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Diastereoselectivity Control Elements. Acyclic Diastereocontrol in Formation and Reactions of γ-Hydroxysulfones

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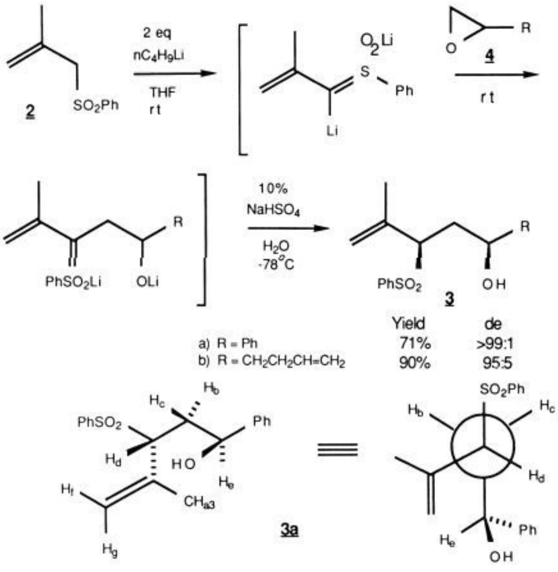
Acyclic diastereocontrol is a key problem in constructing many complex natural products.[1] Our interest in devising methods to substitute sulfones by carbon nucleophiles[2-5] focussed our studies on stereocontrolled alkylations of the anions derived from allyl sulfones.[6] By using an electrophile that possesses a stereogenic or prostereogenic (in the case of carbonyl additions) center, diastereomeric products may result. If one diastereomer such as **1** (R* is a fragment possessing at least one stereogenic center) can be induced to dominate, the possibility to effect substitution of the sulfone either with retention or inversion of configuration or with direct substitution or allyl inversion, as shown in eq 1, would represent a versatile tool for acyclic construction. We wish to report that alkylation of sulfones with epoxides leads to unexpected control of stereochemistry under kinetic or thermodynamic conditions.

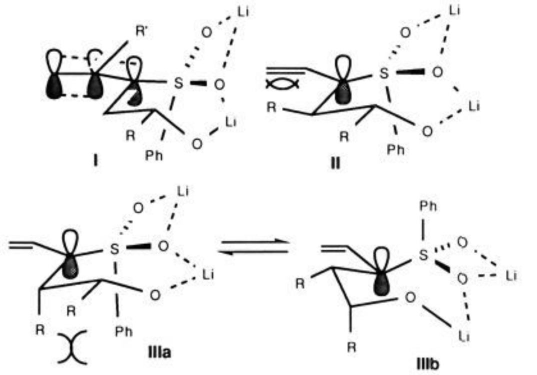
Alkylation of the dianion[7] of methallylphenyl sulfone (**2**) with styrene epoxide leads to a single (>99:1) γ-hydroxysulfone (**3a**).[8] NMR data including NOE difference experiments, detailed in the Supplementary Material, lead us to assign the diastereomer as depicted. Use of 1,5-hexadiene monoepoxide gave similar results (eq 2). The fact that base equilibration of **3b**[8] produces a 76:24 diastereomeric mixture establishes the kinetic nature of the high diastereoselectivity.



The structural requirements for this kinetic selectivity are (1) utilization of a terminal epoxide and (2) branching on the vinyl carbon proximal to sulfone. For example, the sulfone **5** shows excellent kinetic selectivity in the production of γ-hydroxysulfone **6**[8] (97:3) which increases to >99:1 after isolation (eq 3). On the other hand, crotyl sulfone **7** shows a diminished kinetic selectivity in the formation of sulfone **8**[8] (eq 4, 75:25 which increases to 85:15 after isolation).

The reaction of the dianion derived from sulfone **2** with cyclohexene epoxide shows a reduced diastereoselectivity under kinetic conditions (eq 5). Surprisingly, base equilibration (0.1 equiv NaH in THF, room temperature) in this case enhanced that ratio substantially. This thermodynamic control of diastereoselectivity proved to be general for reactions using cis-1,2-disubstituted epoxides with exceptionally high (>99:1) diastereoselectivity for the nonbranched allyl sulfones like crotyl (eq 6). The reaction with *trans*-2,3-butene epoxide showed good kinetic selectivity (eq 6b).

For **11a,c** and **12a,c**, the structural assignments are based upon NMR spectroscopic data (summarized in detail in the Supplementary Material) and molecular mechanics calculations. In addition to such data, in the case of **12b**, X-ray crystallography establishes its stereochemistry and conformation as depicted in the figure.



The kinetic stereoselectivity arises in the protonation of the dianion during quenching. With use of the X-ray structural data[10] and theoretical models[11] for sulfone stabilized anions, the lithium salt of structure I, with the allylic carbon somewhat pyramidalized[10a] toward the sulfone oxygen atoms, would be a reasonable representation for the dianion generated in alkylations with monosubstituted epoxides. The predicted topside protonation for I does produce the observed product. The role of the substituent at the center of the allyl unit to lock the conformation of the phenylsulfonyl portion and, consequently, the remainder of the chain is now apparent. The greater conformational flexibility that exists when R′ = H diminishes the kinetic diastereoselectivity. With cis disubstituted epoxides, the $A_{1,3}$-type interaction[12] in the

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(1) For reviews, see: Braun, M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 24. Heathcock, C. H. *Asymmetric Synth.* **1984**, *3*, 199. Evans, D. A.; Nelson, J. V.; Taber, T. R. *Topics in Stereochem.* **1982**, *13*, 1.

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(5) For copper-mediated reactions, see: Julia, M.; Righini, A.; Verpeaux, J. N. *Tetrahedron* **1983**, *39*, 3283, 3289. Masaki, Y.; Sakuma, K.; Kaji, K. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1171.

(6) Trost, B. M.; Schmuff, N. R. *J. Am. Chem. Soc.* **1985**, *107*, 396.

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(8) All new compounds have been fully characterized spectroscopically. Elemental composition has been established by combustion analysis and/or high resolution mass spectroscopy.

(9) The numbers in parentheses correspond to the ratios for the purified product.

(10) (a) Gais, H.-J.; Vollhardt, J.; Lindnar, H. J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 939. (b) Also, see: Boche, G.; Marsch, M.; Harms, K.; Sheldrick, G. M. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 573. Gais, H.-J.; Lindner, H. J.; Vollhardt, J. *Angew. Chem. Int. Ed. Engl.* **985**, *24*, 859. Grossert, J. S.; Hoyle, J.; Cameron, T. S.; Roe, S. P.; Vincent, B. R. *Can. J. Chem.* **1987**, *65*, 1407.

(11) Bors, D. A.; Streitwieser, A. *J. Am. Chem. Soc.* **1986**, *108*, 1397. Wolfe, S.; Stolow, A.; LaJohn, L. A. *Can. J. Chem.* **1984**, *62*, 1470.

(12) Johnson, F.; Malhotra, S. K. *J. Am. Chem. Soc.* **1965**, *87*, 5492. Malhotra, S. K.; Johnson, F. *J. Am. Chem. Soc.* **1965**, *87*, 5493.

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Scheme I

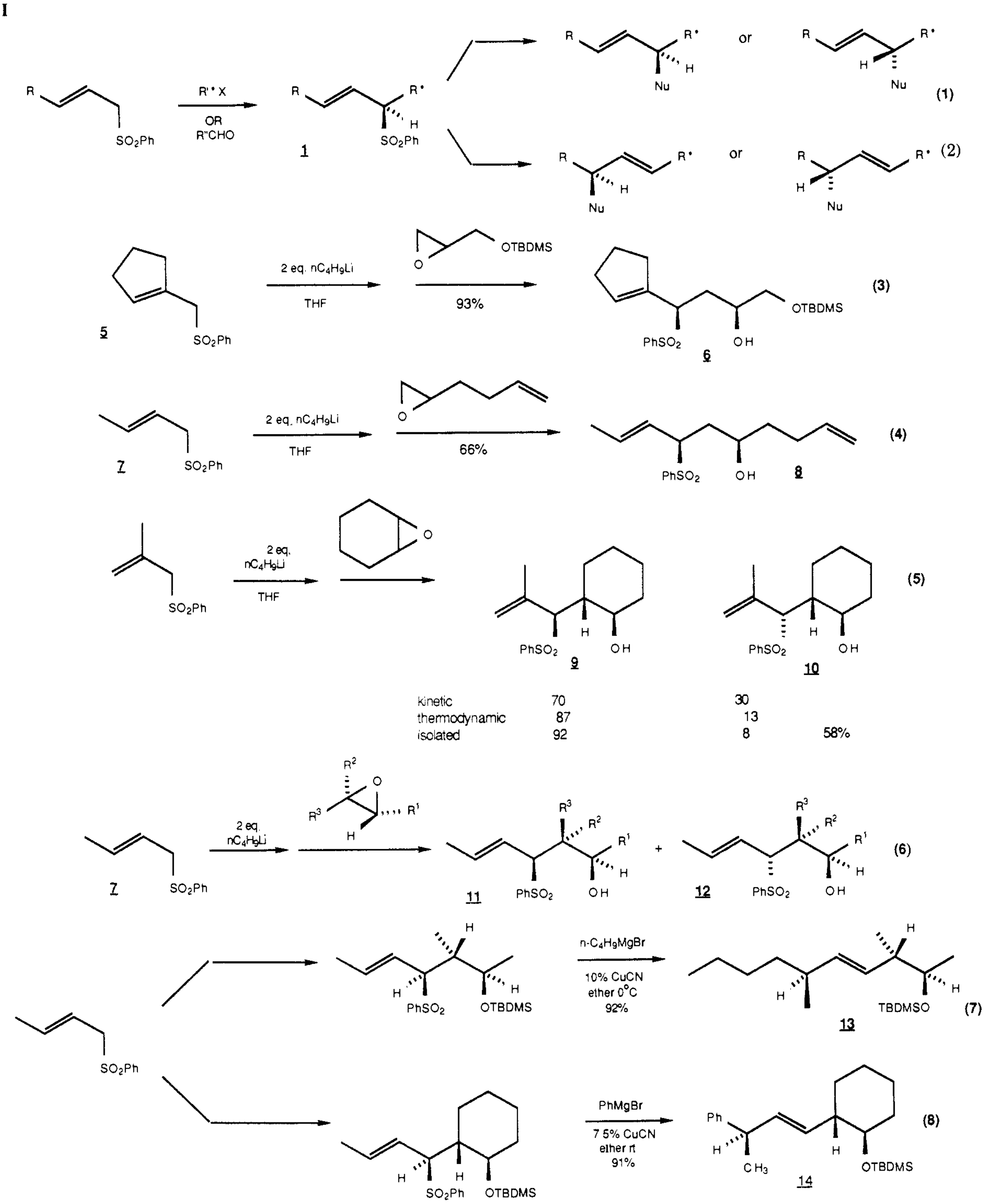

Table I

			diastereomeric ratios **11**:**12**			isolated yield
	R^1	R^2	R^3	kinetic	thermodynamic	isolated	(%)
(a)	CH$_3$	CH$_3$	H	60:40	96:4	>99:>1	71
(b)	CH$_3$	H	CH$_3$	6:94		1:99	62
(c)	(CH$_2$)$_4$		H	60:40	95:5	99:1	86

dianion III generated in their alkylations compares to the unfavorability of having both R groups in axial-like orientations in the conformational flip corresponding to II. Thus, poor kinetic stereoselectivity is observed here too. In this case, thermodynamic equilibration rectifies this deficiency and restores the diastereoselectivity to >95:5. On the other hand, the dianion generated from the trans 1,2-disubstituted epoxide III would be expected to favor IIIb. The predicted protonation from the bottom face of IIIb does generate the observed diastereomeric product, in this case with good diastereoselectivity.

The remarkable ability to obtain γ-hydroxy sulfones with high diastereoselectivity under either kinetic or thermodynamic control offers the flexibility to transfer the stereocontrol to carbon–carbon bond formation by substitution of the sulfone. To illustrate this point, the copper cyanide catalyzed couplings of Grignard reagents depicted in eq 7 and 8 were performed.[13,14] In each case, ^{1}H and

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(13) For copper cyanide in catalytic and stoichiometric allyl couplings, see: Levisalles, J.; Rudler-Chauvin, M.; Rudler, H. *J. Organomet. Chem.* **1977**, *136*, 103. Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1979**, 675. Marino, J. P.; Hatakana, N. *Tetrahedron Lett.* **1979**, 4467. Trost, B. M.; Klun, T. P. *J. Org. Chem.* **1980**, *45*, 4256. Goering, H. L.; Tseng, C. C. *J. Org. Chem.* **1983**, *48*, 3986 Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1984**, *49*, 422.

^{13}C NMR spectroscopic analysis of the products **13** and **14** showed them to be single regio- and stereoisomers. The stereochemistry is assigned based upon analogy to cuprate substitutions of allylic carboxylates.[13] The sequence of diastereocontrolled formation of the γ-hydroxysulfones[15] followed by diastereocontrolled substitution of sulfone illustrates the use of the phenylsulfonyl group as a diastereochemical control element in the alkylation step and as a diastereochemical relay element in the substitution step. In this process, 1,3- and 1,2,3-stereochemistry is first controlled and ultimately transferred into 1,5- or 1,2,5-stereochemistry. The use of epoxides, which are available in highly enantiomerically pure form from achiral allylic alcohols,[16] as the electrophilic partner that gives rise to high diastereocontrol translates this sequence into both an enantio- as well as diastereocontrolled construction of acyclic units.

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Supplementary Material Available: Spectroscopic and analytical data for **3a**, **3b**, **6**, **8**, **9**, **11a**, **11c**, **12b**, **12c**, **13**, and **14** and X-ray data for **12b**; general procedure for alkylation of sulfone dianions and procedure for equilibration illustrated by preparation of **12a** (11 pages). Ordering information is given on any current masthead page.

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(14) Cf. ref 5. To our knowledge, these are the first examples of demonstrating the stereochemistry of copper-mediated substitution of allylic sulfones. The high regioselectivity of these examples contrasts with the earlier results.

(15) For diastereoselectivity in conjugate additions that produce γ-hydroxysulfones, see: Auvray, P.; Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1985**, *26*, 2329.

(16) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

A Folded Metallacyclopentatriene and a Bicapped-Tetrahedral M_2C_4 Cluster Obtained from Coupling of Alkyne Ligands. Structures of $CpMoCl(C_4Ph_4)$ and $(CpMoCl)_2(\mu,\eta^4\text{-}C_4Ar_4)$ (Ar = *p*-Tolyl)

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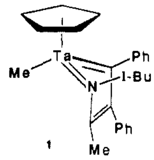
We recently reported[1] the synthesis and structure of **1**, a derivative of a new class of metallacycles, the metallacyclopenta*trienes*. Our EHMO calculations[1,2] suggested that $CpXMC_4R_4$ metallacycles should exhibit the *folded* metallacyclopentatriene structure I for metals with a d^2 electron configuration, whereas a planar metallacyclopentatriene structure II would be the ground-state structure for metals with a d^4 or higher electron configuration and that $CpX_2M(C_4R_4)$ metallacycles would adopt a "normal" metallacyclopentadiene structure III regardless of electron count. (Note, the electron counts are obtained by assigning a -2 charge to the C_4R_4 ligand.)



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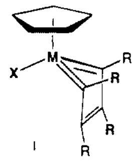

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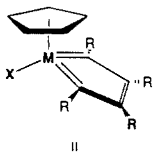

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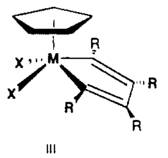


III

Support for these conclusions is afforded by the recent characterizations by Singleton et al.[3] of **2** and **3** which are examples of structure types II and III, respectively. Here, we report the synthesis of the first example of structure I and a novel M_2C_4 cluster.

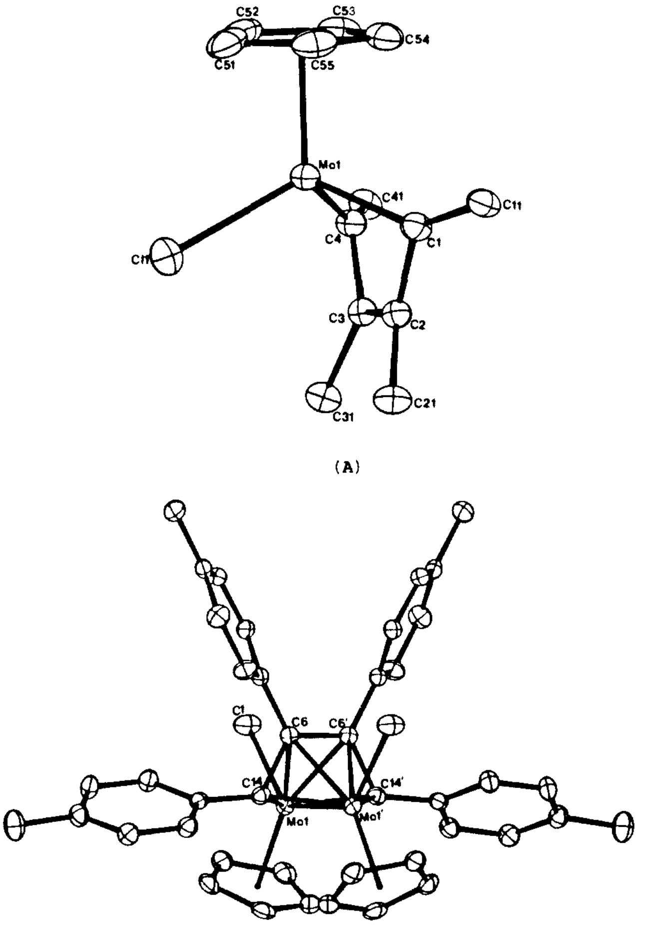
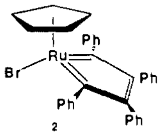
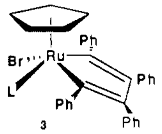


Figure 1. (a) ORTEP plot (50% thermal ellipsoids) for $CpMoCl(C_4Ph_4)$ (only ipso carbons of phenyl rings shown). (b) ORTEP plot (50% thermal ellipsoids) of $(CpMoCl)_2(\mu,\eta^4\text{-}C_4Ar_4)$ (Ar = *p*-tolyl).

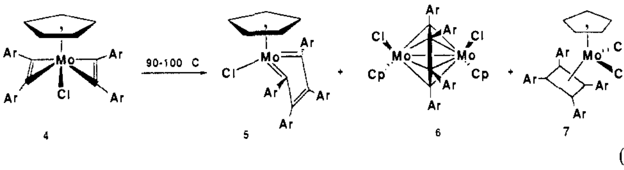


2



3

Heating a toluene solution of **4** (Ar = phenyl or *p*-tolyl) to 90–100 °C for 18 h produces a mixture of compounds **5**, **6**, and **7** (eq 1). Compound **5** may be isolated by fractional crystallization of the solids obtained by removal of the toluene solvent, while **6** and **7** are readily purified by chromatography over SiO_2 with CH_2Cl_2 eluant.[5] Compound **5** is produced preferentially



(1)

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(2) Curtis, M. D., to be submitted for publication.

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(4) Davidson, J. L.; Green, M.; Stone, F. G. A.; Welch, A. J. *J. Chem. Soc., Dalton Trans.* **1976**, 738.

(5) $CpMoCl(C_4Ph_4)$ (**5**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3–7.0 (m, 20 H), 5.71 (s, 5 H); m/z = 554. $Cp_2Mo_2Cl_2$ (C_4Ph_4) (**6**): ^{1}H NMR (300 MHz, acetone-d_6) δ 7.5–6.6 (m, 20 H), 5.49 (s, 10 H); $Cp(\eta^4C_4Ph_4)MoCl_2$ paramagnetic, g = 2.005, A_{Mo} = 36 G. All new compounds give satisfactory elemental analyses.

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