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SN2' ADDITIONS OF CUPRATES TO SULFONE AND ESTER-POLARIZED CYCLOPENTENYLIC SYSTEMS[1]

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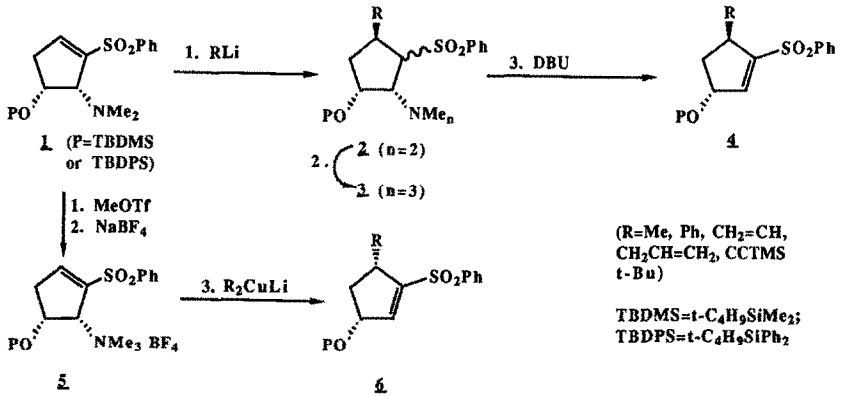
ABSTRACT: The stereochemistry of SN2' addition of cuprates to sulfone and ester-polarized cyclopentenyl systems is shown to depend upon the nature of the leaving group. Allyl ammonium salts usually undergo stereospecific synfacial addition reactions.

In connection with our synthetic program we required an experimental protocol for the conversion of chiral amino vinyl sulfones 1 to cis-substituted vinyl sulfones 6. Our initial finding was that simple organolithium reagents undergo addition to vinyl sulfone 1 with exclusive trans stereochemistry, affording amino sulfones 2 in high yield. Quaternization (to 3) and elimination with DBU provided the trans vinyl sulfones 4 in excellent overall yield. Alternatively, quaternization of the amine moiety of 1 provides ammonium salt 5 which undergoes direct SN2' coupling with cuprate reagents to regio- and stereospecificially produce cis-substituted vinyl sulfones 6.[2]



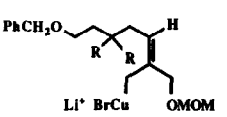
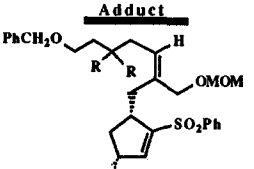
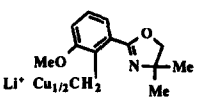
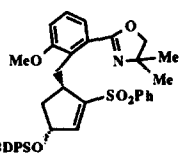
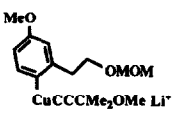
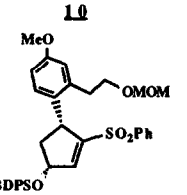
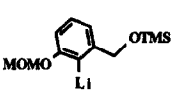
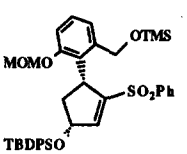
Cuprate reactions with allyl ammonium salt 5 appear highly tolerant of the structure of the reagent.[2-7] Table 1 shows a series of functionalized reagents that have been reacted with 5, resulting in clean conversion to cis-adducts. Several observations were made which seem worthy of comment. Of the reactions listed in Table 1, the most experimentally demanding were those of trisubstituted bromocuprates 7a,b. Since the detailed structure of the parent diallyl cuprate reagent is a matter of some contention[8] and since halocuprates have only seen occasional usage,[9] it seems premature to speculate about the source of the striking α-regiospecificity seen in this reaction.

On a more practical note, we found that copper bromide-dimethyl sulfide which had been stored for any period of time resulted in THF solutions with a distinct yellow or orange color. Reactions which used this material (with or without added LiBr[3,9] or additional sulfide ligands) uniformly gave poorer results than those which use freshly recrystallized reagent (colorless solution).[10] An expedient solution to this problem involved treating the "suspect" copper bromide-dimethyl sulfide, either as a standard solution in THF

or diisopropyl sulfide[11] or directly in the reaction medium,[4] with copper wire. This technique rapidly produces a colorless solution, presumably due to reduction of any copper [II] which might be present, and facilitates reactions of equal quality to those from recently recrystallized reagent.

A final comment about Table 1 relates to aryl lithium reagent 13. In the synthesis of 14 recourse was not made to use of a cuprate reagent since the (presumably chelated) reagent 13 was sufficiently non-basic so as to undergo SN2' addition to allyl ammonium salt 5 without any of the side reactions which normally accompany attempted substitution reactions with more basic reagents.

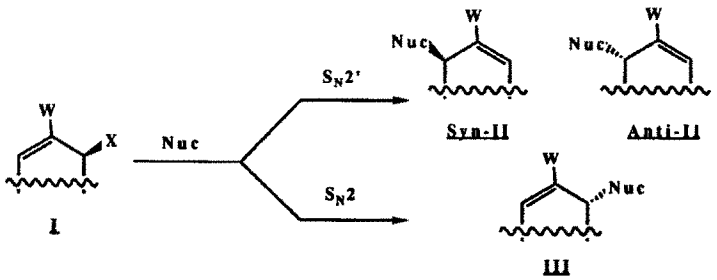
TABLE 1: Reaction of more complex nucleophiles with ammonium salt 5.

Nucleophile	Adduct	Yield	Ref.
			
7a (R=H) 7h (R=Me)	8a (R=H) 8h (R=Me)	75% 79%	3 4
			
9	10	92%	5
			
11	12	79%	6
			
13	14	90%	7

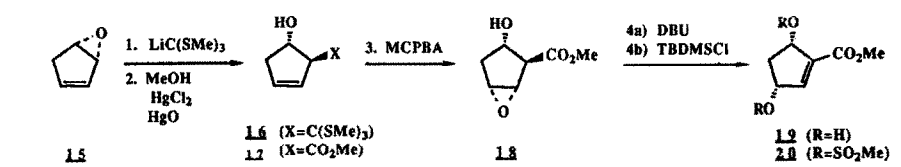
These successful reactions raised several mechanistic questions within the context of the long-established debate regarding the factors favoring SN2 or SN2' pathways in substituted allyl systems.[12] As can readily be seen, the present system has two rather special factors which are readily identifiable: The first of these is the presence of the sulfone moiety at the ß-position of the allyl system. Allyl groups bearing an electron-withdrawing group at this position are disposed toward conjugate-addition at the gamma-position and clearly represent systems especially biased toward SN2' reactivity. Demonstration of this predictable SN2' reactivity was pioneered by Lawton[13] and numerous subsequent authors have used this strategy to great success.[14] The choice of withdrawing groups can be quite wide-ranging,[14] and has included several examples of both cyclic[15] and acyclic[16] vinyl sulfones serving as substrates. A second unique feature in substrate 5 was use of an allyl ammonium salt. Several examples of coupling reactions with acyclic allyl and dienyl

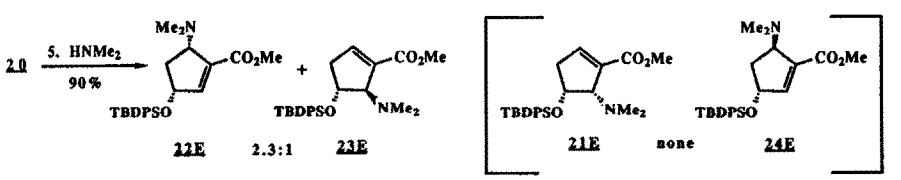
ammonium salts show strong preference for the SN2 transition state,[17] although one of the original Lawton papers also employed a symmetrical allyl ammonium salt that presumably underwent nucleophilic reaction via the SN2' pathway.[13c]

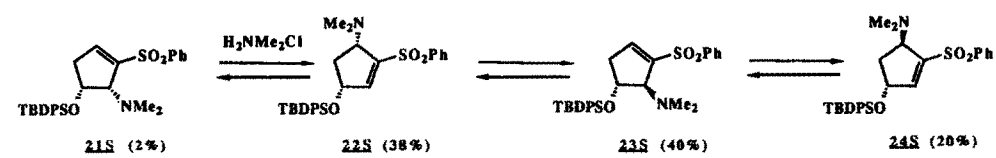
The two factors cited above must be put in context of cuprate coupling in cyclic allylic systems. It has been observed that leaving-group effects are especially important in five and six-membered ring allyl systems; while allylic carboxylates generally react via anti SN2' coupling reactions,[18] allylic urethanes undergo a directed syn SN2' reaction.[19]



Based upon our success with 5, we became interested in exploring the generality of the SN2' reaction with an ester-polarized allyl system. Synthesis of these substrates was based upon methodology established in the vinyl sulfone series.[15] Treatment of cyclopentadiene monoepoxide 15 with lithium tristhiomethyl methide[20] affords trithioorthoester 16 which is hydrolyzed to ester 17 using methanol and mercury [II].[20] Directed epoxidation of 17 gives 18 which upon treatment with DBU and subsequent silylation of the intermediate diol affords vinyl ester 19. Reaction of 19 with methanesulfonyl chloride and triethylamine[21] smoothly generates mesylate 20. Reaction of 20 with dimethylamine in methylene chloride affords a 2.3:1 mixture of easily separable vinyl esters 22E and 23E in 90% yield. We presume this reaction occurs via the intermediacy of adduct 21E, followed by rapid equilibration to the observed mixture, since individual treatment of either isomer with dimethylamine hydrochloride results in reestablishing the 2.3:1 mixture. This mixture is reminiscent of the mixture that is observed upon equilibration of vinyl sulfone 21S.[22]





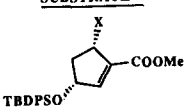
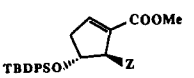
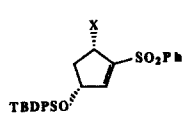
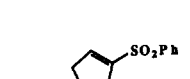
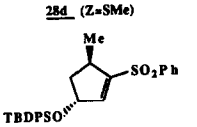


A series of cis-1,4-disubstituted cyclopentene derivatives have been examined with respect to the stereochemistry of their coupling reactions with cuprates and other nucleophiles (see Table 2). The initial substrate employed for this purpose was vinyl ester 20. All reactions afforded products (25a-d) via the anti SN2' transition state. Encouraged by our previous successes with the sulfone-substituted allyl ammonium salt 5, we next examined reaction of allyl ammonium salt 26E with both dimethyl cuprate and methanethiol. The exclusive products again were 25a,25d, respectively bearing the trans 1,2 relationship.

The stereochemical assignment of all substrates and adducts described in this study follows from well-established NMR precedent.[22-24] Specific chemical shift and coupling information is tabulated in the experimental section (Tables 4-9).

Surprised by the absence of the anticipated synfacial addition for the above ammonium salt reactions, we examined the isomeric sulfone-bearing series. Mesylate 27 undergoes anti SN2' displacement with dimethyl cuprate and methanethiol to afford 28a,b, in perfect agreement with the reactions seen with vinyl ester 20. Similarly, dimethylsulfonium salt 29 also affords 28a when reacted with dimethyl cuprate. In an effort to utilize a urethane-directed coupling,[19] compound 30 was treated with dimethyl cuprate. This substrate was quite unreactive at low temperature. More forcing conditions (Table 2) served to largely consume 30, but no addition products were isolated. Taken together, these results suggest that the incoming nucleophiles cannot attain the proper synfacial SN2' trajectory, presumably due to eclipsing interactions with the bulky silyloxy moiety. A final substrate, ammonium salt 31 was also exposed to dimethyl cuprate resulting in product 32, the formal result of direct SN2 coupling. This reaction is especially surprising when contrasted to the cuprate reactions of 26E,29, both of which react via the anti SN2' route.

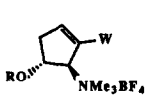
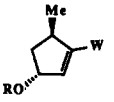
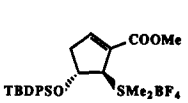
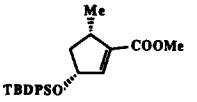
TABLE 2. SN2' Addition to cis-1,4 Disubstituted Cyclopentenes

SUBSTRATE	NUCLEOPHILE	CONDITIONS	ADDUCT	YIELD
				
20 (X=OSO$_2$Me)	Me$_2$CuLi (2 eq.)	0.04M, -78°C, 30min	25a (Z=Me)	77%
20 (X=OSO$_2$Me)	Bu$_2$CuLi (2 eq.)	0.01M, -78°C, 30min	25b (Z=n-Bu)	65%
20 (X-OSO$_2$Me)	[Me$_2$NN=(CH$_3$)CCH$_2$]$_2$CuLi (2eq.)	0.05M, -78°C, 1h	25c (Z=CH$_2$C(CH$_3$)=NNMe$_2$)	47%
20 (X=OSO$_2$Me)	MeSH/Et$_3$N	0.03M, 25°C, 15min	25d (Z=SMe)	76%
26E (X=NMe$_3$BF$_4$)	Me$_2$CuLi (2eq.)	0.01M, -78°C, 20min	25a (Z=Me)	54%
26E (X=NMe$_3$BF$_4$)	MeSH/Et$_3$N	0.01M, 25°C, 20min	25d (Z=SMe)	91%
				
27 (X=OSO$_2$Me)	Me$_2$CuLi (4eq.)	0.025M, -78°C, 3h	28a (Z=Me)	77%
27 (X=OSO$_2$Me)	MeSH/Et$_3$N	0.035M, 25°C 30min	28d (Z=SMe)	73%
29 (X=SMe$_2$BF$_4$)	Me$_2$CuLi (2eq.)	0.03M, -78°C, 1h	28a (Z=Me)	59%
30 (X=OCONHPh)	Me$_2$CuLi (4eq.)	0.05M, -78°C-0°C, 4h	-	recov. 30% 30
31 (X=NMe$_3$BF$_4$)	MeSH/Et$_3$N	0.03M, 25°C, 30min	28d (Z=SMe)	52%
				
31 (X=NMe$_3$BF$_4$)	Me$_2$CuLi (2eq.)	0.06M, -78°C, 10 min	32	50%

While it is premature to indulge in extended speculation vis-a-vis the factors responsible for production of 32, it has been found that 31 reacts with methanethiol to afford 28d, the "normal" SN2' product seen with all other cis-1,4-disubstituted derivatives in Table 2. A further point worth noting is that competition studies have shown that 31 is at least a factor of 100 times less reactive with lithium dimethyl cuprate than are isomeric ammonium salts 5 and 35.[23]

A final series of compounds which were examined in cuprate coupling reactions were the trans-disubstituted cyclopentene derivatives listed in Table 3. As with allyl ammonium salt 5, the allyl ammonium salts 33,35 both undergo rapid synfacial SN2' addition with dimethylcuprate to produce adducts 34,32, respectively. In contrast, allyl sulfonium salt 36 reacts with dimethyl cuprate to only yield the anti SN2' product 37; again demonstrating the dramatic difference between allyl ammonium and sulfonium salts in directing these SN2' reactions.

TABLE 3. SN2' Addition to trans-1,4 Disubstituted Cyclopentenes

SUBSTRATE	NUCLEOPHILE	CONDITIONS	ADDUCT	YIELD
				
33 (R=TBDPS, W=CO_2Me)	Me_2CuLi	0.02M, -78°C, 30min	34 (R=TBDPS, W=CO_2Me)	60%
35 (R=TBDMS, W=SO_2Ph)	Me_2CuLi	0.05M, -78°C, 10min	32 (R=TBDMS, W=SO_2Ph)	92%
				
36	Me_2CuLi	0.02M, -78°C	37	80%

ACKNOWLEDGEMENT: We wish to thank the NIH (GM 32693-05) for support of this research. Access to high-field NMR was provided through the Purdue University Bioloogical Magnetic Resonance Laboratory (NIH RR01077). Mr. Mark Anderson and Mr. David Scarpetti provided spectral assistance. Mass spectral services were provided by Ms. Arlene Rothwell.

EXPERIMENTAL

General Procedures. All reactions were performed under a positive pressure of nitrogen or argon (in flamed-dried flasks for organometallic reactions). Analytical TLC was performed on silica gel 60 F-254 plates. THF and ether were purified by distillation from benzophenone-sodium ketyl under nitrogen in a standing still. All recrystallization, chromatographic and workup solvents were distilled prior to use. Proton NMR spectra were recorded on Perkin-Elmer R-32 (90 MHz), General Electric QE-300 (300 MHz) or Nicolet NT 470 (470 MHz) instruments. Proton chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane as an internal reference (0.0 ppm). All NMR spectra (Tables 4-9) were recorded in $CDCl_3$ solution unless otherwise noted. Infrared spectra were recorded on a Perkin-Elmer 1420 spectrophotomer as $CHCl_3$ solutions, unless otherwise noted, and are reported in micrometers. Melting points were determined on a Meltemp apparatus and are uncorrected.

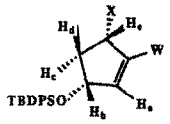


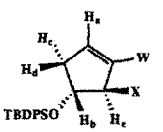
TABLE 4. ^{1}H NMR Chemical Shifts of cis-1,4-Disubstituted Cyclopentenes

COMPOUND	W	X	H_a	H_b	H_c	H_d	H_e
19	COOMe	OH	6.67	4.66	1.86	2.52	4.72
20	COOMe	OMs	6.89	3.79	2.08	2.96	5.55
22E	COOMe	NMe_2	6.52	4.68	1.88	2.10	4.01
26E	COOMe	NMe_3BF_4	6.82	4.74	2.16	2.97	4.74
27	SO_2Ph	OMs	6.90	4.80	2.97	3.05	5.60
29	SO_2Ph	SMe_2BF_4	6.58	4.84	2.23	2.90	4.80
30	SO_2Ph	OCONHPh	6.87	4.70	1.95	2.80	5.65
31	SO_2Ph	NMe_3BF_4	5.91	4.96	2.11	2.75	4.66

TABLE 5. Coupling Constants of cis-1,4-Disubstituted Cyclopentenes

COMPOUND	W	X	J_{ab}	J_{bc}	J_{bd}	J_{cd}	J_{ce}	J_{de}
19	COOMe	OH	~1	3.8	7.5	11.3	3.8	7.5
20	COOMe	OMs	2.1	4.3	7.4	14.6	4.1	7.3
22E	COOMe	NMe_2	1.5	3.7	7.5	15.0	3.0	7.5
26E	COOMe	NMe_3BF_4	~1	2.1	7.5	15.7	2.1	7.5
27	SO_2Ph	OMs	1.8	2.0	5.3	15.4	2.0	5.3
29	SO_2Ph	SMe_2BF_4	1.5	2.8	6.8	15.4	2.8	6.8
30	SO_2Ph	OCONHPh	2.2	2.6	7.5	14.9	3.0	6.0
31	SO_2Ph	NMe_3BF_4	<1	2.5	8.4	16.1	2.1	7.5

TABLE 6. ^{1}H NMR Chemical Shifts of cis-1,2-Disubstituted Cyclopentenes

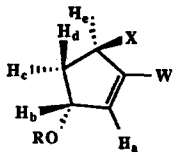


COMPOUND	W	X	H_a	H_b	H_c	H_d	H_e
23S	SO_2Ph	NMe_2	6.82	4.50	2.37	2.71	3.92
23E	COOMe	NMe_2	6.68	4.38	2.10	2.38	3.88
25a	COOMe	Me	6.70	4.10	2.45	2.65	2.96
25d	COOMe	SMe	6.80	4.44	2.47	2.74	3.76
28a	SO_2Ph	Me	6.74	4.06	2.46	2.53	2.60
28b	SO_2Ph	SMe	6.96	4.40	2.53	2.73	3.54
33	COOMe	NMe_3BF_4	7.23	4.71	2.76	3.08	4.20
35	SO_2Ph	NMe_3BF4	6.94	5.04	2.39	3.24	4.25
36	COOMe	SMe_2BF_4	7.27	4.79	2.82	3.16	4.04

TABLE 7. Coupling Constants of cis-1,2-Disubstituted Cyclopentenes

COMPOUND	W	X	J_{ac}	J_{ad}	J_{bc}	J_{bd}	J_{be}	J_{cd}
23S	SO_2Ph	NMe_2	2.1	2.1	2.1	6.3	2.0	18.8
23E	COOMe	NMe_2	4.5	3.0	1.5	6.0	1.5	18.6
25a	COOMe	Me	2.0	3.0	3.1	7.4	2.2	18.6
25d	COOMe	SMe	3.7	4.5	3.0	7.5	2.2	18.6
28a	SO_2Ph	Me	4.8	2.7	2.6	7.5	1.6	18.9
28b	SO_2Ph	SMe	2.7	3.0	3.0	7.1	~1	18.8
33	COOMe	NMe_3BF_4	1.6	<1	2.4	6.4	<1	19.2
35	SO_2Ph	NMe_3BF_4	3.6	<1	<1	4.6	<1	20.3
36	COOMe	SMe_2BF_4	1.5	<1	~1	3.8	<1	19.5

TABLE 8. ^{1}H NMR Chemical Shifts of trans-1,4-Disubstituted Cyclopentenes



COMPOUND	R	W	X	H_a	H_b	H_c	H_d	H_e
24S	TBDPS	SO_2Ph	NMe_2	6.83	4.38	2.32	2.67	3.77
32	TBDMS	SO_2Ph	Me	6.57	5.02	1.03	2.02	2.99
34	TBDPS	COOMe	Me	6.53	5.05	1.83	2.17	3.15

TABLE 9. Coupling Constants of trans-1,4-Disubstituted Cyclopentenes

COMPOUND	R	W	X	J_{ab}	J_{bc}	J_{bd}	J_{cd}	J_{ce}	J_{de}
24S	TBDPS	SO_2Ph	NMe_2	~1	5.6	7.5	14.1	8.4	1.5
32	TBDMS	SO_2Ph	Me	0	5.2	7.0	13.3	8.3	3.1
34	TBDPS	COOMe	Me	3.0	1.5	7.5	11.2	7.3	2.0

trans-2-Tris(methylthio)methyl-cyclopent-3-en-1-ol 16: To a solution of tris-(methylthio)methane (14.6mL, 0.11mmol) in THF (300mL) at -60°C was added dropwise a solution of n-BuLi [72mL, (1.53M in hexane) 0.11mol]. The reaction temperature was maintained below -40°C at all times. After stirring for 40 min, a solution of epoxide 15 (10.0g, 0.12mol) in THF (10mL) was added slowly. Upon complete addition, the reaction mixture was allowed to warm to 0°C whereupon it was quenched by pouring into water. The aqueous layer was extracted with CH_2Cl_2 (200mLx3) and the combined organic extract was washed with brine and dried. Removal of the solvent afforded the crude alcohol suitable for hydrolysis in the next step. Purification was accomplished by SiO_2 chromatography (hexane/Et_2O=1.5:1) to give 19.2g (74%) of 16 as a pale yellow oil. ^{1}HNMR ($CDCl_3$):5.86, 4.98,3.25,2.80,2.47,2.02. MS m/z EI: 189 M^+-SMe (100%).

trans-2-Carbomethoxycyclopent-3-en-1-ol 17: A solution of alcohol 16 (15.0g, 63.1mmol), $HgCl_2$ (60g, 0.22mol), and HgO (23g, 0.107mol) in a 12:1, $MeOH:H_2O$ mixture (1L) was vigorously stirred at room temperature for 48 h. After this interval, the solid precipitates were removed by filtration and the filtrate concentrated in vacuo to 200mL. The concentrate was diluted with a 1:1 mixture of Hexane: EtOAc and washed successively with water, brine, and dried. Removal of the solvent afforded the crude product which was chromatographed over 80g of 60-200 mesh silica gel eluting with 30% (v/v) Et_2O in hexane. These procedures afforded 5.2g (60%) of 17 as a semi-solid. ^{1}HNMR($CDCl_3$):5.85,4.78,3.75,2.86, 2.40. MS m/z CI: 143 (M^++H).

trans-2-Carbomethoxy-cis-2,3-epoxycyclopentan-1-ol 18: To a solution of MCPBA [3.3g, (83%) 16mmol] in 40mL CH_2Cl_2 at 0°C was added a solution of ester 17 (2.2g, 14.5mol) in CH_2Cl_2 (10mL). The reaction was monitored by TLC and upon complete disappearance of 17 (0.5h); the reaction mixture was cooled to -30°C to facilitate chlorobenzoic acid precipitation. The precipitate was removed by filtering and the filtrate was concentrated in vacuo. The residue was chromatographed over 25g of 60-200 mesh silica gel eluting with 30% (v/v) EtOAc in hexane to afford 1.51g (66%) of epoxide 18 as a single diastereomer. ^{1}HNMR ($CDCl_3$):3.70,3.65,3.34,3.12,2.14; IR(μm):2.8,3.3,5.8,6.3,7.0,9.6.

cis-3-(t-Butyldiphenylsilyloxy)-1-carbomethoxy-5-hydroxy-cyclopent-1-ene 19: To a solution of epoxide 18 (237mg, 1.5mmol) in CH_2Cl_2 (3mL) at 0°C was added DBU (228mg, 1.57mmol), followed by TBDPSCl (43mg, 1.57mmol) in CH_2Cl_2 (5mL), and stirred for 6 h. The solution was diluted with CH_2Cl_2 (30mL) and washed with saturated $NaHCO_3$ (3x30 mL) and brine (2x30 mL). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to afford 65mg of crude product as a heavy oil. This material was chromatographed over 10g of 60-200 mesh silica gel eluting with 30% (v/v) Et_2O in hexane. These procedures afforded 487mg (82%) of 19 as a semi-solid.

cis-3-(t-Butyldiphenylsilyloxy)-1-carbomethoxy-5-(methanesulfonyl)cyclopent-1-ene 20: To a solution of alcohol 19 (445mg, 1.12mmol) in THF (10mL) at -78°C was added Et_3N (0.32mL, 2.3mmol) then MsCl (141mg, 1.23mmol). The reaction mixture was stirred at -78°C for 1 h and subsequently warmed to -40°C before quenching by addition of saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3x30 mL) and the combined organic extract was washed with brine (2x30 mL). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to afford 670mg of crude product as a heavy oil which was chromatographed over 10g of 60-200 mesh silica gel eluting with 50% (v/v) Et_2O in hexane. These procedures afforded 400mg (75%) of 20 as a semi-solid.

cis-3-(t-Butyldiphenylsilyloxy)-1-carbomethoxy-5-dimethylaminocyclo-pent-1-ene 22E and trans-4-(t-Butyldiphenylsilyloxy)-2-carbomethoxy-3-dimethylamino-cyclopent-1-ene 23E: The mesylate 20 (115mg, 0.242mmol) in CH_2Cl_2 (8mL) at ambient temperature was treated with gaseous Me_2NH for 12 h. The solution was diluted with CH_2Cl_2 and washed with water (3x20 mL) followed by drying (Na_2SO_4). Concentration of organic layer *in vacuo* afforded 980mg of a mixture of products which were separated by chromatography over 15g 60-200 mesh silica gel eluting with 30% (v/v) Et_2O in hexane. These procedures afforded 642mg (63%) of 22E (R_f=0.24 Et_2O:Hexane=3:7) and 277mg (27%) of 23E (R_f=0.33) as heavy oil. 22E:IR(μm):3.2,3.4,5.8,6.1,6.3,6.9,9.0,9.8. Exact mass calcd for $C_{25}H_{33}NO_3Si$: 423.2229; found 423.2228. 23E:IR(μm):3.2,3.4,5.8,6.1,6.3,6.9,9.0,9.8. Exact mass calcd for $C_{25}H_{33}NO_3Si$: 423.2229; found 423.2229.

trans-4-(t-Butyldiphenylsilyloxy)-2-carbomethoxy-3-methylcyclopent-1-ene 25a: A slurry of copper (I) iodide (576mg, 3.02mmol) in 1.5mL Et_2O at -10°C was treated with MeLi [0.41mL (1.44M in ether), 0.589mmol] for 10 min. The solution was cooled to -78°C, followed by addition of 20 (716mg, 0.151mmol) in Et_2O (2mL) and at -78°C for 30 min. The mixture was added to 25mL 1:1 NH_3-NH_4Cl solution followed by extraction with CH_2Cl_2 (40mL). Drying (Na_2SO_4) and concentration *in vacuo* afforded 60mg of a brown oil which was chromatographed over 5g of 60-200 mesh silica gel eluting with 30% (v/v) Et_2O in hexane. These procedures afforded 46mg (77%) of 25a as a semi-solid. IR(μm):3.2,3.4,5.8,6.1,6.3,7.2,9.8. Exact mass calcd for $C_{24}H_{30}O_3Si$: 394.1964; found: 394.1960.

trans-4-(t-Butyldiphenylsilyloxy)-2-carbomethoxy-3-butylcyclopent-1-ene 25b: A slurry of copper (I) iodide (39.5mg, 0.208mmol) in 1.5mL Et_2O at -10°C was treated with BuLi [0.16mL (2.6M in hexane), 0.416mmol] for 5 min. The solution was cooled to -78°C, followed by addition of 20 (49.2mg, 0.105mmol) in Et_2O (1mL) and at -78°C for 30 min. The mixture was added to 15mL 1:1 NH_3-NH_4Cl solution followed by extraction with CH_2Cl_2 (30mL). Drying (Na_2SO_4) and concentration *in vacuo* afforded 35mg of a brown oil which was chromatographed over 4g of 60-200 mesh silica gel eluting with 10% (v/v) Et_2O in hexane. These

procedures afforded 29.3mg (65%) of 25b. IR(μm):3.2,3.4,5.8,6.1,6.3,7.3,9.8. Exact mass calcd for $C_{27}H_{36}O_3Si$: 436.2433; found: 436.2429.

trans-4-(t-Butyldiphenylsilyloxy)-2-carbomethoxy-3-(2-dimethylhydrazinopropyl)-cyclopent-1-ene 25c: A solution of acetone N,N-dimethylhydrazone (32mg, 0.318mmol) in 2mL Et_2O at -78°C was teated with t-BuLi [0.19mL (1.7M in pentane), 0.318mmol] followed warming to -10°C for 20min. The solution was then transferred to a slurry of copper (I) iodide (31mg, 0.163mmol) in 1mL Et_2O at -10°C for 20 min, followed by addition of 20 (38.7mg, 0.082mmol) in 1mL Et_2O at -78°C for 30 min. The reaction was quenched with 15mL 1:1 NH_3-NH_4Cl solution and extracted with CH_2Cl_2 (30mL). Drying (Na_2SO_4) and concentration *in vacuo* afforded 24mg of a brown oil which was chromatographed over 4g of 60-200 mesh silica gel eluting with 30% (v/v) Et_2O in hexane. These procedures afforded 18mg (47%) of 25c. IR(μm):3.3,3.4,5.5,6.1,7.0,7.2,7.7,9.3. Exact mass calcd for $C_{28}H_{38}N_2O_3Si$: 478.2651; found: 478.2658.

trans-4-(t-Butyldiphenylsilyloxy)-2-carbomethoxy-3-methylthio-cyclopent-1-ene 25d: A solution of 20 (135mg, 0.285mmol) in CH_2Cl_2 (7mL) at ambient temperature was treated with Et_3N (3mL), followed by passage of gaseous MeSH through the mixture for 15 min. The solution was diluted with CH_2Cl_2 (10mL) and washed with water (3x20 mL), followed by drying (Na_2SO_4). Concentration *in vacuo* afforded 112mg of crude product which was chromatographed over 5g of 60-200 mesh silica gel eluting with 30% (v/v) Et_2O in hexane. These procedures afforded 92mg (76%) of 25d as a semi-solid. IR(μm):3.2,3.4,5.8,6.2,6.3,6.8,7.2,7.3,7.8,9.5. Exact mass calcd for $C_{24}H_{30}O_3SSi$: 426.1685; found: 426.1685.

cis-4-(t-Butyldiphenylsilyloxy)-2-carbomethoxy-cyclopent-2-enyl trimethyl-ammonium tetrafluoroborate 26E: A solution of 22E (221mg, 0.522mmol) in CH_2Cl_2 (4mL) at ambient temperature was treated with MeOTf (130mg, 0.79mmol). The solution was stirred for 20 min, followed by addition of saturated $NaHCO_3$ (15mL), and extraction with CH_2Cl_2 (20mLx2). Concentration of organic layer *in vacuo* afforded a white foam which was dissolved in THF (5mL) and stirred with a solution of $NaBF_4$ (4g) in 12mL of water for 30 min. The solution was diluted with CH_2Cl_2 (20mL) and the aqueous layer was extracted with CH_2Cl_2 (3x20 mL). The combined organic layers were concentrated *in vacuo* to afford 246mg (90%) of 26E as a rigid white foam. IR(μm):3.2,3.4,5.8,6.1,6.4,6.6,6.8,7.3,7.7,8.1. Elemental analysis calcd for $C_{26}H_{36}BF_4NO_3Si$: C 59.45, H 6.86, N 2.67; C 59.80, H 7.12, N 2.85.

trans-4-(t-Butyldiphenylsilyloxy)-2-phenylsulfonyl-3-methylcyclopent-1-ene 28a: A slurry of copper (I) iodide (39mg, 0.205mmol) in Et_2O (1.5mL) at -10°C was treated with MeLi [0.30mL (1.4M in ether), 0.43mmol] for 10 min. The solution was cooled to -78°C, followed by addition of $27^{2,28}$ (284mg, 0.0511mmol) in Et_2O (1mL) and stirred at the same temperature for 3 h. The mixture was added to 1:1 NH_3-NH_4Cl (20mL) solution followed by extraction with CH_2Cl_2 (3x15 mL). Drying (Na_2SO_4) and concentration *in vacuo* afforded 25mg of a brown oil which was chromatographed over 2g of 60-200 mesh silica gel eluting with 30% (v/v) EtOAc in hexane. These procedures afforded 17mg (68%) of 28a as a semi-solid. IR(μm):3.2,3.4,6.2,6.8,6.9,7.3,9.0,9.8. Exact mass calcd for $C_{28}H_{32}O_3SSi$ not present; fragment $C_{24}H_{23}O_3SSi$: 419.1841; found 419.1824.

trans-4-(t-Butyldiphenylsilyloxy)-2-phenylsulfonyl-3-methylthio-cyclopent-1-ene 28d: A solution of $27^{2,28}$ (48mg, 0.086mmol) in CH_2Cl_2 (2 mL) at ambient temperature was treated with Et_3N (0.7mL), followed by passage of gaseous MeSH through the mixture for 30 min. The solution was diluted with CH_2Cl_2 (10mL) and

washed with water (3x15 mL), followed by drying (Na_2SO_4). Concentration of the organic layer *in vacuo* afforded a crude product which was chromatographed over 4g 60-200 mesh silica gel eluting with 30% (v/v) Et_2O in hexane. These procedures afforded 32mg (73%) of **28b** as a semi-solid. IR(μm):3.2,3.4,6.2,6.3, 6.8,6.9,7.2,7.3,9.0,9.8. Exact mass calcd for $C_{28}H_{32}O_3S_2Si$ not present; fragment $C_{24}H_{23}O_3S_2Si$: 451.0857; found 451.0850.

cis-4-(t-Butyldiphenylsilyloxy)-2-phenylsulfonyl-2-cyclopentenyl-1-dimethylsulfonium tetrafluoroborate **29**: A solution of **28b** (29mg, 0.0571mmol) in CH_2Cl_2 (2mL) at ambient temperature was treated with MeOTf (14mg, 0.0854mmol). The solution was stirred for 1 h, followed by addition of saturated $NaHCO_3$ (15mL), and extracted with CH_2Cl_2 (3x15 mL). Concentration of the organic layer *in vacuo* afforded a white foam which was dissolved in 3mL of THF and stirred with a solution of $NaBF_4$ (1g) in 2mL of water for 30 min. The solution was diluted with CH_2Cl_2 (20mL) and water (15mL) and the aqueous layer was extracted with CH_2Cl_2 (3x15mL). The combined organic layers were concentrated *in vacuo* to afford 34mg (97%) of **29** as a rigid white foam. IR(μm):2.8,3.2,3.4,6.3,6.4,6.8, 6.9,7.3,7.6,9.4. Elemental analysis calcd for $C_{29}H_{35}BF_4O_3S_2Si$: C 57.00, H 5.70; found C 57.00, H 5.41.

cis-4-(t-Butyldiphenylsilyloxy)-2-phenylsulfonyl-2-cyclopentyl N-phenylcarbamate **30**: A solution of *cis*-4-(t-Butyldiphenylsilyloxy)-1-hydroxyl-2-(phenylsulfonyl)-cyclopent-2-ene[2,22] (300mg, 0.627mmol) in 15mL of CH_2Cl_2 at ambient temperature was treated with PhNCO (200mg, 1.68mmol) followed by Et_3N (0.1mL). The solution was stirred for 30 min, followed by filtration through celite and washing the filter cake with hexane (10mL). The solid was chromatographed over 10g of 60-200 mesh silica gel, eluting with 10% (v/v) EtOAc in hexane. These procedures afforded 247mg (66%) of **30** as a white solid mp:125-6°C. IR(μm):3.0,3.2,3.4,5.8,6.0,6.2,6.9,7.0,7.3,7.6,9.8. MS m/z (CI): M^+ 598.

cis-4-(t-Butyldiphenylsilyloxy)-2-carbomethoxy-2-cyclopentenyltrimethylammonium-tetrafluoroborate **31**: A solution of **22S**[22] (5.0g, 9.89mmol) in CH_2Cl_2 (20mL) at ambient temperature was treated with MeOTf (2.11g, 12.85mmol) moderating the temperature with a water bath. After stirring for 30 min, more MeOTf (0.811g, 4.94mmol) was added. The solution was stirred for 30 min, followed by addition to saturated $NaHCO_3$ (30mL). The organic layer was concentrated *in vacuo*. This residue was dissolved in acetone, (100mL) and treated with a solution of $NaBF_4$ (20g) in 30mL water for 2 h. The solution was diluted with water (100mL) and extracted with CH_2Cl_2 (3x200 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo* to afford 6.0g (100%) of **31** as a rigid white solid. IR(μm):3.3,3.4,6.3,7.6,8.7,9.3.

trans-4-(t-Butyldiphenylsilyloxy)-1-methyl-2-phenylsulfonylcyclopent-2-ene **32**: A slurry of copper (I) iodide (784mg, 4.11mmol) in 4mL THF at -10°C was treated with MeLi [5.92mL (1.4M in ether), 8.22mmol]. The solution was warmed to 0°C for 15 min, followed by transfer *via* cannula to a solution of **31** (500mg, 0.823mmol) in THF (4mL) at -78°C. The orange solution was stirred at -78°C for 10 min. The mixture was added to 40mL 1:1 NH_3-NH_4Cl solution followed by extraction with CH_2Cl_2 (100mL). Drying (Na_2SO_4) and concentration *in vacuo* afforded 0.5g of a brown oil which was chromatographed over 25g of 60-200 mesh silica gel eluting with 5% (v/v) EtOAc in hexane. These procedures afforded 196mg (50%) of **32** as an oil. IR(μm):3.3,3.4,6.3,6.9,7.4,7.6,7.9,9.3.

trans-5-(t-Butyldiphenylsilyloxy)-2-carbomethoxy-cyclopent-2-enyl trimethylammonium tetrafluoroborate 33: A solution of 23E (63mg, 0.15mmol) in CH_2Cl_2 (2mL) at ambient temperature was treated with MeOTf (37mg, 0.225mmol). The solution was stirred for 1.5 h, followed by addition of saturated $NaHCO_3$ (25mL), and extraction with CH_2Cl_2 (20mL). Concentration of organic layer in vacuo afforded a white foam which was dissolved in THF (3 mL) and stirred with a solution of $NaBF_4$ (1g) in 4mL of water for 30 min. The solution was diluted with CH_2Cl_2 (20mL) and water (15mL) and the aqueous layer was extracted with CH_2Cl_2 (3x20 mL). The combined organic layers were concentrated in vacuo to afford 787mg (100%) of 33 as a rigid white solid. IR(μm):3.2,3.4,5.8,6.1,6.3, 6.8,7.0,7.4,8.1,9.8. Elemental analysis calcd for $C_{26}H_{36}BF_4NO_3Si$: C 59.45, H 6.86; N 2.67; found C 59.82, H 7.25, N 2.38.

trans-3-(t-Butyldiphenylsilyloxy)-5-methyl-1-carbomethoxycyclopent-2-ene 34: A slurry of copper (I) iodide (18mg, 0.0945mmol) in Et_2O (1.5mL) at -10°C was treated with MeLi [0.14mL (1.4M in ether), 0.196mmol] for 15 min. The solution was cooled to -78°C, followed by addition of 33 (25.7mg, 0.049mmol) in THF (1mL). After stirring at -78°C for 30 min the mixture was added to 15mL of 1:1 NH_3-NH_4Cl solution followed by extraction with CH_2Cl_2 (3x20 mL). Drying (Na_2SO_4) and concentration in vacuo afforded 18mg of a brown oil which was chromatographed over 1.5g of 60-200 mesh silica gel eluting with 30% (v/v) EtOAc in hexane. These procedures afforded 12mg (60%) of 34 as a heavy oil. IR(μm):3.2, 3.4,5.8,6.1,6.8,7.0,7.4,7.8,9.0,9.8. Exact Mass calcd for $C_{24}H_{30}O_3Si$: 384.1964; found 384.1959.

trans-5-(t-Butyldimethylsilyloxy)-2-phenylsulfonyl-cyclopent-2-enyl trimethylammonium tetrafluoroborate 35: A solution of 23S[22] (207mg, 0.542mmol) in CH_2Cl_2 (1.6mL) was treated with MeOTf (0.134g, 0.814mmol) at ambient temperature for 10 min, followed by addition of saturated $NaHCO_3$ (15mL), and extracted with CH_2Cl_2 (20mL). Concentration of the organic layer in vacuo afforded a white foam which was dissolved in THF (6mL) and stirred with a solution of $NaBF_4$ (5g) in 10mL of water (pH=1, by addition of conc. HBF_4) for 30 min. The solution was diluted with CH_2Cl_2 (20mL) and water (15mL) and the aqueous layer was extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were concentrated in vacuo to afford 245mg (94%) of 35 as a slightly hygroscopic rigid foam. IR(μm):3.3,3.4,6.3,6.8,7.6, 7.9,9.3.

trans-5-(t-Butyldiphenylsilyloxy)-2-carbomethoxy-2-cyclopentenyl dimethylsulfonium tetrafluoroborate 36: A solution of 25d (72mg, 0.169mmol) in CH_2Cl_2 (2mL) at ambient temperature was treated with MeOTf (41mg, 0.0250mmol). The solution was stirred for 1 h, followed by addition of saturated $NaHCO_3$ (20mL) and extraction with CH_2Cl_2 (20mL). Concentration of organic layer in vacuo afforded a white foam which was dissolved in THF (5mL) and stirred with a solution of $NaBF_4$ (1.5g) in 3.5mL of water for 30 min. The solution was diluted with CH_2Cl_2 (20mL) and water (15mL) and the aqueous layer was extracted with CH_2Cl_2 (3x20 mL). The combined organic layers were concentrated in vacuo to afford 84mg (94%) of 36 as a white foam. IR(μm):3.3,3.4,5.8,7.0,7.7,8.2,8.6,9.4. Elemental analysis calcd for $C_{25}H_{33}BF_4SSi$: C 56.90, H 6.25; found C 55.80, H 6.49.

cis-3-(t-Butyldiphenylsilyolxy)-5-methyl-1-carbomethoxycyclopent-2-ene 37: A slurry of copper (I) iodide (26mg, 0.137mmol) in Et_2O (1.5mL) at -10°C was treated with MeLi [0.19mL (1.4M ether), 0.265mmol] for 15 min. The solution was cooled to -78°C, followed by addition of 36 (36mg, 0.068mmol) in THF (1.5mL) and stirred at -78°C for 30 min. The mixture was added to 20mL of 1:1 NH_3-NH_4Cl

solution followed by extraction with CH_2Cl_2 (3x15 mL). Drying (Na_2SO_4) and concentration in vacuo afforded 25mg of a brown oil which was chromatographed over 2g of 60-200 mesh silica gel eluting with 30% (v/v) EtOAc in hexane. These procedures afforded 21.5mg (80%) of 37 as a heavy oil. IR(μm):3.2,3.4,5.8,6.1,6.3, 6.8,7.2,8.9,9.8. Exact mass calcd for $C_{24}H_{30}O_3SSi$: 384.1964; found: 384.1958.

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