forming some initial experiments. Financial support was obtained from the National Swedish Board for Technical Development.

Registry No. 1, 40036-82-6; **2a**, 63753-76-4; **2b**, 109929-30-8; **3**, 109929-31-9; **4a**, 109929-32-0; **4b**, 109929-33-1; **5a**, 109150-98-3; **5b**, 109150-76-7; **7**, 109929-35-3; **10**, 109929-34-2; $Ph_3P{=}CHCOOEt$, 1099-45-2; CMP-KDO synthetase, 37278-28-7.

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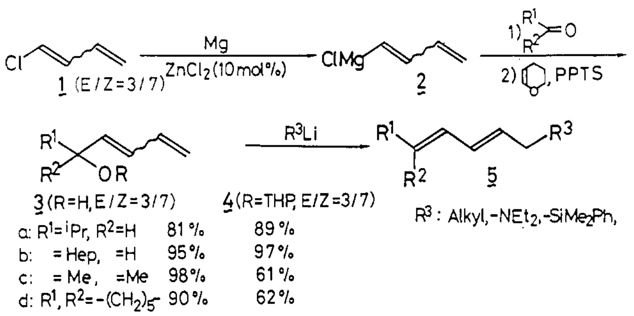
A Facile Stereoselective Synthesis of Internal Conjugated (*E*,*E*)-Dienes Including 2,4-Alkadienylamines, -silanes, and -stannanes

Summary: Tetrahydropyranyl ethers of 2,4-alkadien-1-ols, prepared by the reaction of 1,3-butadienylmagnesium chloride with carbonyl compounds, are regioselectively attacked on the C-5 position by various lithium reagents, such as RLi, R_2NLi, R_3SiLi, and R_3SnLi, under the elimination of lithium tetrahydropyranyl oxide, giving the corresponding (*E*,*E*)-dienes predominantly.

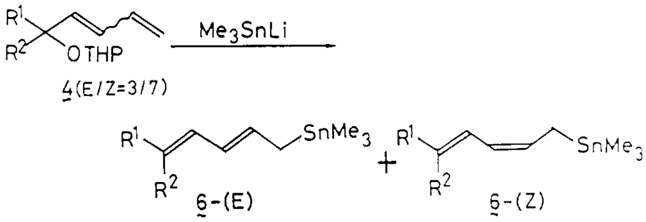
Sir: Regio- and stereoselective synthesis of conjugated dienes has received considerable attention for these decades because these dienes are important both for building blocks of natural products and for components of Diels–Alder reactions.[1,2] Although various reactions including Wittig reaction[2d] as well as transition-metal-catalyzed cross-coupling reaction between alkenylmetals and alkenyl halides have been commonly used,[3] more versatile method for synthesis of conjugated dienes bearing various types of substituents have been needed. This paper describes a novel highly stereoselective synthesis of internal conjugated (*E*,*E*)-dienes from easily accessible 1-chloro-1,3-butadiene,[4] a carbonyl compound, and a lithium reagent as shown in Scheme I.

The Grignard reagent **2** was prepared from 1-chloro-1,3-butadiene (**1**) (*E*/*Z* = 3/7) and magnesium in the presence of zinc(II) chloride.[5] Treatment of a ketone or an aldehyde with **2** gave dienyl alcohol **3** in excellent yield which was converted into tetrahydropyranyl (THP) ether **4** by pyridinium *p*-toluensulfonate (PPTS) catalyst.[6] Among varioius organometallic reagents, alkyllithiums attacked regioselectively on the end of diene unit and afforded internal conjugated dienes **5**.[7] Lithium amide and silyllithium reacted also with **4**, affording 2,4-alkadienylamines[8] and 2,4-alkadienylsilanes,[9] respectively. Results are summarized in Table I.

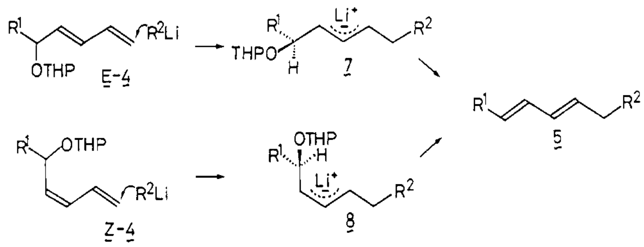
Scheme I



Scheme II



Scheme III



Typical procedure for the formation of Grignard reagent **2** and successive transformation to conjugated dienes **5** is as follows. A mixture of magnesium (24 g, 1.0 mol) and zinc(II) chloride (6.8 g, 0.05 mol) were heated at 130 °C for 2 h under vacuum. Dried tetrahydrofuran (THF, 30 mL) and 1,2-dibromoethane (2.0 mL) were added, and the whole was stirred vigorously under an argon atmosphere.

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(2) (a) For general review, see: Norman, J. F. *Modern Synthetic Methods*; Scheffold, R., Ed.; Verlag, O. S.; Berlin, 1983; pp 139–172. (b) Otera, J.; Misawa, H.; Sugimoto, K. *J. Org. Chem.* **1986**, *51*, 3830. (c) Yamada, S.; Ohsawa, H.; Suzuki, T.; Takayama, H. *J. Org. Chem.* **1986**, *51*, 4934. (d) Schlosser, M.; Tuong, H. B.; Scaub, B. *Tetrahedron Lett.* **1985**, *26*, 311. (e) Ikeda, Y.; Ukai, J.; Ikeda, N.; Yamamoto, H. *Tetrahedron* **1987**, *43*, 723, 731.

(3) (a) Tamao, K.; Sumitani, K.; Kiso, Y.; Zembayashi, M.; Fujioka, A.; Kodama, S.; Nakajima, I.; Minato, A.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1958. Corriu, R. J. P.; Masse, J. P. *J. Chem. Soc., Chem. Commun.* **1972**, 144. (b) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340. (c) Miyaura, N.; Suginome, H.; Suzuki, A. *Tetrahedron Lett.* **1983**, *24*, 1527. (d) Diek, H. A.; Heck, R. F. *J. Org. Chem.* **1975**, *40*, 1083. (e) Larock, R. C. *J. Org. Chem.* **1976**, *41*, 2241. (f) Kanemoto, S.; Matsubara, S.; Oshima, K.; Utimoto, K.; Nozaki, H. *Chem. Lett.* **1987**, 5 and references cited therein.

(4) 1-Chloro-1,3-butadiene, a byproduct in the industrial process of producing chloroprene, was offered from Toyo Soda Manufacturing Co. Ltd.

(5) The preparation of this reagent **2** has not been reported. The method is an analogue to the preparation of Grignard reagent from chloroprene; see: Sultanov, N. T.; Mekhtiev, S. D.; Efedieva, T. G.; Kodzhaova, S. Y.; Aleieva, M. A.; Mamedov, F. A. USSR Patent 280476, 1970; *Chem. Abstr.* **1971**, *74*, 142040. Kondo, K.; Dobashi, S.; Matsumoto, M. *Chem. Lett.* **1976**, 1077. Nunomoto, S.; Yamashita, Y. *J. Org. Chem.* **1979**, *44*, 4788.

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(7) The reaction of methylmagnesium bomide with **4** in the presence of catalytic amount of CuI or $Ni(PPh_3)_2Cl_2$ also gave diene **5**. But the yield was low (<20%).

(8) Decodts, G.; Dressaire, G.; Langlois, Y. *Synthesis* **1979**, 510. Alexakis, A.; Norman, J. F. *Tetrahedron Lett.* **1982**, *23*, 5151. Nikaido, M.; Aslanian, R.; Scavo, F.; Helquist, P.; Åkermark, B.; Bäckvall, J.-E. *J. Org. Chem.* **1984**, *49*, 4738. Meyers, A. I.; Lawson, J. P.; Carver, D. R. *J. Org. Chem.* **1981**, *46*, 3119.

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Table I. Reaction of Alkyllithium, Lithium Amide, and Silyllithium with THP Ether 4

			reaction conditions		product[b]			
run	THP ether	R^3Li	temp, °C	time, h	R^1	R^2	R^3	yield, %[c]
1	**4a**	*n*-BuLi	−78	5	*i*-Pr	H	*n*-Bu	89
2	**4a**	*sec*-BuLi	−78	1	*i*-Pr	H	*sec*-Bu	74
3	**4b**	*n*-BuLi	−78	6	*n*-Hep	H	*n*-Bu	85
4	**4b**	*t*-BuLi	−78	6	*n*-Hep	H	*t*-Bu	76
5	**4c**	*n*-BuLi	−78	7	Me	Me	*n*-Bu	78
6	**4d**	*n*-BuLi	−78	6	$(CH_2)_5$		*n*-Bu	93
7	**4a**	Et_2NLi	0	5	*i*-Pr	H	NEt_2	74
8	**4c**	Et_2NLi	0	7	Me	Me	NEt_2	76
9	**4d**	Et_2NLi	0	7	$(CH_2)_5$		NEt_2	96
10	**4a**	$PhMe_2SiLi$[d]	−78	0.5	*i*-Pr	H	$SiMe_2Ph$	85
11	**4b**	$PhMe_2SiLi$[d]	−78	0.5	*n*-Hep	H	$SiMe_2Ph$	81
12	**4c**	$PhMe_2SiLi$[d]	−78	0.5	Me	Me	$SiMe_2Ph$	90
13	**4d**	$PhMe_2SiLi$[d]	−78	0.5	$(CH_2)_5$		$SiMe_2Ph$	78

[a] THF ether (2.0 mmol), R^3Li (6.0 mmol), and THF (10 mL) were employed. [b] Isomeric purities (>95%) were determined by GLPC and/or ^1H NMR. [c] Isolated yields. [d] THP ether (2.0 mmol), $PhMe_2SiLi$[10] (2.4 mmol), and THF (10 mL) were employed.

Table II. Preparation of Dienylstannane 6[a]

		product			^{119}Sn NMR[b]		
run	THP ether	R^1	R^2	(*E*)-/(*Z*)-**6**	(*E*)-**6**	(*Z*)-**6**	yield, %[c]
1	**4a**	*i*-Pr	H	75/25	+0.6	+6.2	66
2	**4b**	*n*-Hep	H	74/26	+0.5	+4.8	61
3	**4c**	Me	Me	71/29	−2.0	+2.2	53
4	**4d**	$(CH_2)_5$		71/29	−1.1	+4.4	65

[a] THP ether (2.0 mmol), Me_3SnLi[13] (6.0 mmol), and THF (10 mL) were employed. [b] The chemical shifts are given in δ with tetramethylstannane as an internal standard. [c] Isolated yields.

After exothermic reaction subsided, the reaction mixture was diluted by additional THF (350 mL), and then a solution of 1-chloro-1,3-butadiene (**1**; 44 g, 0.5 mol) and 1,2-dibromoethane (4 mL) in THF (70 mL) was added dropwise over 1 h. After the exothermic reaction was over, the whole was heated under reflux for 2 h. A concentration of the resulting solution of **2** was determined by usual manner.[11] A THF (5 mL) solution of 2-methylpropanal (0.72 g, 10 mmol) was treated with **2** (0.45 M, 27 mL, 12.5 mmol) at 0 °C for 30 min. After the usual workup and purification by silica gel column chromatography, dienyl alcohol **3a** (1.02 g, 8.1 mmol) was obtained in 81% yield. A treatment of **3a** with 3,4-dihydro-2*H*-pyran and a catalytic amount of pyridinium *p*-toluenesulfonate gave **4a** (1.51 g, 7.2 mmol) in 89% yield. A hexane solution of *n*-BuLi (1.5 M, 4.0 mL, 6.0 mmol) was added to a solution of **4a** (0.42 g, 2.0 mmol) in dry THF (10 mL) under argon atmosphere at −78 °C. The resulting red solution was stirred for 5 h at the same temperature and gradually warmed up to 0 °C. Aqueous workup followed by purification with silica gel column chromatography gave (*E*,*E*)-2-methyl-3,5-undecadiene (0.29 g, 89%; Table I, run 1).

The conjugated dienes with trialkylstannyl group **6** have not been easily available in spite of a high potential value for organic synthesis.[12] The above described procedure provides a novel method to these dienes as shown in Scheme II. Yields of stannane **6** are good, but the stereoselectivities are moderate as summarized in Table II.

Remarkably, (*E*,*E*)-dienes **5** stereoselectively prepared in high yields irrespective of the stereochemistry of the starting materials **4**. Instead of THP ether **4**, methoxymethyl ether (MEM ether) also gave good results.[14] A treatment of free alcohol **3** with lithium reagents also gave dienes in good yields via lithium alkoxide, but the stereoselectivity is not so high.[15]

Stereoselective formation of dienes can be explained: (1) Rapid nucleophilic attacks of a lithium reagent to s-trans conformers of (*E*)- and (*Z*)-**4** produce **7** and **8**, respectively.[16] (2) Both **7** and **8** afford selectively the (*E*,*E*)-diene **5** by perpendicular elimination of lithium tetrahydropyranyl oxide (Scheme III).

(*E*)-Alkenes are also obtained by the analogous reaction between lithium reagent with THP ether of 1-alken-3-ols. For example, (*E*)-6-pentadecene was obtained by the reaction of *n*-BuLi with 3-(tetrahydropyranyloxy)-1-undecene, but the reaction was very slow (56% yield after 4 days of stirring at room temperature) in comparison with THP ether of dienyl alcohol. Formation of conjugated dienes from THP ether of 1,4-alkadien-3-ols is conceivable, but this procedure was not promising, since the starting material, the THP ether of 1,4-alkadien-3-ols, was unstable, and the proton on C-3 was easily abstracted by the action of *n*-BuLi, giving a complex mixture.

Registry No. (*E*)-**1**, 16503-25-6; (*Z*)-**1**, 10033-99-5; (*E*)-**3a**, 109928-88-3; (*Z*)-**3a**, 109928-89-4; **3a** (methoxymethyl ether), 109929-21-7; (*E*)-**3b**, 109928-90-7; (*Z*)-**3b**, 109928-91-8; (*E*)-**3c**, 69514-47-2; (*Z*)-**3c**, 69514-48-3; (*E*)-**3d**, 88920-69-8; (*Z*)-**3d**, 109928-92-9; (*E*)-**4a**, 109928-93-0; (*Z*)-**4a**, 109928-94-1; (*E*)-**4b**, 109928-95-2; (*Z*)-**4b**, 109928-96-3; (*E*)-**4c**, 109928-97-4; (*Z*)-**4c**, 109928-98-5; (*E*)-**4d**, 109928-99-6; (*Z*)-**4d**, 109929-00-2; (*E*,*E*)-**5a** (R^3 = *n*-Bu), 109929-01-3; (*E*,*E*)-**5a** (R^3 = *sec*-Bu), 109929-02-4;

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(13) Tamborski, C.; Ford, F. E.; Soloski, E. J. *J. Org. Chem.* **1963**, *28*, 237.

(14) Methoxymethyl ether of 6-methyl-1,3-heptadien-5-ol (**3a**) and lithium diethylamide gave diethyl[(*E*,*E*)-6-methyl-2,4-heptadienyl]amine in 71% yield (0 °C, 6 h; Table I, run 7).

(15) A treatment of 6-methyl-1,3-heptadien-5-ol (**3a**) with 4 equiv of *n*-BuLi gave a mixture of (*E*,*E*)-2-methyl-3,5-undecadiene and (*E*,*Z*)-2-methyl-3,5-undecadiene in 79% yield. The ratio of these stereoisomers was 72:28 (*E*,*E*/*E*,*Z*).

(16) The reactions of alkyllithium or lithium amide with 1,3-butadiene are reported: Schue, F.; Bywater, S. *Bull. Soc. Chim. Fr.* **1970**, 271. Glaze, W. H.; Hanicak, J. E.; Moore, M. L.; Chaudhuri, J. *J. Organomet. Chem.* **1972**, *44*, 39. Takabe, K.; Katagiri, T.; Tanaka, J. *Tetrahedron Lett.* **1972**, 4009. Imai, N.; Narita, T.; Tsuruta, T. *Tetrahedron Lett.* **1971**, 3517.

(*E*,*E*)-**5a** (R^3 = NEt_2), 109929-06-8; (*E*,*E*)-**5a** (R^3 = $SiMe_2Ph$), 109929-08-0; (*E*,*Z*)-**5a** (R^3 = *n*-Bu), 109959-45-7; (*E*,*E*)-**5b** (R^3 = *n*-Bu), 109929-03-5; (*E*,*E*)-**5b** (R^3 = *t*-Bu), 109929-04-6; (*E*,*E*)-**5b** (R^3 = $SiMe_2Ph$), 109929-09-1; (*E*)-**5c** (R^3 = *n*-Bu), 78500-35-3; (*E*)-**5c** (R^3 = NEt_2), 101456-04-6; (*E*)-**5c** (R^3 = $SiMe_2Ph$), 109929-10-4; (*E*)-**5d** (R^3 = *n*-Bu), 109929-05-7; (*E*)-**5d** (R^3 = NEt_2), 109929-07-9; (*E*)-**5d** (R^3 = $SiMe_2Ph$), 109929-11-5; (*E*,*E*)-**6a**, 109929-12-6; (*Z*,*E*)-**6a**, 109929-13-7; (*E*,*E*)-**6b**, 109929-14-8; (*Z*,*E*)-**6b**, 109929-15-9; (*E*)-**6c**, 109929-16-0; (*Z*)-**6c**, 109929-17-1; (*E*)-**6d**, 109929-18-2; (Z)-**6d**, 109929-19-3; $Br(CH_2)_2Br$, 106-93-4; MeCH(CHO)Me, 78-84-2; *n*-BuLi, 109-72-8; *sec*-BuLi, 598-30-1; *t*-BuLi, 594-19-4; Et_2NLi, 816-43-3; $PhMe_2SiLi$, 3839-31-4; Me_3SnLi, 17946-71-3; octanal, 124-13-0; acetone, 67-64-1; cyclohexanal, 2043-61-0; pyridinium *p*-toluenesulfonate, 24057-28-1; (E)-6-pentadecene, 74392-31-7; 3-(tetrahydropyranoxy)-1-undecene, 109929-20-6.

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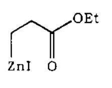
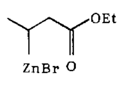
Unsaturated Ester Synthesis via Cu(I)-Catalyzed Allylation of Zinc Esters

Summary: CuCN-catalyzed allylation of ethyl β-(iodozincio)propionate (**1**), ethyl β-(bromozincio)butyrate (**2**), ethyl γ-(iodozincio)butyrate (**3**), and ethyl δ-(iodozincio)pentanoate (**4**) with allylic halide or tosylate provides ethyl 5-hexenoates, ethyl 6-heptenoates, and ethyl 7-octenoates in high yields. Regioselectivity of the allylation and the reaction of **3** with propargyl tosylate are also discussed.

Sir: Recently we have shown that β-zinc ester **1** and γ-zinc ester **3** can be generated by a direct metalation of the corresponding iodides with Zn–Cu.[1] This method was found general for the generation of the higher homologues (δ- (**4**), ϵ-, and ζ-zinc esters) and secondary C–Zn derivatives (e.g., **2**). Here we report allylation of **1**–**4**, which, in principle, coupled with a vinylation,[2] might constitute a general entry to the synthesis of unsaturated acid derivatives with olefin at any desired position more remote than the γ-position of carbonyl (eq 1).[3]



1



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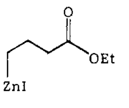

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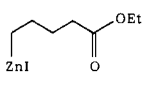
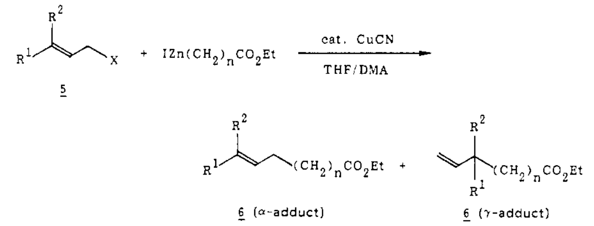
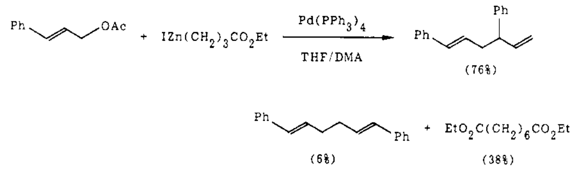


4



(1)

Owing to low nucleophilic reactivity, allylation has been successful for some organozincs, which possess a polarized C–Zn bond: direct allylation of (trifluoromethyl)zinc bromide[4] and Pd(0)-catalyzed allylation of α-zinc ester[5] and phenylzinc chloride.[6] Making contrast to the latter two examples, the Pd(0)-catalyzed allylation of **3** resulted in a self-coupling, and no expected product **6** was detected (eq 2).[7] However, cuprous cyanide[8] was found to nicely catalyze the allylation of zinc esters **1**–**4** (eq 1).[9] Results are summarized in Table I.[10] The allylation was undertaken either at 60 °C for 1 h (conditions A) or at room temperature overnight (conditions B). Under the conditions B, the zinc esters **1**–**4** were filtered under nitrogen to remove an excess of Zn–Cu before treating with **5**. Without the filtration, a homocoupling of allylic halide becomes a serious side reaction. Tosylates were directly used after preparation by treatment of the corresponding alcohols with 1 equiv of *n*-BuLi (*n*-hexane solution) in THF at −78 °C and then with 1 equiv of tosyl chloride at 0 °C. These tosylates readily undergo an exchange reaction with chloride ion at an ambient temperature, and an allylation agent in these experiments is a composite of a tosylate and a chloride (vide infra). The yields of **6** are generally high, irrespective of the wide structural variety of **5**. In the absence of CuCN, the yield of **6** was low (e.g., ethyl 3-(2′-cyclohexenyl)propionate in 33% yield at 60 °C for 2 h, cf. entry 3).



(2)

The regioselectivity for the unsymmetrical **5** was rather poor except for the cases in entries 14 and 15 and insensitive to the change in reaction conditions (entries 5 vs. 6), the kind of leaving groups (entries 6–8), and the structures of **5** and zinc esters. Generally the nucleophile was preferentially introduced to the γ-position. This general trend is apparent especially by a comparison of a pair of results (crotyl vs. α-methallyl tosylates, entries 10

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[1] Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Tetrahedron Lett.* **1985**, *26*, 5559.

[2] Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Tetrahedron Lett.* **1986**, *27*, 955.

[3] The chemistry of ϵ- and ζ-zinc esters is very similar to that of **1**–**4**, and hence only **1**–**4** were treated in this manuscript.

[4] Wiemers, D. M.; Burton, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 832.

[5] Baldrini, G. P.; Mengoli, M.; Tagliavini, E. *Tetrahedron Lett.* **1986**, *27*, 4223.

[6] Chatterjee, S.; Negishi, E. *J. Org. Chem.* **1985**, *50*, 3406.

[7] Similar homocoupling was reported for Grignard reagents, allylic halides, and $FeCl_3$, $CoCl_2$, $NiCl_2$, or $CuCl_2$: Ohbe, Y.; Matsuda, T. *Tetrahedron* **1973**, *29*, 2989.

[8] For CuCN-mediated (stoichiometric) allylation of 4-pentenylzinc, see: Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1986**, *27*, 4427, 4431.

[9] One example of allylation of methyl α-methyl-β-(halozincio)propionate was reported without experimental details: Nakamura, E.; Sekiya, K.; Kuwajima, I. *Tetrahedron Lett.* **1987**, *28*, 337.

[10] The reaction was performed as follows (entry 3, Table I): To a solution of 2-cyclohexenyl tosylate (1.2 mmol, see the text) were successively added 18 mg (0.2 mmol) of CuCN in 2 mL of dry THF and a solution of **1**, which had been prepared by heating a mixture of 1.5 mmol of ethyl 3-iodopropionate and 2.3 mmol of Zn–Cu in THF (4 mL)–DMA (*N*,*N*-dimethylacetamide, 2.2 mmol) at 60 °C for 3 h under nitrogen. The mixture was stirred at 60 °C for 1 h. After dilution with ether, washing with aqueous $NaHCO_3$, and drying over $MgSO_4$, followed by evaporation of the solvents, the residue was purified by column chromatography over silica gel (hexane–ether gradient) to provide ethyl 3-(2′-cyclohexenyl)propionate in 82% yield based on 2-cyclohexenol.

0022-3263/87/1952-4418$01.50/0