mL, $CHCl_3$)).[20] The optical purity of (S)-2 (93% ee) was determined by conversion of a portion of this material to the bis-((R)-O-acetylmandelate) derivatives in $CDCl_3$ as described by Brintzinger et al.[9] and integration of the cyclopentadienyl resonances observed in the ^1H NMR spectrum of the mixture.

Preparation of Compounds 4a and 4b and Reaction with Aldehydes: General Procedure. Titanocene dichloride 2 (190 mg, 0.5 mmol) was suspended in 2 mL of dry THF under argon. n-Propylmagnesium bromide (275 μL, 2.0 M in ether, 0.55 mmol) was added dropwise by syringe at room temperature to give a homogeneous brown red solution with some gas evolution being observed. The solution was heated with a hot air gun for several minutes until gas evolution ceased. The resulting purple-brown solution was cooled to room temperature. Crotylmagnesium chloride (250 μL, 1.8 M in THF, 0.45 mmol) was added dropwise by syringe to give a deep purple solution. After stirring for 30 min at room temperature, the aldehyde (0.5 mmol) was added neat by syringe. The resulting brown solution was stirred at room temperature for 1 h and 0.7 mL of a solution of concentrated HCl in THF (2.0 M, 1.4 mmol) added dropwise by syringe with vigorous stirring. Dry air was bubbled through the mixture for about a minute to give a red suspension. Anhydrous $MgSO_4$ was added, and the mixture was swirled briefly and filtered, washing with THF. The filtrate was concentrated in vacuo and taken up in hexane–ether, 1:1, and filtered (to remove salts and compound 2), washing with additional hexanes. The filtrate was concentrated in vacuo to give the crude homoallylic alcohols and some additional titanocene dichloride 2. The titanocene dichloride could be precipitated by washing the oily solid with pentane and filtering again, washing with pentane. The pentane was removed in vacuo, and the crude homoallylic alcohols were purified by passage through a short column of silica gel, eluting with hexanes–ethyl acetate, 11:1. Under these conditions no fractionation of diastereomers is observed.[4] The original filter cake that contained compound 2 and magnesium salts was washed with CH_2Cl_2, and the filtrate was combined with additional compound 2 that had been removed by precipitation from pentane. The filtrate was concentrated to dryness in vacuo; recovery was generally 80–90% of spectroscopically pure material. Material was accumulated from run to run and crystallized from hexanes–toluene prior to reuse. No decrease in optical activity was observed if care was exercised to avoid exposure to light.

Preparation and Analysis of (3,5-Dinitrophenyl)carbamates. 3,5-Dinitrobenzoyl azide (62.0 mg, 0.25 mmol) was heated in 1.0 mL of dry toluene at reflux for 15 min. A solution of the homoallylic alcohol (0.2 mmol) in 3 × 1.0 mL of toluene was added dropwise by syringe. The resulting solution was heated at reflux for 4 h and then cooled to room temperature. The solution was diluted with ether (10.0 mL) and washed with cold 2 M HCl, aqueous $NaHCO_3$, and brine. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude mixture was passed through a short silica gel column, eluting with hexanes–ethyl acetate, 5:1, to remove a polar yellow impurity. The eluate was concentrated in vacuo, and the carbamate derivatives, homogeneous by ^1H NMR, were dissolved in ~20 mL of 90:10 hexanes–isopropyl alcohol and separated on a Pirkle Covalent [D]-naphthylalanine column (Regis Chemicals Ltd., 5 μm, 25 cm by 4.6 mm i.d.). The separation conditions and retention times are summarized in Table II.

Preparation of Mosher's Acid Esters. The homoallylic alcohol (1.0 mmol) dissolved in 5 mL of dry dichloromethane was added to a solution of (R)-α-methoxy-α-(trifluromethyl)phenylacetyl chloride (287 mg, 1.1 mmol), 4-(dimethylamino)pyridine (120 mg, 1.1 mmol) and triethylamine (480 mg, 4.7 mmol) in 5 mL of dichloromethane. The solution was stirred at room temperature or heated at reflux until the alcohol was consumed as judged by TLC analyses (silica gel, hexanes–ethyl acetate, 10:1). With sterically hindered alcohols (e.g. derived from reagent 4b and pivaldehyde) it was necessary to add additional acid chloride and DMAP to ensure complete reaction. After reaction was complete, the solutions were cooled, diluted with ether, washed with cold, 1 M HCl, saturated $NaHCO_3$, and brine, and the organic phase was dried over $MgSO_4$. Concentration in vacuo provided crude products which were analyzed by ^1H NMR spectroscopy in benzene-d_6 to determine diastereomer ratios. The relevant chemical shifts and assignments of the signals integrated are summarized in Table III.

Acknowledgment. We would like to thank the Natural Sciences and Engineering Research Council of Canada for financial support of this work.

(20) At these concentrations photoracemization of compound 2 is extremely rapid and exposure to visible light must be avoided prior to measurement.

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Stereoselectivity of Organometallic Reagents Addition to 7-Oxabicyclo[2.2.1]hept-5-en-2-one[1]

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The reaction between 7-oxabicyclo[2.2.1]hept-5-en-2-one and a variety of organolithium, Grignard, and organocuprate reagents is described. Organolithium and Grignard reagents yield the expected endo alcohols with high selectivity. Alternatively, lithium organocuprates add with high stereoselectivity to the hindered endo face of the carbonyl functionality to afford the corresponding exo alcohols.

The past few years have witnessed an upsurge of interest in the chemistry of derivatives of 7-oxabicyclo[2.2.1]heptane,[2] important starting materials for syntheses of natural products and derivatives of biological interest.[3] Within this context, oxanorbornenic substrates 1 and 2 (Chart I)

Chart I

1 2

are especially versatile starting materials for the preparation of a number of natural products.[4] These synthetic

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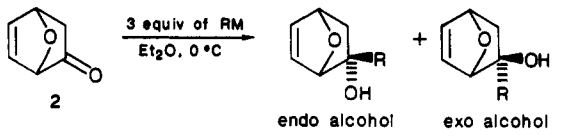
Table I. Reaction of 7-Oxabicyclo[2.2.1]hept-5-en-2-one with Organolithium and Grignard Reagents



2 endo alcohol exo alcohol

entry	R	M	products endo	products exo	endo:exo ratio	yield,[a] %
1	Me	Li	3	4	20:1	95
2	Me	MgI	3			95
3	Et	MgI	5			75
4	*n*-Bu	Li	6	7	11:1	90[b]
5	*n*-Bu	MgBr	6			90[c]
6	*i*-Pr	MgI	8			90
7	CH_2=CH	MgBr	9			70[d]
8	CH_2=$CHCH_2$	MgBr	10			65[d]
9	Ph	MgBr	11			80
10	Ph	Li	11	12	3.6:1	90
11	2-furyl	Li	13	14	9:1	78
12	1-naphthyl	Li	15	16	9:1	85
13	NC-CH_2	Li	17			75[e]
14	*n*-C_4H_9-C≡C	Li	18	19	9:1	88

[a] Yields refer to pure isolated products. [b] Reaction carried out with 1 equiv of *n*-butyllithium. [c] An 8% yield of 7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol was also isolated from this reaction. [d] In these cases, small amounts of byproducts were isolated in low yield (10–15%). The structure of these compounds has not been researched. [e] The reaction was carried out in THF from −78 °C to 0 °C.

intermediates ("naked sugars"[4a]) are now readily available[5] even optically pure;[6] however, the reactivity of these systems remains unexplored in many aspects. Thus, while the stereochemical outcome of nucleophilic additions of organolithium and Grignard reagents to other bicyclic ketones is a well-documented process,[7] a similar study has not been effected for 7-oxanorbornenic ketones.[8]

The paramount importance of controlling the diastereoselectivity of the addition of C-nucleophiles to carbonyl compounds[9] and the synthetic potential of oxanorbornenic systems prompted us to investigate the stereoselectivity of the carbonyl alkylation of 7-oxabicyclo[2.2.1]hept-5-en-2-one. It was envisioned that the unique structural features of the substrate would enable us to design appropriate nucleophiles to achieve endo and exo attacks with high diastereoselectivity.

Reaction of 7-Oxabicyclo[2.2.1]hept-5-en-2-one with Organolithium and Grignard Reagents. It is generally accepted that the stereochemical outcome of organometallic compound addition to bicyclic ketones is controlled by two main factors: steric interactions and torsional strain. These two factors reinforce each other in 7-unsubstituted substrates and exo attack is highly favored; however, when there is a substituent on position 7, syn to the carbonyl functionality, a nucleophile attempting to enter the molecule from the exo direction encounters such severe steric strain that exo attack is essentially precluded.[7] Based upon these precedents, we anticipated that the reaction between 7-oxanorbornenone, **2**, and organolithium and Grignard reagents would lead to endo alcohols with high selectivity.

The results obtained in the initial part of our investigation are summarized in Table I. Grignard reagents (entries 2, 3, and 5–9) afforded the expected endo alcohols[10] in high yield and with complete stereoselectivity. Simple lithium derivatives (entries 1 and 4) produced predominantly endo mixtures of products,[11] in clear contrast with the behavior reported for norbornenic substrates.[7] Aromatic organolithium reagents (entries 10–12) displayed a similar stereoselectivity, and small amounts of the corresponding exo isomers (**12**, **14**, **16**) were obtained. Entry

(1) For a preliminary communication, see: Arjona, O.; Fernández de la Pradilla, R.; Manzano, C.; Pérez, S.; Plumet, J. *Tetrahedron Lett.* **1987**, *28*, 5547.

(2) For a recent review, see: Lipshutz, B. H. *Chem. Rev.* **1986**, *86*, 795.

(3) For some leading references, see: (a) Das, J.; Vu, T.; Harris, D. N.; Ogletree, M. L. *J. Med. Chem.* **1988**, *31*, 930. (b) Wilson, N. L.; Jones, R. L.; Marr, C. G.; Muir, G. *Eur. J. Med. Chem.* **1988**, *23*, 359. (c) Novak, B. M.; Grubbs, R. H. *J. Am. Chem. Soc.* **1988**, *110*, 960. (d) Jung, M. E.; Street, L. J. *Heterocycles* **1988**, *27*, 45. (e) Reymond, J.-L.; Vogel, P. *Tetrahedron Lett.* **1988**, *29*, 3695. (f) Murai, A.; Tanimoto, N.; Sakamoto, N.; Masamune, T. *J. Am. Chem. Soc.* **1988**, *110*, 1985.

(4) (a) For a short synthesis of L-daunosamine, see: Warm, A.; Vogel, P. *J. Org. Chem.* **1986**, *51*, 5348. (b) For a synthesis of (+)- and (−)-methyl nonactate, see: Warm, A.; Vogel, P. *Helv. Chim. Acta* **1987**, *70*, 690. (c) For a synthesis of D- and L-ribose derivatives, see: Wagner, J.; Vieira, E.; Vogel, P. *Helv. Chim. Acta* **1988**, *70*, 624. (d) For a synthesis of (±)-castanospermine, see: Reymond, J.-L.; Vogel, P. *Tetrahedron Lett.* **1989**, *30*, 705.

(5) (a) Vieira, E.; Vogel, P. *Helv. Chim. Acta* **1982**, *65*, 1700. (b) Moore, J. A.; Partain, E. *J. Org. Chem.* **1983**, *48*, 1105. (c) Brion, F. *Tetrahedron Lett.* **1982**, *23*, 5299. (d) Nugent, W. A.; McKinney, R. J.; Harlow, R. L. *Organometallics* **1984**, *3*, 1315.

(6) (a) Vieira, E.; Vogel, P. *Helv. Chim. Acta* **1983**, *66*, 1865. (b) Black, K. A.; Vogel, P. *Helv. Chim. Acta* **1984**, *67*, 1612. (c) Takayama, H.; Iyobe, A.; Koizumi, T. *J. Chem. Soc., Chem. Commun.* **1986**, 771. (d) Saf, R.; Faber, K.; Penn, G.; Griengl, H. *Tetrahedron* **1988**, *44*, 389.

(7) (a) Boone, J. R.; Ashby, E. C. *Top. Stereochem.* **1979**, *11*, 53. (b) Ashby, E. C.; Laemmle, J. T. *Chem. Rev.* **1975**, *75*, 521.

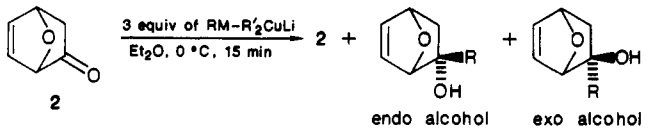
(8) For other additions to the carbonyl group of oxabicyclic ketones, see: (a) Additions of complex metal hydrides to 7-oxabicyclo[2.2.1]heptan-2-one, Moursonides, J.; Wege, D. *Aust. J. Chem.* **1983**, *36*, 2473. (b) Hydride reductions of 5,6-*exo*-epoxy-7-oxabicyclo[2.2.1]heptan-2-one: Le Drian, C.; Vogel, P. *Helv. Chim. Acta* **1988**, *71*, 1399. (c) Additions of nitrogen nucleophiles: Arjona, O.; Mallo, A.; Manzano, C.; Plumet, J.; Galbis, J.; Jaime, C. *J. Chem. Soc., Perkin Trans. 2* **1988**, 865. (d) Additions of dichloroketene: Arjona, O.; Fernández de la Pradilla, R.; Pérez, S.; Plumet, J. *Tetrahedron* **1988**, *44*, 1235. (e) Addition of methyllithium to 3,3-dimethyl-7-oxabicyclo[2.2.1]heptan-2-one: Buchbauer, G.; Holbik, H. *Heterocycles* **1988**, *27*, 1217. (f) Addition of the lithium anion of (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenyl sulfoximide to 5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]heptan-2-one, see ref 4c.

(9) For a new approach to predicting the stereochemistry of the addition of nucleophiles to chiral aldehydes and ketones, see: (a) Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 908. (b) Wu, Y.-D.; Houk, K. N.; Trost, B. M. *J. Am. Chem. Soc.* **1987**, *109*, 5560.

(10) This behavior is consistent with literature data for norbornenic systems. See, for example: (a) Brown, W. L.; Fallis, A. G. *Tetrahedron Lett.* **1985**, *26*, 207. (b) Jung, M. E.; Hatfield, G. L. *Tetrahedron Lett.* **1983**, *24*, 2931.

(11) These reactions were generally carried out with a 3-fold excess of organometallic reagent. However, when **2** was reacted with *n*-BuLi under those conditions, only trace amounts of **6** and **7** were isolated. The structure of the major product has not been firmly established but it appears to be produced by opening of the oxygen bridge. Research in this direction is currently under way.

Table II. Reaction of 7-Oxabicyclo[2.2.1]hept-5-en-2-one with Organocuprate Reagents



			products				
				alcohols			
entry	RM	R'	2, %	endo	exo	endo:exo ratio	yield,[a] %
1	MeLi	Me		3	4	1:6	80
2	*n*-BuLi	*n*-Bu			7		70
3	PhLi	Ph		11	12	10:1	80
4		Me		3	4	1:6	85
5		*n*-Bu			7		75
6		Ph		11	12	1:6	85
7		1-naphthyl		15	16	1:6	70
8[b]	Ph_3CuLi_2		40		12		40
9[b]		Ph	80				
10[c]		Me	5	3	4	1:5	75
11[d]	MeLi	Me		3	4	1:2	66
12[d]		Me	40	3	4	1:1	40
13	MeCu		90				
14[e]	$MeCu{\cdot}BF_3$		95				
15[f]	$Me_2CuMgBr$			3			75
16[e]	$Me_2CuLi{\cdot}BF_3$		40	3			40
17[g]	MeCuCNLi		37	3			40
18[h]	$Me_2CuCNLi_2$		65	3	4	2:1	24

[a] Yields refer to pure isolated alcohols. [b] The reaction was carried out in dimethyl sulfide. [c] The reaction was carried out with 2 equiv of Me_2CuLi. [d] The reaction was carried out at −78 °C and was difficult to reproduce. [e] The reaction was carried out at −78 °C. [f] Identical results were obtained in THF at −23 °C. [g] The reaction was slower than when Me_2CuLi was utilized. TLC analysis after 2 h showed only starting material. The results indicated correspond to 24 h at room temperature. [h] The reaction was allowed to proceed for 1 h.

10 shows that the stereochemical outcome of the process is highly dependent on the specific lithium derivative involved. This and the decrease of endo selectivity observed for organolithium reagents may be related to a number of factors, such as a different state of aggregation of the reagent and an earlier occurrence of the transition state in the reaction coordinate.

Axial-selective nucleophiles, such as acetylides[12] and lithiated acetonitrile,[13] failed to produce the corresponding exo isomers in a stereoselective fashion. Thus, while the reaction with the latter afforded exclusively endo alcohol **17**, predominantly endo mixtures of **18** and **19** were obtained with hexynyllithium (entry 14).

The stereochemical assignment of these adducts followed their postulated mechanism of formation, by analogy with literature data for norbornenic ketones, as well as their ^1H and ^{13}C NMR spectral data. These assignments will be discussed in detail below.

Reaction of 7-Oxabicyclo[2.2.1]hept-5-en-2-one with Organocuprate Reagents. The second stage of this study addressed the stereoselective preparation of exo oxanorbornenic alcohols. For this purpose, the reagent developed by Macdonald and Still,[14] prepared by addition of methyllithium to lithium dimethylcuprate, was perceived as an appealing possibility. It was envisioned that coordination of the "unreactive"[15] cuprate species with the carbonyl group[16] and with the oxygen bridge[17] should block the exo face of **2**, thus forcing nucleophilic attack by methyllithium to occur from the hindered endo face of the molecule. The results of the reaction between several organocuprates and 7-oxanorbornenone (**2**) are indicated in Table II.

When **2** was treated with 3 equiv of MeLi–Me_2CuLi, (entry 1), a mixture of endo and exo alcohols, **3** and **4** in a 1:6 ratio was obtained. The introduction of a *n*-butyl group was effected in a similar fashion (entry 2); these results seemed to confirm our hypothesis. However, the reaction of **2** with PhLi–Ph_2CuLi (entry 3) was devoid of the high exo selectivity encountered before and a 10:1 mixture of **11** and **12** was realized, perhaps indicating that nucleophilic addition was taking place faster than complexation in this case;[18] this high endo selectivity is in sharp contrast with the outcome of the addition of PhLi (Table I, entry 10).[19]

In order to verify that the cuprate reagent did not react with the carbonyl group, the reaction of **2** with Me_2CuLi was examined (entry 4). Surprisingly, a mixture of **3** and **4** was obtained in identical ratio as when MeLi–Me_2CuLi had been utilized; analogous behavior was observed for

(12) See for example: (a) Fleming, I.; Terret, N. K. *J. Organomet. Chem.* **1984**, *264*, 99. (b) Kuwajima, I.; Nakamura, E.; Hashimoto, K. *Tetrahedron* **1983**, *39*, 975.

(13) (a) Trost, B. M.; Flórez, J.; Jebaratnam, D. J. *J. Am. Chem. Soc.* **1987**, *109*, 613. (b) Trost, B. M.; Flórez, J.; Haller, K. J. *J. Org. Chem.* **1988**, *53*, 2394.

(14) (a) Macdonald, T. L.; Still, W. C. *J. Am. Chem. Soc.* **1975**, *97*, 5280. (b) Macdonald, T. L.; Still, W. C. *Tetrahedron Lett.* **1976**, 2659.

(15) Lithium organocuprates were generally unreactive toward saturated ketones. For some reports of organocuprate/ketone additions, see: (a) Scott, L. T.; Cotton, W. D. *J. Chem. Soc., Chem. Commun.* **1973**, 320. (b) Goldsmith, D. J.; Sakano, I. *Tetrahedron Lett.* **1974**, 2857. (c) House, H. D.; Chu, C. Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460. (d) Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1975**, 3897.

(16) (a) Ashby, E. C.; Noding, S. A. *J. Org. Chem.* **1979**, *44*, 4371. (b) Lipshutz reports that the addition of 3 equiv of RLi to CuI affords only R_2CuLi and free RLi. See: Lipshutz, B. H. *Synthesis* **1987**, 325.

(17) It has been recently reported that an ortho-methoxymethyl substituent in a methyl cinnamate system intramolecularly assists the conjugate addition of Me_2CuLi. See: Hallnemo, G.; Ullenius, C. *Tetrahedron Lett.* **1986**, *27*, 395. For a recent report describing a highly diastereoselective conjugate addition of organocopper reagents on cinnamates bearing a chiral oxazolidine or imidazolidine ring, see: Alexakis, A.; Sedrani, R.; Mangeney, P.; Normant, J. F. *Tetrahedron Lett.* **1988**, *29*, 4411.

(18) There are numerous examples in the literature of the "anomalous" behavior of vinyl and phenyl cuprates. See, for example: Marino, J. P.; Jaén, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 3165.

(19) The enhanced endo selectivity observed for the addition of PhLi–Ph_2CuLi in ether (positive Gilman test) presumably implies that alkylation of PhLi is taking place on a ketonic reactive species different from the one operative for the addition of PhLi. See ref 14 and 16.

Table III. Selected ^1H NMR and ^{13}C NMR Data for Endo and Exo Oxanorbornenic Alcohols

	R		R
3	Me	**4**	
6	*n*-Bu	**7**	
11	Ph	**12**	

	^1H NMR (δ ppm)			^{13}C NMR (δ ppm)		
	CH_3	H-3_{endo}	H-3_{exo}	CH_3	C-2	C-1
3	1.53	1.21	1.95	27.5	74.8	84.0
4	1.21	1.43	1.82	23.3	76.0	86.9
6		1.13	1.97		78.4	83.2
7		1.47	1.78		79.1	86.3
11		1.55	2.39		78.1	85.1
12		2.16	2.11		79.8	87.0

n-Bu_2CuLi (entry 5). Furthermore, the use of Ph_2CuLi (entry 6) resulted in a predominantly exo mixture of **11** and **12** (1:6), and the reaction with (1-Naphthyl)$_2$CuLi took place in a similar manner. In all cases (entries 4–7) the reactions were instantaneous.

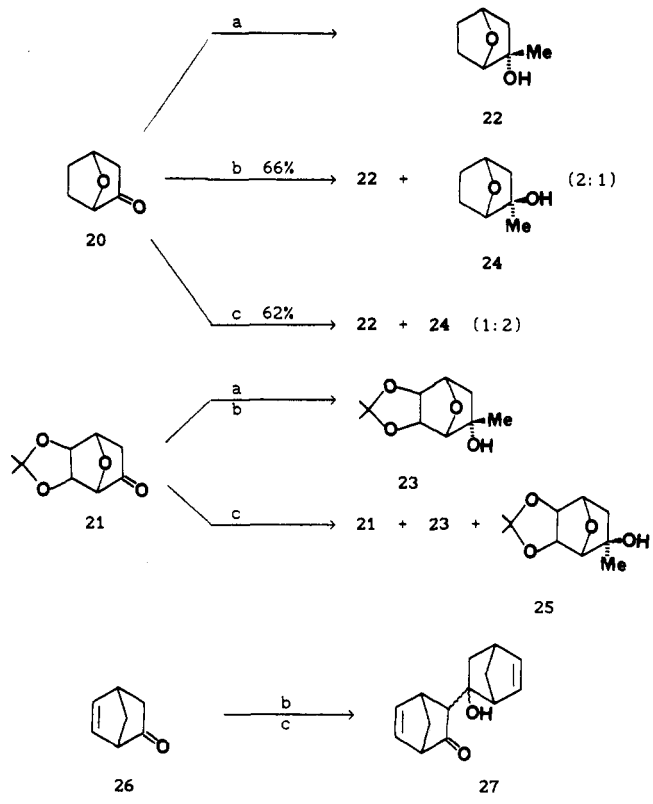
The use of Ph_3CuLi_2, generated in dimethyl sulfide according to Bertz' procedure[20] resulted in 40% of exo alcohol **12** along with 40% of recovered ketone (entry 8). Ph_2CuLi in dimethyl sulfide proved to be even less reactive for this alkylation (entry 9), and the starting material was isolated in 80% yield.

The reaction of **2** with simple lithium organocuprates in an instantaneous manner and in high yields is unprecedented in the literature. The dramatic reversal of stereoselectivity, with respect to organolithium and Grignard reagents, is a unique phenomenon.[14] These unexpected results prompted us to further investigate this process. Some of the experiments carried out are shown in Table II (entries 10–12).

The effect of the stoichiometry of the reaction was examined (entries 1 and 10), and 3 equiv of cuprate was found to produce the best results. The need of excess reagent may be interpreted in terms of the proposed complexation (vide supra). The solvent employed was next taken into consideration. It was encountered that an ether–hexane, 1:1, solvent mixture provided the same result as ether. However the use of THF resulted in quantitative recovery of **2**; this observation is also consistent with the proposed complexation since **2** would not be expected to compete with THF for coordination sites on the cuprate. Lowering the reaction temperature to −78 °C (entries 11 and 12) caused a decrease of both the yield and diastereoselectivity of the reaction; this may be rationalized in terms of a less efficient formation of the proposed complex. The unlikely possibility that epimerization of the alcohols could be taking place was conclusively ruled out by subjecting both epimers **3** and **4** to a variety of reaction conditions (MeLi, MeLi–Me_2CuLi, and Me_2CuLi). No sign of epimerization was detected by ^1H NMR spectroscopy after several days.

The utilization of other organocopper reagents was then addressed, and the results of this part of the study are summarized in Table II (entries 13–18). The use of alkylorganocopper reagents (entry 13) did not lead to significant yields of products, nor did the organocopper–Lewis acid reagent, MeCu·BF_3[21] (entry 14). The use of Grignard reagents as precursors for the cuprates led to exclusive formation of the endo alcohols (entry 15).[22] As shown in Table II, $Me_2CuLi·BF_3$[21] (entry 16) did not afford exo alcohols either. Cyanocuprates[23] and higher order mixed cyanocuprates[16] (entries 17 and 18) were found to be quite unreactive.

Scheme I[a]



[a] Reagents: (a) MeLi; (b) MeLi–Me_2CuLi; (c) Me_2CuLi.

Assignment of configuration of the addition products derived from ^1H NMR and ^{13}C NMR chemical shift correlations. Table III contains selected spectroscopic data for representative isomeric oxanorbornenic alcohols. It was observed that the exo isomer **4** (R = Me) presents a remarkably shielded methyl group (1.21 ppm); this is consistent with the expected influence of the anisotropic double bond, a well-established phenomenon in norbornenic analogues.[24] Generally, exo isomers (**4**, **7**, **12**) presented significant downfield shifts for H-3_{endo} and upfield shifts for H-3_{exo}, as indicated in Table III. Further evidence supporting the assigned stereochemistry was obtained from the differential reactivity of **3** and **4** with benzenesulfenyl chloride. Whereas endo alcohol **3** led to the formation of a tricyclic oxetane by intramolecular cyclization, exo isomer **4** led to the corresponding addition product.[25] ^{13}C NMR data also proved useful in assigning

(20) We thank one of the referees for suggesting this experiment, as well as the use of Ph_3Cu_2Li and $Ph_3Cu_2Li·2BF_3·Et_2O$. (See: Lipshutz, B. H.; Ellsworth, E. L.; Siahaan, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 1351). The former species produced a good yield of endo isomer **11**, while the latter afforded only recovered starting material. With respect to the generation of Ph_3CuLi_2 in dimethyl sulfide (negative Gilman test), see: (a) Bertz, S. H.; Dabbagh, G. *J. Am. Chem. Soc.* **1988**, *110*, 3668. (b) Bertz, S. H.; Dabbagh, G. *Tetrahedron* **1989**, *2*, 45.

(21) For a recent review, see: Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 947.

(22) For a detailed study on magnesium methylcuprates, see: Ashby, E. C.; Goel, A. B. *J. Org. Chem.* **1983**, *48*, 2125.

(23) See for example: Marino, J. P.; Fernández de la Pradilla, R.; Laborde, E. *J. Org. Chem.* **1987**, *52*, 4898.

(24) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon Press: Oxford, 1969; p 84.

(25) Arjona, O.; Fernández de la Pradilla, R.; Pérez, R. A.; Plumet, J.; Viso, A. *Tetrahedron Lett.* **1987**, *28*, 5549.

stereochemistry. The signal for the methyl group appears at higher field for the exo isomer **4** than for the endo isomer **3**, due to steric compression. In addition, C-2 and C-1 appear at lower field for the exo isomers **4**, **7**, and **12** than for the endo isomers.[26] The stereochemistry of the other oxanorbornenic carbinols was assigned by correlation of their spectra with those of **3**, **4**, **6**, **7**, **11**, and **12**.

In order to ascertain the influence of the carbon–carbon double bond on the stereochemical outcome of the process, the reaction of oxanorbornanic derivatives **20** and **21**[5a] (Scheme I) with methyllithium was studied. In both cases, exclusive formation of the endo alcohols **22** and **23** was observed. While our work was in progress, the reaction between methyllithium and 3,3-dimethyl-7-oxabicyclo-[2.2.1]heptan-2-one has been reported to produce the corresponding endo alcohol;[8e] this observation is in agreement with the results described above.

To determine the generality of the organocuprate alkylation, the behavior of oxanorbornanic ketones **20** and **21** with organocuprate reagents was examined and the results obtained are shown in Scheme I. 7-Oxanorbornanone, **20**, afforded fair yields of mixtures of saturated alcohols **22** and **24** (the structure of which was secured by hydrogenation of the unsaturated precursors **3** and **4** and chromatographic separation) in different ratios, depending upon the precise nucleophile utilized. However, the stereoselectivity of the reaction was severely diminished, and, furthermore, these reactions were hard to reproduce and afforded variable yields of aldol dimers. Even more disappointing results were encountered for isopropylidenedioxy derivative **21**, which led to endo product **23** or to intractable mixtures of recovered starting material, **23**, **25**, and several other uncharacterized products, depending upon the reaction conditions. Since exo carbinols **24** and **25** are readily avaible from unsaturated precursor **4**, the synthetic importance of these reactions is limited, and, therefore, they were not researched any further. Nevertheless, these tests contributed to defining the limitations of the methodology. Another substrate examined was bicyclo[2.2.1]hept-5-en-2-one, **26**, which, under both sets of conditions, afforded complex mixtures of products from which **27** was isolated (60%) as a mixture of two isomers, indicating that enolization was the predominant reaction pathway in this case.[27]

The above results indicate that the steric and electronic requirements of the endo alkylation of derivatives of 7-oxanorbornane are very strict. It appears that both the oxygen bridge and the carbon–carbon double bond are crucial to achieve good stereoselectivities. Furthermore, the peculiar reactivity of 7-oxanorbornenic systems is underlined by the fact that, in contrast with the results of Yamamoto, use of the bulky aluminum reagent MAD, followed by addition of methyllithium,[28] led to endo methylcarbinol **3**, with identical stereoselectivity to that encountered for methyllithium. This observation and the results encountered for axial selective nucleophiles[12,13] indicate that there must be a delicate interplay of steric and electronic factors responsible for the unique endo alkylation of 7-oxabicyclo[2.2.1]hept-5-en-2-one with lithium organocuprates described in the present report.[29]

(26) This trend is observed for related norbornenic systems. See, for example: Schneider, H.-J.; Weigand, E. F.; Becker, N. *J. Org. Chem.* **1988**, *53*, 3361.

(27) For a report describing the alkylation and oligomerization of the lithium enolate of 2-norbornenone, see: Horner, J. H.; Vera, M.; Grutzner, J. B. *J. Org. Chem.* **1986**, *51*, 4212. See also: Tureček, F.; Brabec, L.; Korvola, J. *J. Am. Chem. Soc.* **1988**, *110*, 7984.

(28) Maruoka, K.; Itoh, T.; Sakurai, M.; Nonoshita, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 3588.

Conclusions

The alkylation of 7-oxabicyclo[2.2.1]hept-5-en-2-one, **2**, with Grignard reagents produces endo alcohols with very high selectivity. On the other hand, the unprecedented addition of simple lithium organocuprates to bicyclic ketone **2**, albeit limited in scope, provides a straightforward entry for the stereoselective preparation of exo oxanorbornenic alcohols.

Experimental Section

General Methods. All reactions were carried out under a positive pressure of dry nitrogen or dry argon, using freshly distilled solvents under anhydrous conditions unless otherwise stated. Reagents and solvents were handled by using standard syringe techniques. Diethyl ether and tetrahydrofuran were distilled from lithium aluminum hydride, dimethyl sulfide from Na, hexane and ethyl acetate from phosphorus pentoxide, and methylene chloride from calcium hydride. Commercial methyllithium (low halide solution in ether), butyllithium (solution in hexane) phenyllithium (solution in benzene–ether, 70–30%), and vinylmagnesium bromide (solution in tetrahydrofuran) were purchased from Aldrich, Merck, or Fluka and titrated[30] prior to use. Reagent-grade copper iodide and copper bromide were purchased from Aldrich and used without further purification. Analytical TLC was carried out on 0.20 mm E. Merck precoated silica gel plates (60F-254), with detection by UV light, iodine, or acidic vanillin solution. Column chromatography was performed with E. Merck 230–400 mesh or 70–230 mesh silica gel. Melting points were determined on a Büchi 512 apparatus and are uncorrected. Mass spectra were recorded on a Varian MAT-711 instrument. Infrared spectra were recorded on either a Perkin-Elmer 781 or 257 grating spectrophotometers; band positions are indicated in wavenumbers. ^{1}H NMR spectra were recorded on a Varian T-60A, a Bruker AM-200, or a Varian XL-300 instrument, using $CDCl_3$ as solvent. ^{13}C NMR spectra were measured on a Varian FT-80-A, using $CDCl_3$ as solvent, and are completely decoupled. In both, ^{1}H NMR and ^{13}C NMR, chemical shifts are reported in δ units downfield from tetramethylsilane. The following abbreviations are used to describe peak patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

General Procedure for the Reaction between 7-Oxabicyclo[2.2.1]hept-5-en-2-one and Organolithium and Grignard Reagents. To a solution of 3 equiv of organolithium (or organomagnesium) reagent in anhydrous ether (10 mL/mmol of ketone), at 0 °C, was added 1 equiv of ketone dissolved in anhydrous ether (5 mL/mmol of ketone). The mixture was stirred at 0 °C for 15 min and then quenched with a saturated NH_4Cl solution. The organic layer was decanted, and the aqueous layer was extracted with ethyl acetate (3 × 10 mL/mmol of ketone). The combined organic solution and extracts were washed with a saturated NaCl solution and dried over anhydrous $MgSO_4$. Concentration under reduced pressure gave a crude product, which was purified by column chromatography on silica gel, using the appropriate eluent.

General Procedure for the Reaction between 7-Oxabicyclo[2.2.1]hept-5-en-2-one and Organocuprate Reagents. To a well-stirred suspension of CuI (3 equiv) in anhydrous ether (40 mL/mmol of ketone), at 0 °C, was slowly added the corresponding organolithium derivative (8.8 equiv for reactions with RLi–R_2CuLi and 5.8 equiv for reactions with R_2CuLi). The mixture was stirred at 0 °C for 10 min, after which time a solution of 1 equiv of ketone in anhydrous ether (5 mL/mmol of ketone) was added dropwise. The reaction mixture was stirred for 15 min and then quenched with a saturated NH_4Cl solution. The solid residue was removed by filtration and carefully washed with ethyl acetate. The organic layer was decanted, and the aqueous layer was extracted with

(29) For a report describing the unexpectedly high trans diastereofacial selectivity encountered for cuprate additions to 5-methoxy-2-cyclopentenone, see: Smith, A. B. III; Dunlap, N. K.; Sulikowski, G. A. *Tetrahedron Lett.* **1988**, *29*, 439. In this contribution, the observed selectivity is accounted for in terms of a novel stereoelectronic effect.

(30) Watson, S. C.; Eastham, J. E. *J. Organomet. Chem.* **1967**, *9*, 165.

dichloromethane (3 × 20 mL/mmol of ketone). The combined organic extracts were washed with a saturated NaCl solution and dried over anhydrous $MgSO_4$. Concentration under reduced pressure gave a crude product, which was purified by column chromatography on silica gel, using the appropriate eluent.

2-*exo*-Methyl-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (3). From 250 mg (2.27 mmol) of **2** and methyllithium (1.6 M in ether) was isolated 272 mg of **3** (95%) as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1; R_f 0.18) (endo:exo ratio, 20:1). The use of methylmagnesium iodide resulted in exclusive formation of the endo isomer in similar yields: IR (neat) 3450, 3040–2860, 1000 cm^{-1}; ^1H NMR δ 6.58 (dd, 1 H, J = 5.9, 1.7 Hz, H-5), 6.47 (dd, 1 H, J = 5.9, 1.7 Hz, H-6), 4.92 (dd, 1 H, J = 4.8, 1.5 Hz, H-4), 4.42 (d, 1 H, J = 1.5 Hz, H-1), 1.95 (dd, 1 H, J = 11.7, 4.8 Hz, H-3_{exo}), 1.60 (br, 1 H, OH), 1.53 (s, 3 H), 1.21 (d, 1 H, J = 11.7 Hz, H-3_{endo}); ^{13}C NMR δ 136.8, 133.0, 84.0, 79.2, 74.8, 42.3, 27.5. Anal. Calcd for $C_7H_{10}O_2$: C, 66.64; H, 7.99. Found: C, 66.50; H, 7.81.

2-*endo*-Methyl-7-oxabicyclo[2.2.1]hept-5-en-2-*exo*-ol (4). From 440 mg (4 mmol) of **2** and MeLi–Me_2CuLi was isolated 403 mg of **4** (80%) as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.17) (endo:exo ratio, 1:6). These isomers could not be separated. Similar results were obtained from the reaction of **2** with Me_2CuLi (85%), generated from CuI or CuBr; IR (neat) 3420, 3040–2860, 1320, 1230, 1100, 900, 710 cm^{-1}; ^1H NMR δ 6.38 (dd, 1 H, J = 5.9, 1.5 Hz, H-5), 6.32 (dd, 1 H, J = 5.9, 1.6 Hz, H-6), 4.96 (d, 1 H, J = 4.8 Hz, H-4), 4.43 (s, 1 H, H-1), 2.06 (br, 1 H, OH), 1.82 (dd, 1 H, J = 12.1, 4.8 Hz, H-3_{exo}), 1.43 (d, 1 H, J = 12.1 Hz, H-3_{endo}), 1.21 (s, 3 H); ^{13}C NMR δ 137.2, 132.7, 86.9, 78.1, 76.0, 42.4, 23.3. Anal. Calcd for $C_7H_{10}O_2$: C, 66.64; H, 7.99. Found: C, 66.56; H, 7.82.

2-*exo*-Ethyl-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (5). From 250 mg (2.27 mmol) of **2** and ethylmagnesium iodide was isolated 238 mg of **5** (75%) as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.25): IR (neat) 3450, 3060–2900, 1000, 895, 710, 675 cm^{-1}; ^1H NMR δ 6.53 (m, 2 H, H-5, H-6), 4.98 (d, 1 H, J = 4.0 Hz, H-4), 4.50 (s, 1 H, H-1), 1.98 (dd, 1 H, J = 10.0, 4.0 Hz, H-3_{exo}), 1.83 (q, 2 H, J = 7.0 Hz), 1.72 (br, 1 H, OH), 1.17 (d, 1 H, J = 10.0 Hz, H-3_{endo}), 1.04 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 137.7, 133.4, 82.7, 79.4, 78.5, 41.1, 32.7, 8.1. Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.48; H, 8.68.

2-*exo*-*n*-Butyl-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (6). From 500 mg (4.54 mmol) of **2** and *n*-butylmagnesium bromide were isolated 687 mg of **6** (90%) as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.30) and 61 mg of 7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (8%). The use of 1 eqiuv of *n*-butyllithium resulted in a 90% yield of a mixture of **6** and the exo isomer **7** (endo:exo ratio, 11:1): IR (neat) 3600, 3450, 3040–2860, 1320, 1020, 670 cm^{-1}; ^1H NMR δ 6.56 (dd, 1 H, J = 5.8, 1.7 Hz, H-5), 6.43 (dd, 1 H, J = 5.8, 1.7 Hz, H-6), 4.88 (dd, 1 H, J = 4.8, 1.0 Hz, H-4), 4.73 (dd, 1 H, J = 1.7, 0.7 Hz, H-1), 1.97 (dd, 1 H, J = 11.8, 4.8 Hz, H-3_{exo}), 1.79–1.71 (m, 2 H), 1.53–1.31 (m, 5 H), 1.13 (d, 1 H, J = 11.8 Hz, H-3_{endo}), 0.90 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 138.0, 133.4, 83.2, 79.5, 78.4, 41.6, 40.0, 26.2, 23.0, 13.9. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.21; H, 9.72.

2-*endo*-*n*-Butyl-7-oxabicyclo[2.2.1]hept-5-en-2-*exo*-ol (7). From 330 mg (3 mmol) of **2** with *n*-BuLi–*n*-Bu_2CuLi was isolated 353 mg of **7** (70%), as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.28), contaminated with a small amount of an inseparable byproduct whose spectral data was different from the data of the endo isomer **6**. Similar results were obtained from the reaction of **2** with *n*-Bu_2CuLi (75%): IR (neat) 3450, 3020–2840, 1460, 1310, 1170, 1080, 855, 730 cm^{-1}; ^1H NMR δ 6.40 (dd, 1 H, J = 5.8, 1.5 Hz, H-5), 6.34 (dd, 1 H, J = 5.8, 1.4 Hz, H-6), 4.99 (d, 1 H, J = 4.8 Hz, H-4), 4.53 (s, 1 H, H-1), 2.35–2.20 (br, 1 H, OH), 1.78 (dd, 1 H, J = 12.1, 4.8 Hz, H-3_{exo}), 1.47 (d, 1 H, J = 12.1 Hz, H-3_{endo}), 1.49–1.26 (m, 6 H), 0.90 (m, 3 H); ^{13}C NMR δ 137.3, 132.6, 86.3, 79.1, 77.6, 41.6, 37.3, 26.2, 22.7, 13.5. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 72.40; H, 10.03.

2-*exo*-Isopropyl-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (8). From 250 mg (2.27 mmol) of **2** and isopropylmagnesium iodide was isolated 314 mg of **8** (90%) as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.28): IR (neat) 3610, 3470, 3040–2890, 1025, 1000, 670 cm^{-1}; ^1H NMR δ 6.61 (dd, 1 H, J = 5.8, 1.7 Hz, H-5), 6.48 (dd, 1 H, J = 5.8, 1.8 Hz, H-6), 4.92 (dd, 1 H, J = 4.9, 1.7 Hz, H-4), 4.69 (d, 1 H, J = 1.8 Hz, H-1), 2.05 (dd, 1 H, J = 12.0, 4.9 Hz, H-3_{exo}), 1.91 (heptuplet, 1 H, J = 6.8 Hz, H-1′), 1.55–1.45 (br, 1 H, OH), 1.10 (d, 1 H, J = 12.0 Hz, H-3_{endo}), 1.04 (d, 3 H, J = 6.8 Hz), 1.01 (d, 1 H, J = 6.8 Hz); ^{13}C NMR δ 137.4, 134.0, 81.2, 80.6, 79.1, 39.8, 35.1, 17.3, 16.9. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.20; H, 9.09.

2-*exo*-Vinyl-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (9). From 330 mg (3 mmol) of **2** and vinylmagnesium bromide (1 M in THF) was isolated 289 mg of **9** (70%) as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.41) along with a small amount (30 mg) of an uncharacterized byproduct: IR (neat) 3400, 3080, 3020–2800, 1640, 1315, 1220, 1005, 790, 705 cm^{-1}; ^1H NMR δ 6.66 (dd, 1 H, J = 5.9, 1.66 Hz, H-5), 6.50 (dd, 1 H, J = 5.9, 1.6 Hz, H-6), 6.17 (dd, 1 H, J = 17.3, 10.7 Hz, H-1′), 5.35 (d, 1 H, J = 17.3 Hz, H-2′t), 5.16 (d, 1 H, J = 10.7 Hz, H-2′c), 5.03 (d, 1 H, J = 4.9 Hz, H-4), 4.55 (s, 1 H, H-1), 2.86 (br, 1 H, OH), 2.18 (dd, 1 H, J = 12.0, 4.9 Hz, H-3_{exo}), 1.33 (d, 1 H, J = 12.0 Hz, H-3_{endo}); ^{13}C NMR δ 143.8, 137.7, 133.2, 110.9, 84.7, 79.1, 77.0, 41.8. Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.29. Found: C, 69.39; H, 7.15.

2-*exo*-Allyl-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (10). From 330 mg (3 mmol) of **2** and allylmagnesium bromide was isolated 276 mg of **10** (65%) as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.47) along with a small amount (40 mg) of an uncharacterized byproduct: IR (neat) 3435, 3080, 3040–2800, 1640, 1435, 1320, 920, 805, 710 cm^{-1}; ^1H NMR δ 6.58 (dd, 1 H, J = 5.8, 1.7 Hz, H-5), 6.44 (dd, 1 H, J = 5.8, 1.7 Hz, H-6), 5.97 (ddt, 1 H, J = 17.8, 9.5, 7.2 Hz, H-2′), 5.25–5.14 (m, 2 H, H-3′c, H-3′t), 4.93 (dd, 1 H, J = 4.8, 1.0 Hz, H-4), 4.54 (dd, 1 H, J = 1.6, 0.6 Hz, H-1), 2.58–2.54 (m, 2 H, 2 H-1′), 2.01 (dd, 1 H, J = 11.8, 4.8 Hz, H-3_{exo}), 1.21 (d, 1 H, J = 11.8 Hz, H-3_{endo}); ^{13}C NMR δ 137.2, 133.2, 132.8, 117.9, 81.9, 78.9, 76.5, 44.2, 40.5. Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 71.20; H, 8.10.

2-*exo*-Phenyl-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (11). From 250 mg (2.27 mmol) of **2** and phenylmagnesium bromide was isolated 341 mg (80%) of **11** as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.38). The use of phenyllithium (2 M in benzene–ether, 70–30%) resulted in a 90% yield of a mixture of **11** and the exo isomer **12** (endo:exo ratio, 3.6:1): IR (neat) 3450, 3100–2900, 1600, 1490, 1445, 1315, 1060, 850, 780–760, 700 cm^{-1}; ^1H NMR δ 7.61–7.56 (m, 2 H, H-Ar), 7.32–7.17 (m, 3 H, H-Ar), 6.68 (dd, 1 H, J = 5.8, 1.7 Hz, H-5), 6.54 (dd, 1 H, J = 5.8, 1.7 Hz, H-6), 5.05 (d, 1 H, J = 4.9 Hz, H-4), 4.70 (s, 1 H, H-1), 2.39 (dd, 1 H, J = 12.2, 4.9 Hz, H-3_{exo}), 1.82 (br, 1 H, OH), 1.55 (d, 1 H, J = 12.2 Hz, H-3_{endo}); ^{13}C NMR δ 146.6, 138.3, 134.1, 127.7, 126.3, 125.0, 85.1, 79.1, 78.1, 45.2. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.30; H, 6.28.

2-*endo*-Phenyl-7-oxabicyclo[2.2.1]hept-5-en-2-*exo*-ol (12). From 110 mg (1 mmol) of **2** and Ph_2CuLi was isolated 160 mg of a 1:6 mixture of **11** and **12** after filtration through silica gel (85%). These were later separated by chromatography (hexane–ethyl acetate, 1:1, R_f 0.31) to afford 137 mg of pure **12** as a light yellow oil. The reaction with PhLi–Ph_2CuLi led to a 10:1 mixture of **11** and **12** (80%). The reaction with Ph_3CuLi_2 in dimethyl sulfide led to **12** (40%) and **2** (40%): IR (neat) 3450, 3100–2950, 1445, 1205, 1195, 910, 900, 700 cm^{-1}; ^1H NMR δ 7.34–7.19 (m, 5 H, H-Ar), 6.42 (dd, 1 H, J = 5.9, 1.6 Hz, H-5), 6.02 (dd, 1 H, J = 5.9, 1.8 Hz, H-6), 5.10 (dd, 1 H, J = 4.0, 1.0 Hz, H-4), 4.70 (dd, 1 H, J = 1.8, 0.9 Hz, H-1), 2.97 (br, 1 H, OH), 2.16 (d, 1 H, J = 12.5 Hz, H-3_{endo}), 2.11 (dd, 1 H, J = 12.5, 4.0 Hz, H-3_{exo}); ^{13}C NMR δ 141.2, 137.2, 133.0, 127.5, 126.8, 126.2, 87.0, 79.8, 78.0, 42.5. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.42; H, 6.30.

2-*exo*-(2-Furyl)-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (13). From 250 mg (2.27 mmol) of **2** and 2-furyllithium (prepared from furan and *n*-butyllithium) was isolated 315.8 mg (78%) of an inseparable 9:1 mixture of **13** and the exo isomer **14** after chromatography (hexane–ethyl acetate, 2:1, R_f 0.18): IR (neat) 3400, 3100–2850, 1500, 1315, 1220, 1075, 1000 cm^{-1}; ^1H NMR δ 7.40 (d, 1 H, J = 0.8 Hz, H-5′), 6.67 (dd, 1 H, J = 5.8, 1.4 Hz, H-5), 6.53 (dd, 1 H, J = 5.8, 1.5 Hz, H-6), 6.36–6.26 (m, 2 H, H-3′, H-4′), 5.05 (d, 1 H, J = 4.8 Hz, H-4), 4.94 (s, 1 H, H-1), 2.57 (dd, 1 H, J = 12.0, 4.8 Hz, H-3_{exo}), 2.3–2.0 (br, 1 H, OH), 1.54 (d, 1 H, J

= 12.0 Hz, H-3$_{endo}$); ^{13}C NMR δ 157.8, 141.4, 137.5, 132.8, 109.8, 105.5, 83.0, 79.1, 74.9, 40.9. Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.40; H, 5.66. Found: C, 67.53; H, 5.72.

2-*exo*-(1-Naphthyl)-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (15). From 330 mg (3 mmol) of **2** and 1-lithionaphthalene (prepared from 1-bromonaphthalene and *n*-BuLi) was isolated 607.5 mg (85%) of crude product as a yellowish oil (endo:exo ratio, 9:1). These isomers were separated by chromatography (hexane–ethyl acetate, 1:1, R_f 0.32) to afford 545 mg of pure **15** as a white solid (mp 66–67 °C): IR (KBr) 3360, 3080–2930, 1600, 1505, 1315, 1065, 1015 cm^{-1}; ^{1}H NMR δ 8.46–8.41 (m, 1 H, H-Ar), 7.89–7.76 (m, 2 H, H-Ar), 7.60–7.38 (m, 4 H, H-Ar), 6.80 (dd, 1 H, J = 5.8, 1.7 Hz, H-5), 6.62 (dd, 1 H, J = 5.8, 1.8 Hz, H-6), 5.49 (d, 1 H, J = 1.7 Hz, H-1), 5.02 (dd, 1 H, J = 4.8, 0.7 Hz, H-4), 2.52 (dd, 1 H, J = 11.9, 4.8 Hz, H-3$_{exo}$), 2.15 (br, 1 H, OH), 2.07 (d, 1 H, J = 11.9 Hz, H-3$_{endo}$); ^{13}C NMR δ 140.7, 138.8, 134.8, 133.6, 131.6, 128.6, 128.1, 126.7, 125.2, 125.1, 124.4, 121.5, 82.0, 79.3, 78.3, 44.1. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.79; H, 6.06.

2-*endo*-(1-Naphthyl)-7-oxabicyclo[2.2.1]hept-5-en-2-*exo*-ol (16). From 330 mg (3 mmol) of **2** and (1-naphthyl)$_2$CuLi was isolated 500 mg (70%) of crude product as a yellowish oil (endo:exo ratio, 1:6). These isomers were separated by chromatography (hexane–ethyl acetate, 1:1, R_f 0.27) to afford 428 mg of pure **16** as a white solid (mp 85–86 °C): IR (KBr) 3400, 3060–2850, 1600, 1505, 1315, 1065 cm^{-1}; ^{1}H NMR δ 8.50–8.47 (m, 1 H, H-Ar), 7.86–7.79 (m, 2 H, H-Ar), 7.57–7.26 (m, 4 H, H-Ar), 6.42 (dd, 1 H, J = 5.9, 1.7 Hz, H-5), 6.34 (dd, 1 H, J = 5.9, 1.7 Hz, H-6), 5.34 (s, 1 H, H-1), 5.18 (d, 1 H, J = 4.8 Hz, H-4), 2.95–2.80 (br, 1 H, OH), 2.64 (dd, 1 H, J = 12.2, 4.8 Hz, H-3$_{exo}$), 2.25 (d, 1 H, J = 12.2 Hz, H-3$_{endo}$); ^{13}C NMR δ 138.2, 137.0, 134.1, 133.6, 131.7, 128.6, 128.4, 126.0, 125.6, 125.3, 124.1, 123.9, 86.6, 81.2, 77.9, 43.4. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.78; H, 6.07.

2-*exo*-(Cyanomethyl)-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (17). From 110 mg (1 mmol) of **2** and $LiCH_2CN$ (prepared from LDA and CH_3CN at −78 °C) in tetrahydrofuran (15 mL) was isolated 113 mg (75%) of **17** as a white solid (mp 100–101 °C) after chromatography (hexane–ethyl acetate, 1:1, R_f 0.17): IR (KBr) 3340, 3040–2860, 2250, 1410, 1320, 1300, 1245, 1090, 1000 cm^{-1}; ^{1}H NMR δ 6.68 (dd, 1 H, J = 5.7, 1.4 Hz, H-5), 6.49 (dd, 1 H, J = 5.7, 1.6 Hz, H-6), 5.01 (dd, 1 H, J = 4.8, 0.5 Hz, H-4), 4.64 (d, 1 H, J = 0.6 Hz, H-1), 2.84 (s, 2 H, CH_2), 2.72 (s, 1 H, OH), 2.10 (dd, 1 H, J = 12.2, 4.8 Hz, H-3$_{exo}$), 1.39 (d, 1 H, J = 12.2 Hz, H-3$_{endo}$); ^{13}C NMR δ 138.5, 132.4, 117.6, 82.7, 79.8, 76.2, 41.6, 29.8. Anal. Calcd for $C_8H_9O_2N$: C, 63.56; H, 6.00; N, 9.26. Found: C, 63.63; H, 6.15; N, 9.31.

2-*exo*-(1-Hexynyl)-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (18) and 2-*endo*-(1-Hexynyl)-7-oxabicyclo[2.2.1]hept-5-en-2-*exo*-ol (19). From 330 mg (3 mmol) of **2** and 1-lithio-1-hexyne (prepared from 1-hexyne and *n*-BuLi) was isolated 507 mg (88%) of crude product as a yellowish oil (endo:exo ratio, 9:1). These isomers were separated by chromatography (hexane–ethyl acetate, 1:1).

18: R_f 0.31 (hexane:ethyl acetate, 1:1); IR (neat) 3400, 2990–2860, 2215, 1310, 1065, 1020, 900 cm^{-1}; ^{1}H NMR δ 6.57 (dd, 1 H, J = 5.8, 1.7 Hz, H-5), 6.42 (dd, 1 H, J = 5.8, 1.6 Hz, H-6), 5.02 (dd, 1 H, J = 4.8, 1.5 Hz, H-4), 4.81 (d, 1 H, J = 1.5 Hz, H-1), 2.83 (br, 1 H, OH), 2.44 (dd, 1 H, J = 11.7, 4.8 Hz, H-3$_{exo}$), 2.25–2.18 (m, 2 H), 1.49 (d, 1 H, J = 11.7 Hz, H-3$_{endo}$), 1.71–1.33 (m, 4 H), 0.90 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 137.0, 132.5, 85.0, 83.9, 83.2, 79.1, 70.4, 44.2, 30.1, 21.4, 17.9, 13.0. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 75.18; H, 8.43.

19: R_f 0.27 (hexane–ethyl acetate, 1:1); IR (neat) 3400, 2990–2840, 2220, 1310, 1065, 1020, 900 cm^{-1} ^{1}H NMR δ 6.39 (m, 2 H, H-5, H-6), 5.01 (d, 1 H, J = 4.8 Hz, H-4), 4.65 (s, 1 H, H-1), 2.60 (br, 1 H, OH) 2.30–1.93 (m, 4 H), 1.60–1.05 (m, 4 H), 1.05–0.80 (m, 3 H); ^{13}C NMR δ 137.9, 133.5, 87.4, 85.2, 80.5, 78.6, 71.5, 45.7, 30.4, 21.7, 18.2, 13.4. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 74.83; H, 8.25.

2-*exo*-Methyl-7-oxabicyclo[2.2.1]heptan-2-*endo*-ol (22). From 336 mg (3 mmol) of **20** and methyllithium (1.6 M in ether) was isolated 326 mg of **22** (85%) as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.28): IR (neat) 3420, 3000–2840, 1445, 1370, 1200, 990, 875 cm^{-1}; ^{1}H NMR δ 4.49 (t_{ap}, 1 H, J = 5.40 Hz, H-4), 4.00 (d, 1 H, J = 4.8 Hz, H-1), 3.00 (br, 1 H, OH), 2.33–2.21 (m, 1 H, H-3$_{exo}$), 1.85–1.44 (m, 4 H, H-5, H-6), 1.40 (d, 1 H, J = 12.1 Hz, H-3$_{endo}$), 1.36 (s, 3 H); ^{13}C NMR δ 83.1, 77.3, 76.6, 45.9, 28.9, 28.8, 22.2. Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.40; H, 9.25.

2-*exo*-Methyl-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]heptan-2-*endo*-ol (23). From 320 mg (1.79 mmol) of **21** and methyllithium (1.6 M in ether) was isolated 232 mg of **23** (65%) as a white solid (mp 108–110 °C) after chromatography (hexane–ethyl acetate, 2:1, R_f 0.24): IR (KBr) 3520, 3000–2820, 1205, 1050 cm^{-1}; ^{1}H NMR δ 4.97 (d, 1 H, J = 5.6 Hz, H-6), 4.37 (d, 1 H, J = 5.6 Hz, H-5), 4.34 (d, 1 H, J = 6.6 Hz, H-4), 3.91 (d, 1 H, J = 0.5 Hz, H-1), 1.80 (dd, 1 H, J = 12.8, 6.6 Hz, H-3$_{exo}$), 1.72 (s, 1 H, OH), 1.47 (d, 3 H, J = 0.5 Hz), 1.45 (s, 3 H), 1.31 (d, 3 H, J = 0.5 Hz), 1.30 (d, 1 H, J = 12.8 Hz, H-3$_{endo}$); ^{13}C NMR δ 110.4, 85.0, 81.1, 80.0, 77.9, 74.8, 40.2, 28.9, 25.3, 24.4. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.79; H, 8.13.

2-*endo*-Methyl-7-oxabicyclo[2.2.1]heptan-2-*exo*-ol (24). From the hydrogenation (Pd/C) of 410 mg (3.25 mmol) of a mixture of **3** and **4** (1:6 ratio) was obtained 328 mg of **24** (79%) as a light yellow oil after chromatography (hexane–ethyl acetate, 1:1, R_f 0.24): IR (neat) 3420, 3000–2860, 1478, 1440, 1355, 1180, 1085, 930, 880 cm^{-1}; ^{1}H NMR δ 4.66–4.43 (m, 1 H, H-4), 4.23–4.06 (m, 1 H, H-1), 3.03 (s, 1 H, OH), 2.06–1.47 (m, 6 H), 1.32 (s, 3 H); ^{13}C NMR δ 85.8, 78.7, 76.6, 49.1, 29.1, 23.5, 21.9. Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.55; H, 9.50.

Reaction of Bicyclo[2.2.1]hept-5-en-2-one (26) with MeLi–Me_2CuLi and Me_2CuLi. From 216 mg (2 mmol) of **26**[31] and MeLi–Me_2CuLi was isolated 259 mg (60%) of aldol dimer **27** as a yellowish solid (mp 102–105 °C) after chromatography (hexane–ethyl acetate, 5:1, R_f 0.36). Identical results were obtained with Me_2CuLi (52%): IR (KBr) 3440, 3070, 3020–2880, 1735, 1450, 1255, 1100, 725 cm^{-1}; ^{1}H NMR δ 6.56 (dd, 1 H, J = 6.0, 3.0 Hz), 6.36 (dd, 1 H, J = 6.0, 3.0 Hz), 6.26–5.90 (m, 2 H), 3.66 (m, 1 H), 3.16 (m, 1 H), 3.03–2.26 (m, 3 H), 2.26–0.93 (m, 7 H); ^{13}C NMR δ 215.3, 145.0, 144.9, 140.6, 140.5, 133.3, 133.0, 132.8, 132.3, 82.2, 55.9, 55.6, 51.8, 51.4, 51.0, 50.4, 48.6, 47.5, 44.2, 43.8, 43.5, 42.9, 42.5; mass spectrum, m/e 216 (M), 85 (base). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.74; H, 7.46. Found: C, 77.89; H, 7.72.

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