = n-C_4H_9 (2a)	-78 °C, 30 min (lutidine)	69:31	72:28	76
		L = C_5H_9 (2b)	0 °C, 30 min	82:18	84:16	86
B		L = n-C_4H_9 (2a)	25 °C, 1 h	>99:1	>97:3	82
C		L = n-C_4H_9 (2a)	-78 °C, 30 min 0 °C, 30 min	>99:1	>97:3	82
D		L = n-C_4H_9 (2a)	-78 °C, 30 min 0 °C, 1 h	45:55	44:56	(92)
		L = C_5H_9 (2b)	0 °C, 30 min	19:81	18:82	87
E		L = n-C_4H_9 (2a)	35 °C, 2 h	>99:1	>97:1	65
F		L = n-C_4H_9 (2a)	-78 °C, 1 h	--	33:67	(71)
		L = n-C_5H_9 (2b)	-78 °C, 1 h	--	32:68	74
G		L = n-C_4H_9 (2a)	0 °C, 30 min	≤ 5:95	10:90	80
		L = C_5H_9 (2b)	0 °C, 30 min	≤ 5:95	5:95	90

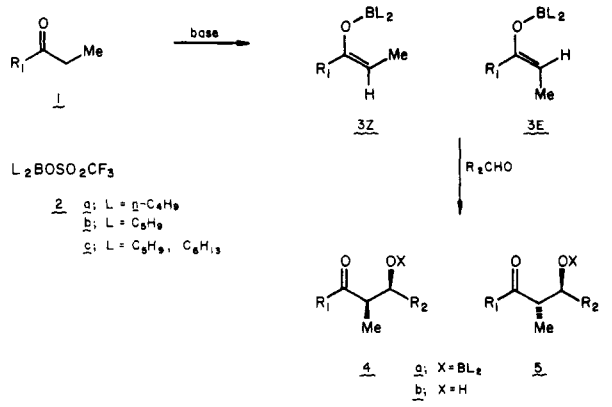
[a] Except where noted, diisopropylethylamine was employed as the enolization base. [b] Enolate ratios were determined by conversion of **3Z-3E** mixtures to the corresponding trimethylsilyl enol ethers via successive treatment with methyllithium (3 equiv) and chlorotrimethylsilane and subsequent comparison with authentic samples by GLC. [c] Aldol ratios were determined by ^1H NMR. [d] Values reported are isolated yields. Values in parentheses refer to yields determined by ^1H NMR relative to internal standard.

onstrated that, for specified (*Z*)- and (*E*)-lithium enolates (R_1 sterically demanding), excellent diastereoselection could be attained in the formation of *erythro*- and *threo*-aldol adducts respectively; however, for less bulky enolate substituents (R_1 = C_2H_5, *i*-C_3H_7, C_6H_5, OMe, N(*i*-$C_3H_7)_2$), diastereoselection has been generally observed to be greatly diminished.[1-4] Owing to the fact that metal-oxygen bond lengths for these and related metal enolates (M = Li, MgL, ZnL, AlL_2) are relatively long (~1.9-2.2 Å),[5a] as are the M-L bond lengths (M-C ~ 2-2.2 Å),[5b] the origin of the observed stereoselection *could* be largely due to $R_1 \leftrightarrow R_2$ interactions.

In an effort to confer greater stereochemical control in kinetically controlled aldol processes, we have studied the steric effects conferred upon these reactions by the metal center. Accordingly, maximal pseudo-1,3-diaxial $R_2 \leftrightarrow$ L interactions in the transition states T_2 and T_3 might be achieved by *minimizing* M-O and M-L bond lengths (*D*) and *maximizing* the bulk of the metal ligands.[6] Dialkylboron enolates (M = BL_2),[7] which may be readily prepared under mild conditions from ketones and dialkylboron triflates (**2**),[7a] satisfy the above criteria (D_{B-O} = 1.36-1.47, D_{B-C} = 1.5-1.6 Å),[8] and one case, **3Z** and **3E** (R_1 = Ph), has been reported to undergo condensation with propionaldehyde (R_2 = Et) to give **4a** and **5a**, respectively (cf. Scheme II).[7b]

The present study demonstrates the generality of employing boron enolates in stereoselective aldol condensations and the utility of boron triflates **2** in the selective *enolization* of ketones and thio esters. The representative aldol condensations summarized in Table I were carried out according to the following general procedure. To equimolar quantities of **2a**[7a] and diisopropylethylamine (1.1 equiv), as a 0.5 M solution in anhydrous ether at −78 °C under argon, is added 1 equiv of ketone. After the reaction mixture was stirred for 30 min at −78 °C, a white precipitate of amine triflate indicates enolate formation; if no precipitate is observed, the reaction mixture is warmed to 0 °C or room temperature. Under these conditions there is no apparent equilibration of (*Z*)- and (*E*)-enolates; however, if the solution is subsequently heated at reflux (1-3 h), enolate equilibration may be achieved. The resultant enolate solution is cooled to −78 °C, 1 equiv of aldehyde is added, and the solution is stirred for 30 min at − 78 °C followed by 1-2 h at 0 °C. The resultant boron chelates **4a** are most efficiently oxidized to the ketols **4b** by the addition of 1.5 equiv of MoO_5·py·HMPA, MoOPH[9] (30 min, 0 °C; 45 min, 25 °C),

Scheme II



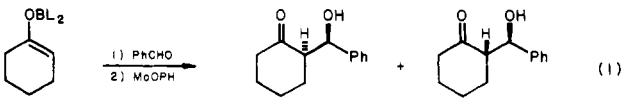
followed by the addition of 1 N aqueous sodium hydroxide solution. In our hands this oxidant is superior to the classical hydrogen peroxide procedure.[7a] For boron triflate **2b**,[10] enolization at 0 °C rather than −78 °C appears to be necessary. Control experiments were carried out to ensure that the product ratios were a result of complete kinetic stereoselection. In all cases examined it was found that the primary aldol products **4a** and **5a** were quite stable (34 °C, 3 h, Et_2O) and that subsequent conversion of these boron chelates into the hydroxy ketones **4b** and **5b** proceeded *without* loss of stereochemistry.

A number of conclusions may be drawn from the data in Table I. Entry A underlines two important points which have influenced subsequent studies. First, in the reaction of diethyl ketone with boron triflate **2a** (L = *n*-Bu), the *kinetic* enolate ratio is a function of the base employed in the enolization process (EtN(*i*-Prop)$_2$, **3Z**:**3E** ≥ 99:1; lutidine, **3Z**:**3E** = 69:31). Second, with a given amine base (EtN(*i*-Prop)$_2$), the boron ligand (L) in the triflate reagent **2** exerts a pronounced effect upon the kinetic enolate ratio (L = *n*-Bu, **3Z**:**3E** = 99:1; L = C_5H_9, **3Z**:**3E** = 84:16). We surmise that the consequence of boron ligand effects on the kinetic enolization process may well be generalizable (cf. entry D). With the exception of entry E, the conditions reported in the table reflect apparent kinetic control during the enolization process. Under kinetic conditions (−78 °C → 0 °C), *tert*-butylethyl ketone afforded, in low conversion, an enolate ratio of *Z*:*E* ~ 25:75; however, in refluxing ether, enolization and attendant enolate equilibration resulted in the production of the pure (*Z*)-enolate (entry E).

Given the illustrated dialkylboron enolates of defined structure, the resultant aldol diastereoselection observed with benzaldehyde is excellent. It is readily apparent that, for a given aldehyde, enolate steric parameters, R_1 (Scheme I), can be varied without loss of aldol diastereoselection. These results are in marked contrast to those of Heathcock and co-workers in their investigations with lithium enolates.[2] These comparative observations between boron and lithium enolates support our hypothesis that metal center steric effects are important in conferring enhanced diastereoselection to the condensation process. In general, we have found that (*Z*)- boron enolates exhibit *higher* levels of diastereoselection (erythro:threo ≥ 30) than (*E*)-boron enolates (threo:erythro = 2 − 19). Corresponding trends have been noted with lithium enolates.[1c,2]

The modest levels of diastereoselection observed with cyclohexanone (entry F) were surprising. Accordingly, this system was chosen to study the interplay between boron ligand structure and the role of solvent effects on kinetic aldol stereoselectivity (Table II). For a given boron ligand (entries A, B) there appears to be a small but consistent solvent effect (c.f. entries C, D). Nonpolar solvents, in general, may affect compression of the diastereoisomeric transition states and confer

Table II.[11] Aldol Condensation of **6** With Benzaldehyde (Eq 1). Ligand and Solvent Effects

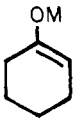
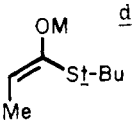
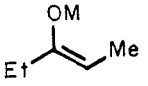


(1)

entry	$L_1L_2BOSO_2CF_3$ (**2**)	conditions,[a] solvent, temp (°C)	ratio[b] of **7**:**8**	yield, %,[c] of **7** + **8**
A	L_1, L_2 = *n*-C_4H_9 (**2a**)	ether, −78	33:67	71
B	L_1, L_2 = *n*-C_4H_9 (**2a**)	pentane, −78	17:83	100
C	$L_1, L_2 = C_5H_9$ (**2b**)	ether, −78	32:68	(74)
D	$L_1, L_2 = C_5H_9$ (**2b**)	pentane, −78	15:85	80
E	$L_1 = C_5H_9$, $L_2 = C_6H_{13}$ (**2c**)	CH_2Cl_2, −78	6:94	68
F	$L_1 = C_5H_9$, $L_2 = C_6H_{13}$ (**2c**)	THF, −78 to −30	<4:96	94 (73)

[a] All reactions employed diisopropylethylamine as a base. [b] Ratios determined by ^1H NMR (ref 4). [c] NMR yields; those in parentheses are isolated yields.

Table III.[11] Influence of Metal Center on Kinetic Aldol Reactions with Benzaldehyde

Enolate	Metal, M	Ratio[a] Erythro:Threo
	Li[b]	50:50
	$Al(C_2H_5)_2$[c]	50:50
	$B(C_5H_9)C_6H_{13}$	<4:96
 [d]	Li[e]	60:40
	$B(C_5H_9)_2$	5:95
 [f]	Li[g]	80:20
	B(n-$C_4H_9)_2$	>97:3

[a] Ratios determined by ^1H NMR. [b] Carried out at −20 °C (5 min) in DME (ref 4). [c] Reference 6b. [d] Reference 13. [e] Carried out at −70 °C (5 min) in THF. [f] Prepared from the (*Z*)-trimethylsilyl enol ether (ref 1c) and methyllithium. [g] Carried out at −70 °C (10 s) in THF.

greater reaction stereoselectivity. In a given solvent little enhancement in stereoselectivity was observed in changing the boron ligand from *n*-butyl to cyclopentyl (entries B, D); however, with the cyclopentyl thexyl enolate, prepared from boron triflate **2c**[12] (entries E, F), a *significant* improvement in reaction stereoselectivity was observed. Modestly increased aldol diastereoselection induced via boron ligand structural changes was also noted with *tert*-butyl thiopropionate (entry G, Table I).

Table III summarizes the results of three kinetic enolate condensations with benzaldehyde where a direct comparison can be made upon the influence of the metal upon the degree of diastereoselection. It is evident that the boron enolates are superior to the corresponding lithium enolates in stereoselective bond construction.

Although the aforementioned studies were carried out with

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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(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).
(5) (a) J. O. Thomas, R. Tellgren, and J. Almlöf, *Acta Crystallogr., Sect. B*, **31**, 1946 (1975); G. B. Johansson and O. Lindqvist, *ibid.*, **32**, 412 (1976); G. de With, S. Harkema, and G. H. van Hummel, *ibid.*, **32**, 1980 (1976); (b) R. G. Vranka and E. L. Amma, *J. Am. Chem. Soc.*, **89**, 3121 (1967); R. L. Gerteis, R. E. Dickerson, and T. L. Brown, *Inorg. Chem.*, **3**, 872 (1964); E. Weiss, *J. Organomet. Chem.*, **2**, 314 (1964).
(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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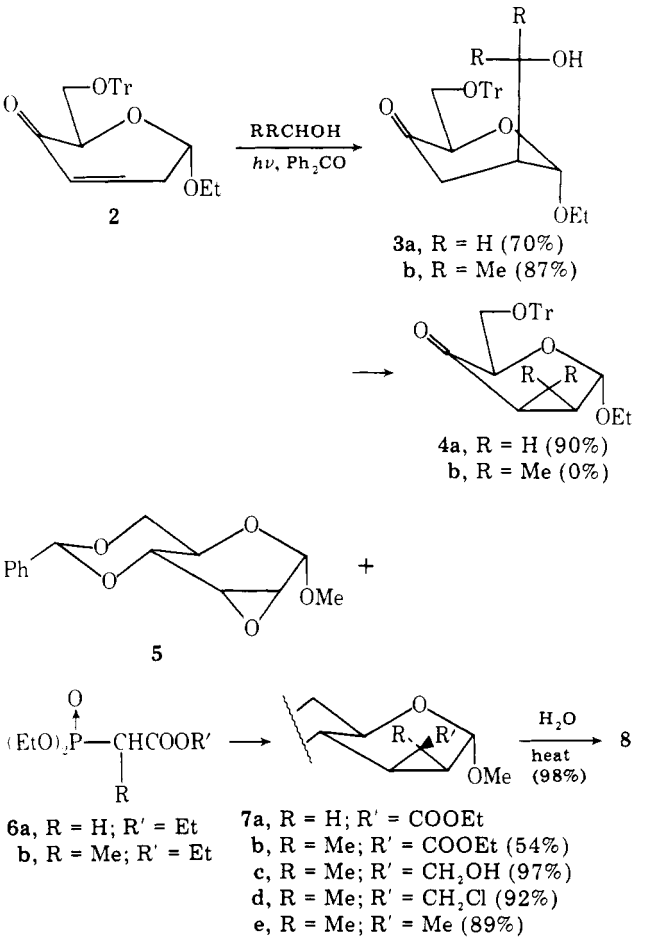
Annulated Pyranosides as Chiral Synthons for Carbocyclic Systems. Enantiospecific Routes to Both (+)- and (−)-Chrysanthemumdicarboxylic Acids from a Single Progenitor

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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