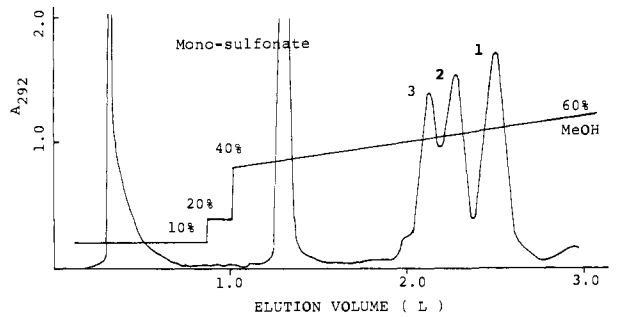
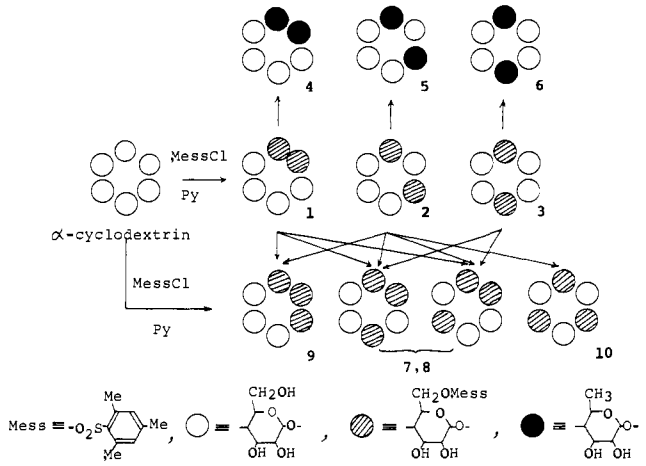


Figure 1. Reversed-phase column chromatography of the mixture obtained from the reaction of α-cyclodextrin with mesitylenesulfonyl chloride. A stepwise followed by a linear gradient elution of MeOH was applied. "Monosulfonate" represents 6-deoxy-6-[(mesitylsulfonyl)oxyl]-α-cyclodextrin.

Scheme I



as shown in Scheme I. Trimesitylenesulfonates (**7–10**) were prepared as standard compounds for the assignments; sulfonation of α-cyclodextrin (1 g) with 27 mol excess of mesitylenesulfonyl chloride (6 g)[5] gave four trimesitylenesulfonates (**7–10**) with three dimesitylenesulfonates (**1–3**) as an overlapped pattern of those shown in Figure 2.[9] Separation by use of the reversed-phase column gave pure **7** (66 mg), **8** (96 mg), and a mixture of **9** and **10**, from which pure **9** (58 mg) and **10** (4 mg) were isolated by a preparative reversed-phase HPLC.[6] All of the isolated **7–10** were assigned to be regioisomeric trimesitylenesulfonates (6A6B6C, 6A6B6D, 6A6B6E, and 6A6C6E isomers) from their ^{1}H NMR.[10] Additional monomesitylenesulfonations of the dimesitylenesulfonates (**1–3**) were employed as criteria of assignments of **1–3** and also **7–10**. The additional monosulfonation of 6A6B-, 6A6C-, or 6A6D-di-mesitylenesulfonates should produce three (6A6B6C, 6A6B6D, and 6A6B6E), four (6A6B6C, 6A6B6D, 6A6B6E, and 6A6C6E), or two (6A6B6D and 6A6B6E) trimesitylenesulfonates, respectively (see Scheme I). HPLC analyses (Figure 2)[9] showed that **1**, **2**, or **3** gave three (**7–9**), four (**7–10**), or two (**7** and **8**) products, respectively. Therefore, we assigned **1** as a 6A6B,[11] **2** as a 6A6C, **3** as a 6A6D, **7** as a 6A6B6D (or 6A6B6E), **8** as a 6A6B6E (or 6A6B6D), **9** as a 6A6B6C, and **10** as a 6A6C6E isomer.

Thus, the primary difunctionalized α-cyclodextrins are now easily available by the present convenient method. Also, authentic primary trisubstituted α-cyclodextrin can be derived from **7–10**.

(9) The HPLC column content is shown in ref 6.

(10) They showed quite similar NMR spectra although the spectra somewhat differed from one another in chemical shift ranges of aromatic protons (6H, m). **7**; δ 6.96–7.20, **8**; δ 6.96–7.16, **9**; δ 6.96–7.20, **10**; δ 7.00–7.16. The best differentiation method which we know is the HPLC of which column content is described in ref 6 and is commercially available.

(11) The 6A6B structure of **1** was independently determined by an enzymatic degradation of **1** by Taka-amylase to give 6',6''-dideoxy-6',6''-bis-[(mesitylsulfonyl)oxy]maltotriose. This method will be reported in near future.

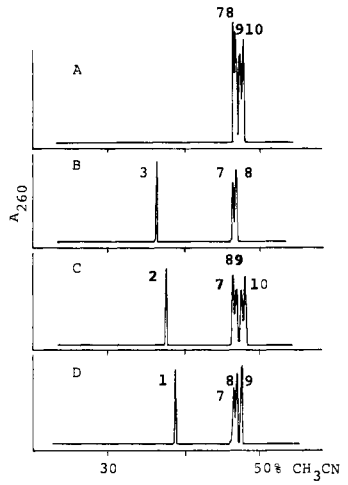


Figure 2. Reversed-phase HPLC of trimesitylenesulfonates of α-cyclodextrin prepared from α-cyclodextrin (2A) and the reaction mixture of the additional monosulfonated **3** (2B), **2** (2C), or **1** (2D). A gradient elution with water–aqueous CH_3CN was applied.

Our separation method by use of the reversed-phase column is quite suitable not only for the separation of the regioisomers but also for the elimination of the unreacted cyclodextrin and salts such as pyridinium mesitylenesulfonate. Moreover, the absolute method of isomer determination described here would be applicable for regioisomeric substitutions on the compounds (cyclophanes, crown ethers, cryptands, etc.) that are made up of several same constitutes.[12]

Acknowledgment. We are indebted to Japan Maise Products Co. Ltd. for generous gift of α-cyclodextrin.

(12) A similar absolute method of isomer determination was described by Körner in assignment of disubstituted benzenes by the conversion of them to the trisubstituted benzenes. Körner, G. *Gazz. Chim. Ital.* **1874**, *4*, 305.

Electronic Control of Stereoselectivity. 23. Stereochemically Selective Course of [6 + 4] and [3 + 4] Cycloadditions to Isodicyclopentadiene[1]

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Isodicyclopentadiene (**1**) is now recognized to favor endo-face selectivity during [4 + 2] cycloaddition to all dienophiles[3] except triazolinediones.[1,4] Guided by semiempirical calculations and photoelectron spectroscopic measurements, Gleiter has rationalized this behavior in terms of a strong σ/π interaction that causes the ψ_1 π orbital of the diene to be disrotatorily tilted toward the methano bridge.[3a,5] It follows that a less destabilizing four-

(1) Part 21. Paquette, L. A.; Green, K. E.; Hsu, L.-Y. *J. Org. Chem.*, in press.

(2) Author to whom inquiries concerning the X-ray crystal structure analysis should be directed.

(3) (a) Gleiter, R.; Paquette, L. A. *Acc. Chem. Res.* **1983**, *16*, 328. (b) Paquette, L. A. In "Stereochemistry and Reactivity of Pi systems"; Watson, W. H., Ed.; Verlag Chemie International: Deerfield Beach, FL, 1983; 41–73.

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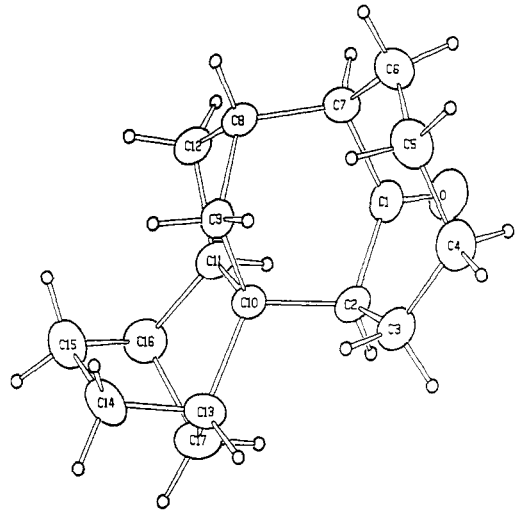
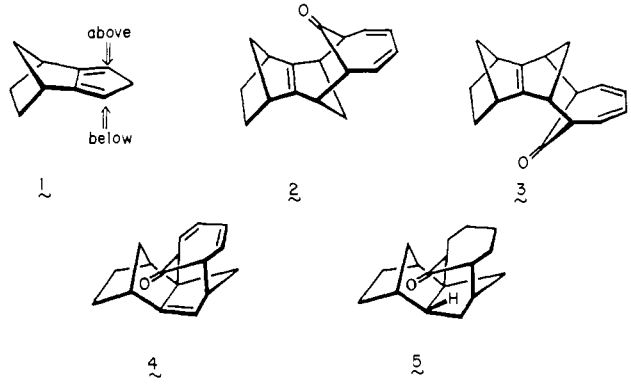
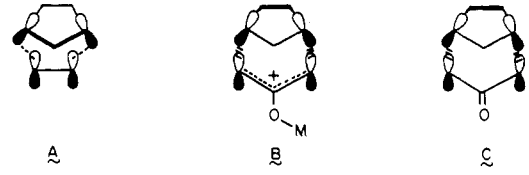


Figure 1. ORTEP drawing of **5**. Non-hydrogen atoms are drawn with 50% probability ellipsoids. Hydrogen atoms have been drawn artificially small.

electron interaction develops if dienophile addition occurs from below plane (**1**). A greater mismatch of orbital alignment is



encountered there (A),[6] since the nonbonded C_1–C_4 distance in



typical cyclopentadiene rings (2.19–2.32 Å)[7] far exceeds that of normal dienophilic double bond lengths (1.30 Å for maleic anhydride).[8]

Because the preceding argument is not universally accepted,[9] we have deemed it relevant to examine the stereochemical course of [4 + 3] and [6 + 4] cycloadditions to **1**. Two oxyallyl cations and tropone were selected. The bonding centers of these new reaction partners reside at distances somewhat greater than that across the cyclopentadiene ring (e.g., the C_2–C_7 gap in tropone is 2.55 Å).[10] As a consequence, the effect operative in A, if important to the stereochemical outcome, should be reversed since the relevant filled orbitals will now interact most intensely in antibonding fashion on the endo face (B and C). We now report that a decided preference for exo-face bonding materialize in these interesting examples. *No comparable crossover in stereoselection has previously been demonstrated for cycloaddition processes differing solely in the non-diene component.*

Table I. Metal-Promoted [3 + 4] Cycloadditions of PhCHBrCOCHBrPh to **1**

reducing agent	product distribution, %[a]					face selectivity, exo:endo
	6	**7**	**8**	**9**	**10**	
NaI, Cu[b]	3	7	0.4	75	15	90:10
$Fe_2(CO)_9$[c]		6	14	5	25	94:6
Zn–Cu[d]		9	38	35	28	91:9

[a] These values are normalized to reflect the relative amounts of the adducts in the individual mixtures. [b] Aqueous acetonitrile (1:1), room temperature, 5 h (69%); **1**/dibromo ketone/NaI/Cu (2:1:4:3). [c] C_6H_6, 60 °C, 36 h (18%); **1**/dibromo ketone/$Fe_2(CO)_9$ (2:1:1.3). [d] Anhydrous glyme, reflux, 15 h (6%); **1**/dibromo ketone/Zn–Cu (1:1:excess).

When **1** was stirred with 1 equiv of tropone in dry benzene solution at room temperature for 9 days, 50% of the hydrocarbon entered into cycloaddition.[11] The three resulting adducts were chromatographically separated. The two more prevalent ketones **2** (71%) and **3** (15%) were identified as planar-symmetric molecules on the basis of their ^1H and ^{13}C NMR spectra.[12] Their differing stereochemistries were deduced from chemical shift data and confirmed by X-ray analysis.[13] The third component (10%), obtianed as a viscous oil, was recognized to be a [6 + 4] addend to a [1,5]-hydrogen shifted isomer of **1**.[14] Since its total saturation over 10% Pd–C afforded a crystalline solid unequivocally characterized as **5** by X-ray analysis (Figure 1), formulation of **4** as the unusual exo ketone illustrated was verified.

When α,α'-dibromo ketones are reduced in the presence of dienes, [3 + 4] cyclocoupling results.[15] Different metals can be expected to stabilize the 2-oxyallyl intermediate to varying extents. To allow for this possibility, solutions of **1** and bis(α-bromobenzyl)ketone were independently treated with NaI and Cu powder, $Fe_2(CO)_9$, and zinc–copper couple. Although adducts **6–10** were indeed formed in differing amounts (Table I), their composite ratios reveal at least a 9:1 preference for exo-face selectivity. The individual ketones were separated chromatographically; **6**, **7**, and **9** were characterized by X-ray analysis.[13] Identification of **8** (unsymmetric) and **10** (planar symmetric) was achieved by epimerization of **9** ($NaOCH_3$, CH_3OH, reflux, 2 days). Expectedly, the conformation of any individual cyclohexanone ring is dictated by the sterically imposed need to orient the phenyl substituents equatorially if at all possible.

(6) A relevant energy diagram can be found in: Böhm, M. C.; Carr, R. V. C.; Gleiter, R.; Paquette, L. A. *J. Am. Chem. Soc.* **1980**, *102*, 7218.

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(9) See, for example: (a) Rondan, N. G.; Paddon-Row, M. N.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2436. (b) Watson, W. H.; Galloy, J.; Bartlett, P. D.; Roof, A. A. M. *Ibid.* **1981**, *103*, 2022. (c) Mahaim, C.; Vogel, P. Helv. *Chim. Acta* **1982**, *65*, 866.

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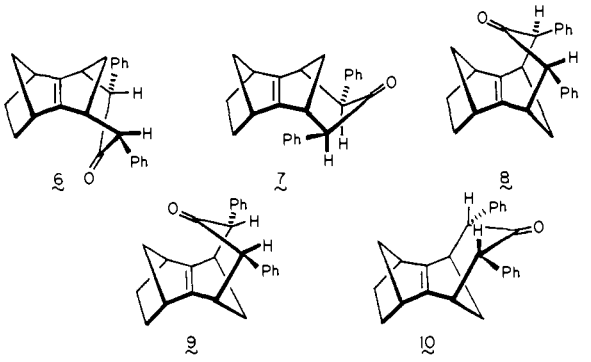
(11) The [6 + 4] cycloaddition of tropone to cyclopentadiene is well-known. (a) Cookson, R. C.; Drake, B. V.; Hudec, J.; Morrison, A. *J. Chem. Soc., Chem. Commun.* **1966**, *15*. (b) Itô, S.; Fujisi, Y.; Okuda, T.; Inoue, Y. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1351. Itô, S.; Sakan, K.; Fujisi, Y. *Tetrahedron Lett.* **1970**, 2873. (c) Tanida, H.; Pfaendler, H. R. *Helv. Chim. Acta* **1972**, *55*, 3062.

(12) **2**: mp *105.5*–106 °C; 300-MHz ^1H NMR ($CDCl_3$) δ 6.01–5.96 (m, 2 H), 5.76–5.69 (m, 2 H), 3.37–3.34 (m, 2 H), 2.97–2.95 (m, 2 H), 2.82–2.80 (br s, 2 H), 2.32 (d, J = 12 Hz, 1 H), 1.78–1.73 (m, 2 H), 1.61–1.51 (m, 2 H), 1.32 (d, J = 12 Hz, 1 H), 1.13 (dd, J = 7 and 2.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 209.21 (s), 154.08 (s), 128.97 (d), 126.55 (d), 58.26 (d), 53.60 (t), 46.89 (d), 40.76 (d), 39.35 (t), 26.32 (t)ppm. **3**: mp 112 °C; 300-MHz ^1H NMR ($CDCl_3$) δ 6.04–6.00 (m, 2 H), 5.78–5.72 (m, 2 H), 3.24–3.21 (m, 2 H), 3.10–3.07 (m, 2 H), 2.91 (br s, 2 H), 2.10 (d, J = 11 Hz, 1 H), 1.65–1.46 (m, 4 H), 1.17 (d, J = 8 Hz, 1 H), 0.86 (dd, J = 7.5 and 2.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 208.89 (s), 152.35 (s), 129.36 (d), 126.61 (d), 56.60 (d), 52.06 (t), 47.97 (d), 41.97 (d), 36.67 (t), 25.81 (t)ppm.

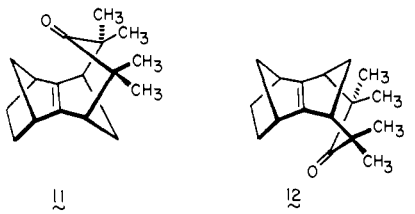
(13) Paquette, L. A.; Hsu, L.-Y.; Gallucci, J. C.; Korp, J. D.; Bernal, I.; Kravetz, T. M.; Hathaway, S. J. *J. Am. Chem. Soc.*, following paper in this issue.

(14) (a) Subramanyam, R.; Bartlett, P. D.; Iglesias, G. Y. M.; Watson, W. H.; Galloy, J. *J. Org. Chem.* **1982**, *47*, 4491. (b) Paquette, L. A.; Williams, R. V.; Carr, R. V. C.; Charumilind, P.; Blount, J. F. *Ibid.* **1982**, *47*, 4566. (c) Bartlett, P. D.; Wu, C. *J. Am. Chem. Soc.* **1983**, *105*, 100.

(15) (a) Noyori, R.; Hayakawa, Y. *Org. React. (N. Y.)* **1983**, *29*, 163. (b) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 819.



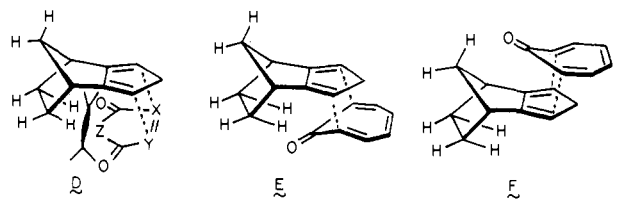
Comparable exposure of **1** to the tetramethyloxyallyl cation ($Fe_2(CO)_9$ generation) resulted in the isolation of **11** and **12** (ratio 4:1). The directionality of carbon–carbon bond formation in these



symmetrical adducts (^{13}C NMR) was established by subjecting **11** to X-ray analysis.[13]

Thus, intermolecular [6 + 4] and [3 + 4] cycloadditions to **1** can be used to assemble norbornenyl-fused 4-cycloheptenones. The carbon frameworks of these end products reflect a face selectivity preference (above plane) that is opposite to that (below plane) observed for the majority of [4 + 2] processes involving this diene. Accordingly, the present observations are consonant with the Gleiter theory.

An alternative hypothesis is that above-plane stereoselectivity in **1** should always be preferred on steric grounds. Indeed, we now recognize that the ethano bridge structurally inhibits endo [4 + 2] addition as in D, whereas the methano bridge does not



do so on all occasions. We have reasoned earlier[1] that highly reactive dienophiles (e.g., triazolinediones and maleic anhydride) prefer above-plane bonding to **1** because the associated early transition states place heavy emphasis on stabilizing secondary orbital effects and consequently are more demanding of the Alder (endo) capture. An overriding sensitivity to *long*-range steric factors therefore develops in these specific instances. However, [6 + 4] cycloadditions unambiguously adhere to exo-bonding schemes.[11,16] Accordingly, tropone has available to it only options E and F. Comparable transition states are less strongly favored in [3 + 2] cycloadditions.[17] A great deal less prima facie evidence for steric control in either transition state is apparent. In fact, the prevalence of **8** and **9** indicates that above-plane oxyallyl cation approach to **1** parallels that in F. From the relative proportions of **6** and **7**, the 180° alternative (i.e., C–O bond externally oriented) is preferred during below-plane cycloaddition.

Since product equilibrations could not be effected, adduct formation seemingly occurs under kinetic control. The role of product stability on the observed stereoselection remains unclear, but is probably not significant. For example, ketones **6–12** differ insignificantly in their pyramidalized central double bond geometry.[13,18] Consequently, to the extent that long-range steric control can be discounted, orbital tilting within **1** must continue to be reckoned with as a force that contributes to π-face stereoselectivity.[19]

Supplementary Material Available: Tables listing crystallographic details for **5**, final positional and thermal parameters, bond distances, bond angles, $|F_o|$, and $|F_c|$ (23 pages). Ordering information is given on any current masthead page.

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(18) In an ancillary experiment, **2** was noted to decompose in C_6H_6 solution at 80 °C, while **3** proved stable to these conditions.

(19) The authors thank the National Cancer Institute (Grant CA-12115) for generous finanical support.

Interrelationship of π-Bond Tilting and the Stereochemical Disposition of Substituents at C-2 and C-7 within Norbornyl-Fused 4-Cycloheptenones[1]

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The pyramidalization of alkenes is currently a subject of intense interest.[3] X-ray crystal analysis of several *syn*-sesquinorbornenes has provided evidence that this ring system experiences large deviations from planarity about its central double bond.[4] To a lesser extent, structurally simpler norbornenes likewise exhibit equilibrium nonplanar character.[5] In contrast, most,[4a,c,d] though not all,[6,7] *anti*-sesquinorbornenes possess an essentially flat π bond. Photoelectron spectra obtained on parent hydrocarbons **1** and **2** reveal their IP's to be significantly lower than expected.[8]

(1) Electronic Control of Stereoselectivity. 24. For Part 23, see: Paquette, L. A.; Hathaway, S. J.; Kravetz, T. M.; Hsu, L.-Y. preceding paper in this issue.

(2) These authors are responsible for the X-ray crystal structure analyses reported herein: (a) compounds **6** and **8**, (b) compounds **7** and **9**, (c) compounds **4** and **5**.

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