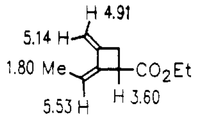
methylenecyclobutane and some of its "simple" alkyl-substituted derivatives have been known for some time and have been studied quite extensively, particularly from a physical organic viewpoint.[2] However, the methods that have been employed to prepare these materials are generally cumbersome, inefficient, and stereochemically ambiguous. Furthermore, the synthetic utility of 1,2-dialkylidenecyclobutane systems has not been investigated. The methodology outlined here provides substances of general structures **7** and **10** efficiently and in a completely stereocontrolled fashion.

Alkylation (lithium diisopropylamide, tetrahydrofuran–hexamethylphosphoramide, −78 → 0 °C; 2,3-dibromopropene, −78 °C, 1 h) of the ester **5a**[3] provided (72%) the β,γ-unsaturated ester **6a**[5] as a single product. In similar fashion, **5b–d**[3] were converted smoothly and exclusively into **6b–d** (78%, 95%, 91%), while **5e**[3] was transformed into **6e** (69%). On the other hand, alkylation of the (*Z*)-3-(trimethylstannyl)-2-alkenoates **8**[3] afforded only the *E* alkylation products **9**, in yields varying from 74% to 89%. In all cases, the conversions **5a–d** → **6a–d** and **8** → **9** were completely stereoselective.

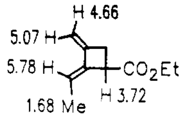
Since it is well established[6] that couplings between the ^{117}Sn and ^{119}Sn isotopes and a vicinal olefinic proton are much stronger when the R_3Sn group and the proton are trans than when they are cis, the stereochemistry of compounds **6** and **9** was readily established by ^{1}H NMR spectroscopy. Thus, the coupling constants $^3J_{Sn-H^*}$ in the ^{1}H NMR spectra of **6a–c** and **9a–c** are 128–131 and 72–74 Hz, respectively. The corresponding values for **6d** and **9d** are 88 and 36 Hz, respectively.

Treatment of each of the substances **6a–c,e** and **9a–c** with 5 mol % of $(Ph_3P)_4Pd$[7] in dry *N,N*-dimethylformamide at 80 °C for 1 h provided the corresponding cyclobutane derivatives **7a–c,e** and **10a–c**, respectively. In each case, the reaction was clean and efficient; the isolated yields of purified products ranged from 70% to 95%. Attempted ring closure of **6d** and **9d** under the conditions given above gave none of the desired products. However, when the reactions were carried out with 10 mol % of $(Ph_3P)_4Pd$ in the presence of 1 equiv of Et_3N and the crude products were purified by column chromatography on silica gel (elution with 1:8 ether–petroleum ether containing 1% Et_3N), the products **7d** and **10d** were obtained in yields of 71% and 68%, respectively. Structurally, the latter substances are particularly interesting, since they contain at C-2 a "hidden" aldehyde (enol ether) function.

The expectation that compounds **7a–d** and **10** possessed the indicated stereochemistry was readily verified by ^{1}H NMR spectroscopy. For example, in a NOE difference experiment, irradiation at δ 1.80 in the ^{1}H NMR spectrum of **7a** caused enhancement of the signals at δ 5.53 and 5.14.



7a



10a

On the other hand, in the ^{1}H NMR spectrum of **10a**, separate irradiations at δ 1.68 and 5.78 increased the intensity of the resonances at δ 5.78 and 3.72 and at δ 1.68 and 5.07, respectively.

Since β-trimethylstannyl α,β-unsaturated esters **5** and **8** containing many different (functionalized) R groups are readily available,[4b,c] it is clear that the methodology outlined above can potentially produce, in a stereospecific manner, a wide variety of functionalized alkyl 2,3-dimethylenecyclobutanecarboxylate derivatives. We are currently investigating further possibilities and are studying the chemistry of these novel substances.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada for financial support and to the University of British Columbia for a Graduate Fellowship (to Y.-F.L.).

Supplementary Material Available: Representative experimental procedures for the preparation of and spectral data for compounds **6a**, **7a**, **9a**, and **10a** (3 pages). Ordering information is given on any current masthead page.

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[2] See, for example: Heimbach, P.; Schimpf, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 206. Gajewski, J. J.; Shih, C. N. *J. Org. Chem.* **1972**, *37*, 64. Gajewski, J. J.; Shih, C. N. *J. Am. Chem. Soc.* **1972**, *94*, 1675. Berson, J. A.; Petrillo, E. W., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 636. Gajewski, J. J. *J. Am. Chem. Soc.* **1975**, *97*, 3457. Kelso, P. A.; Yeshurun, A.; Shih, C. N.; Gajewski, J. J. *J. Am. Chem. Soc.* **1975**, *97*, 1513. Levek, T. J.; Kiefer, E. F. *J. Am. Chem. Soc.* **1976**, *98*, 1875. van Straten, J. W.; van Norden, J. J.; van Schaik, T. A. M.; Franke, G. Th.; de Wolf, W. H.; Bickelhaupt, F. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 105. Pfeffer, H.-U.; Klessinger, M. *Chem. Ber.* **1979**, *112*, 890. Denis, J. M.; Niamayoua, R.; Vata, M.; Lablache-Combier, A. *Tetrahedron Lett.* **1980**, *21*, 515. Gajewski, J. J.; Benner, C. W.; Stahly, B. N.; Hall, R. F.; Sato, R. I. *Tetrahedron*, **1982**, *38*, 853. Dolbier, W. R., Jr.; Burkholder, C. R. *J. Org. Chem.* **1984**, *49*, 2381. Peelen, F. C.; Landheer, I. J.; de Wolf, W. H.; Bickelhaupt, F. *Recl.: J. R. Neth. Chem. Soc.* **1986**, *105*, 326. Roth, W. R.; Lennartz, H.-W.; Vogel, E.; Leiendecker, M.; Oda, M. *Chem. Ber.* **1986**, *119*, 837. Muller, P.; Rodriguez, D. *Helv. Chim. Acta* **1986**, *69*, 1546. Fukazawa, Y.; Fujihara, T.; Usui, S.; Shiobara, Y.; Kodama, M. *Tetrahedron Lett.* **1986**, *37*, 5621.

[3] Compounds **5** were prepared by reaction of the corresponding α,β-acetylenic esters with $[Me_3SnCuCN]Li$[4a] (THF, −78 °C; NH_4Cl-H_2O), while **8a–c** were derived by treatment of $RCH_2C\equiv CCO_2Et$ with $[Me_3SnCuSPh]Li$[4a] (THF, −48 °C; NH_4Cl-H_2O).[4b,c] Treatment of $MeOCH_2OCH_2C\equiv CCO_2Et$ with $[Me_3Sn(2\text{-thienyl})CuCN]Li_2$[4d] (THF, −78 °C; NH_4Cl-H_2O) provided **8d**.

[4] (a) Piers, E.; Morton, H. E.; Chong, J. M. *Can. J. Chem.* **1986**, *65*, 78. (b) Piers, E.; Morton, H. E. *J. Org. Chem.* **1980**, *45*, 4263. (c) Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron Lett.* **1981**, *22*, 4905. (d) Piers, E.; Tillyer, R. D., unpublished work. See: Lipshutz, B. H.; Koerner, M.; Parker, D. A. *Tetrahedron Lett.* **1987**, *28*, 945 for corresponding alkyl higher order cuprates.

[5] All compounds reported herein exhibited spectra in full accord with structural assignments.

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[7] For a previous study on the Pd(0)-catalyzed cyclization of vinylstannane–enol triflates, see: Piers, E.; Friesen, R. W.; Keay, B. A. *J. Chem. Soc., Chem. Commun.* **1985**, 809. For the intermolecular coupling of vinylstannanes with vinyl halides, see: Stille, J. K.; Groh, B. L. *J. Am. Chem. Soc.* **1987**, *109*, 813.

Polymer-Bound Ephedrine as an Efficient Chiral Catalyst for the Enantioselective Addition of Dialkylzincs to Aldehydes

Summary: Polymer-bound ephedrine catalyzed the enantioselective addition of dialkylzincs to aldehydes. Optically active secondary alcohols in up to 89% ee were obtained.

Sir: Polymer supported catalysts have attracted increasing interest.[1] Their workup and recovery are easier than monomeric reagents. They are also analogous to biolog-

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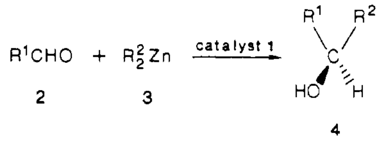
[1] For reviews: Mathur, N. K.; Narang, C. K.; Williams, R. E. *Polymers as Aids in Organic Chemistry*; Academic: New York, 1980. Pittman, C. U., Jr. "Polymer Supported Catalysts" In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon: Oxford, 1982; Chapter 55, pp 553–611.

Table I. Enantioselective Addition of 2 to 3



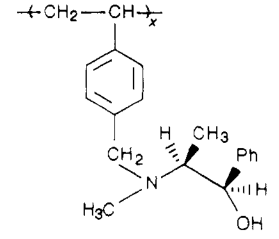
					4		
entry	R^1	R^2		yield, %	$[\alpha]_D$ (*c*, solvent)	% ee[a]	config
1	C_6H_5	Et	**a**	83	$[\alpha]^{24}$ +40.5° (5.21, $CHCl_3$)	89	*R*
2	*p*-ClC_6H_4	Et	**b**	78	$[\alpha]^{27}$ + 20.1° (5.03, C_6H_6)	83	*R*
3	*p*-$MeOC_6H_4$	Et	**c**	75	$[\alpha]^{26}$ +18.1° (5.07, C_6H_6)	54	*R*
4	*o*-$MeOC_6H_4$	Et	**d**	79	$[\alpha]^{26}$ +27.6° (2.03, $C_6H_5CH_3$)	51	*R*[b]
5	2-naphthyl	Et	**e**	78	$[\alpha]^{26}$ +23.7° (5.35, C_6H_6)	56	*R*
6	$CH_3(CH_2)_5$	Et	**f**	71	$[\alpha]^{27}$ −2.06° (3.79, $CHCl_3$)	21	*R*
7[c]	$CH_3(CH_2)_5$	Et	**f**	67	$[\alpha]^{23}$ +5.88° (6.57, $CHCl_3$)	61	*S*
8	C_6H_5	Me	**g**	43	$[\alpha]^{26}$ +14.3° (1.12, c-C_5H_{10})	33	*R*

[a] Based on the reported values of $[\alpha]_D$ +45.45° (*c* 5.15, $CHCl_3$) for (*R*)-**4a**;[7] $[\alpha]_D$ −10.4° (*c* 5, C_6H_6) for (*S*)-**4b** in 43% ee;[8] $[\alpha]_D$ −17.2° (*c* 5, C_6H_6) for (*S*)-**4c** in 51% ee;[8] $[\alpha]^{20}{}_D$ +47.0° (*c* 1, $C_6H_5CH_3$) for **4d** in 87% ee;[9] $[\alpha]^{20}{}_D$ −18.81° (C_6H_6) for (*S*)-**4e** for 44.7% ee;[10] $[\alpha]^{24}{}_D$ +9.6° (*c* 8.3, $CHCl_3$) for (*S*)-**4f**;[11] $[\alpha]^{20}{}_D$ −43.1° (*c* 7.19, c-C_5H_{10}) for (*S*)-**4g**.[12] [b] Configuration is tentatively assumed. [c] Catalyst was prepared from (1*S*, 2*R*)-2-(*N*-ethylamino)-1-phenylpropan-1-ol instead of (1*R*, 2*S*)-(−)-ephedrine.

ically active macromolecules, i.e., enzymes.

In spite of many efforts, optical yields have been low to moderate in *catalytic* asymmetric *carbon–carbon* bond-forming reactions such as the Michael addition,[2] hydrocyanation,[3] and hydroformylation.[4] Recently *monomeric* chiral amino alcohols[5] have been reported to be effective catalysts in the enantioselective addition of dialkylzincs to aldehydes.

We report that *polymer-bound* ephedrine (**1**), obtainable in one step in either enantiomeric form from inexpensive (+)- or (−)-ephedrine, is an efficient catalyst for the enantioselective addition of dialkylzincs to aldehydes.



1

Catalyst 1 was prepared from (1*R*, 2*S*)-(−)-ephedrine and chloromethylated polystyrene (1% divinylbenzene, chlorine content 0.8 mmol/g, 100–200 mesh) according to the literature procedure (K_2CO_3, reflux 2 days, toluene was used instead of DMF).[6]

Enantioselective addition of diethylzinc to benzaldehyde using **1** as catalyst (10 mol % ephedrine to aldehyde) in hexane at room temperature afforded (*R*)-1-phenylpropanol (**4a**), $[\alpha]^{24}{}_D$ +40.5° (*c* 5.21, $CHCl_3$) [lit.[7] $[\alpha]_D$ +45.45° (*c* 5.15, $CHCl_3$)], in 83% chemical yield and in 89% enantiomeric excess (ee). Catalyst 1 was easily removed from the reaction mixture by a simple filtration. The recovered catalyst was found to be also effective. As shown in Table I, other aryl aldehydes were alkylated enantioselectively in moderate to high ee's. An aliphatic aldehyde (heptanal) also afforded optically active secondary alcohol.

In a typical procedure, benzaldehyde (0.12 mL, 1.18 mmol) was added to a suspension of 1 (171 mg, 10 mol % ephedrine to aldehyde) in hexane (3 mL) in an ice bath. After 10 min, Et_2Zn (2.55 mmol, 2.55 mL of 1 M hexane solution) was added over a period of 10 min. The reaction mixture was stirred at room temperature for 2 days and quenched by an addition of 1 M HCl. The catalyst was removed by filtration and washed several times with dichloromethane. Recovery of 1 was 95% after alkaline treatment. The aqueous layer was extracted with dichloromethane. The combined organic solvent was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was purified by silica gel TLC [hexane:AcOEt = 5:1 (v/v) as developing solvent].

Thus, catalyst 1 gave better results than the recently reported *monomeric* *N*-alkylephedrine (maximum 80% ee for **4a**, ~0% ee for aliphatic aldehyde).[13] To the best of our knowledge, the degree of the present asymmetric induction is the highest for carbon–carbon bond-forming reactions using chiral synthetic polymers as catalysts.

Registry No. **2a**, 100-52-7; **2b**, 104-88-1; **2c**, 123-11-5; **2d**, 135-02-4; **2e**, 66-99-9; **2f**, 111-71-7; **3a**, 1078-58-6; **3g**, 544-97-8; **4a**, 1565-74-8; **4b**, 110611-21-7; **4c**, 105836-14-4; **4d**, 105836-13-3; **4e**, 112576-12-2; (*R*)-**4f**, 61925-50-6; (*S*)-**4f**, 61925-49-3; **4g**, 1517-69-7; (1*S*,2*R*)-2-(ethylamino)-1-phenylpropan-1-ol, 37577-32-5; (1*R*,2*S*)-(−)-ephedrine, 299-42-3.

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