reflection of [3]**1** and (020) of [4]**1** correspond closely to molecular lengths. Absence of diffraction in this region from [*n*]**1** is due to the lack of uniform chain length in the polymer. Reflections (110) of [3]**1** and (100) of [4]**1** reveal a separation of $\sim$5.2 Å between parallel molecular axes. The polymer has a strong peak at this *d* value, indicating that the staffs of varying lengths pack in a similar manner. Reflections (006) of [3]**1** and (080) of [4]**1** arise from intrastaff repetition of the bicyclic cages; in the polymer, $d \simeq 3\ 1/3$ Å. The comparison leaves no doubt that poly([1.1.1]propellane) indeed is a mixture of [*n*]staffanes with larger values of *n*, as deduced originally[1] from the CP-MAS $^{13}$C NMR spectrum.

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## Rearrangement Approach to Bridgehead Substitution of 1-Methoxybicyclo[2.2.2]oct-5-en-2-ones

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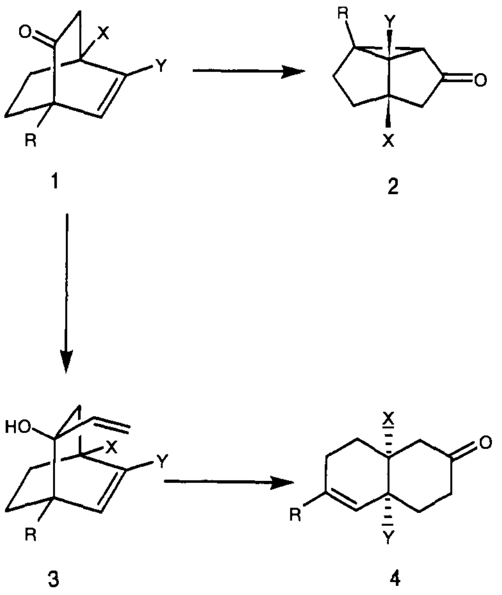
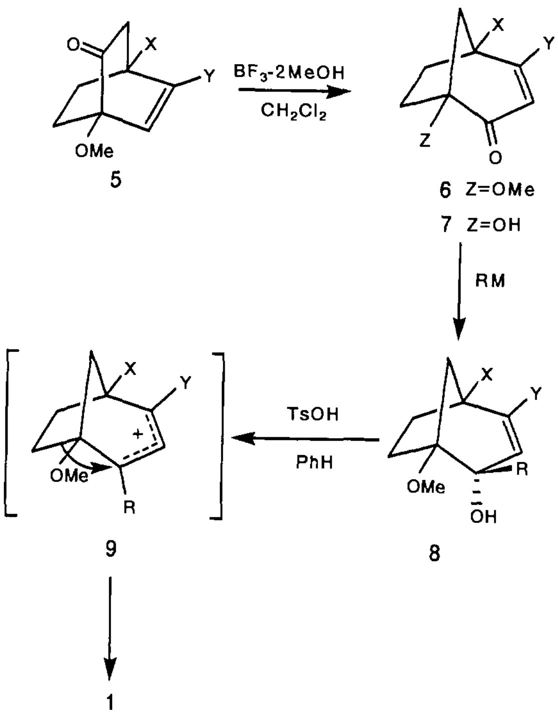
Bicyclo[2.2.2]oct-5-en-2-ones (**1**) are potential compounds which are convertible into [5-5] fused-ring systems (**2**) by the triplet sensitized photochemical process, oxa-di-$\pi$-methane rearrangement,[1] and also into [6-6] fused-ring systems (**4**) via vinylation followed by the oxy-Cope rearrangement of the *exo*-alcohols (**3**).[2] In connection with our studies on rearrangement strategies from bridged polycyclic compounds to [*m*-*n*] fused-ring natural products,[3] we were interested in principal preparation of compounds **1**. Straightforward routes to **1** seem to involve Diels–Alder reaction of 1,3-cyclohexadienes and ketene equivalents.[4] However, selective preparation of even a simply substituted 1,3-cyclohexadiene generally requires many steps.[5] Furthermore, the mode of substituents of the bicyclic ketones, thus obtained, depends upon the regioselectivity of the Diels–Alder reaction that we cannot reverse easily. To compensate these weak points, we must develop a new method for introduction of a substituent at the desired position, including the bridgehead carbon, of the bicyclic system. We wish to report herein formal bridgehead substitution of 1-methoxybicyclo[2.2.2]oct-5-en-2-ones (**5**), derived stereoselectively from anisoles by the Diels–Alder strategy including Birch reduction followed by selective isomerization into 1-methoxy-1,3-cyclohexadienes.[6]

**Scheme I**



**Scheme II**



Scheme II shows our rearrangement approach to the bridgehead substitution. The first step is a Lewis-acid-mediated pinacol-type transformation of **5** into the thermally more stable conjugated ketones **6**. When **5a** (X = Me, Y = H) was treated with $BF_3$–$2CH_3OH$ (1.2 equiv) in dry $CH_2Cl_2$ at room temperature for 1–2 h, the desired ketone **6a** was obtained in 90% yield along with **7a** (3%) due to ether cleavage.[7] The second step is introduction of a desired bridgehead substituent by treatment with an organometallic reagent (RM) adding in a 1,2-manner. A reaction of **6a** with MeLi gave the *endo*-alcohol **8a** (R = X = Me, Y = H) in 72% yield. The final step is a pinacol-type rearrangement which proceeds stereoselectively. The alcohol **8a** was converted into the bridgehead methyl ketone **1a** in 52% yield by treatment with TsOH (0.1 equiv) in boiling benzene for 5 min. This outcome

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(1) For recent reviews, see: Schaffner, K.; Demuth, M. *Modern Synthetic Method*; Scheffold, R., Ed.; Splinger-Verlag: Berlin, 1986; Vol 4, pp 61–88, pp 89–124.

(2) (a) Berson, J. A.; Jones, M., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 5017–5018, 5019–5021. (b) Gregson, P. G.; Mirrington, R. N. *J. Chem. Soc., Chem. Commun.* **1973**, 598–599. (c) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765–4766. (d) Gregson, R. P.; Mirrington, R. N. *Aust. J. Chem.* **1976**, *29*, 2037. (e) Evans, D. A.; Golob, A. M.; Mandel, N. S.; Mandel, G. S. *Ibid.* **1978**, *100*, 8170–8174. (f) Hirota, H.; Kitano, M.; Komatsubara, K.; Takahashi, T. *Chem. Lett.* **1987**, 2079–2080.

(3) Uyehara, T.; Yamada, J.; Ogata, K.; Kato, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 211–216. Uyehara, T.; Yamada, J.; Kato, T.; Bohlmann, F. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 861–867. Uyehara, T.; Kabasawa, Y.; Furuta, T.; Kato, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 539–543. Uyehara, T.; Kabasawa, Y.; Kato, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2521–2528. Uyehara, T.; Yamada, J.; Furuta, T.; Kato, T.; Yamamoto, Y. *Tetrahedron* **1987**, *43*, 5605–5620. Uyehara, T.; Furuta, T.; Kabasawa, Y.; Yamada, J.; Kato, T.; Yamamoto, Y. *J. Org. Chem.* **1988**, *54*, 3669–3673.

(4) For a review, see: Ranganathan, S.; Ranganathan, D.; Mehrotra, A. K. *Synthesis* **1977**, 289–296.

(5) See, for example: reference 2d.

(6) Evans, D. A.; Scott, W. L.; Truesdale, L. K. *Tetrahedron Lett.* **1972**, 121–124. Birch, A. J.; Dastur, K. P. *Tetrahedron Lett.* **1972**, 4195–4198; *J. Chem. Soc., Perkin Trans. 1* **1973**, 1650–1652. Monti, S. A.; Chen, S.-C.; Yang, Y.-L.; Yuan, S.-S.; Bourgeois, O. P. *J. Org. Chem.* **1978**, *43*, 4062–4069.

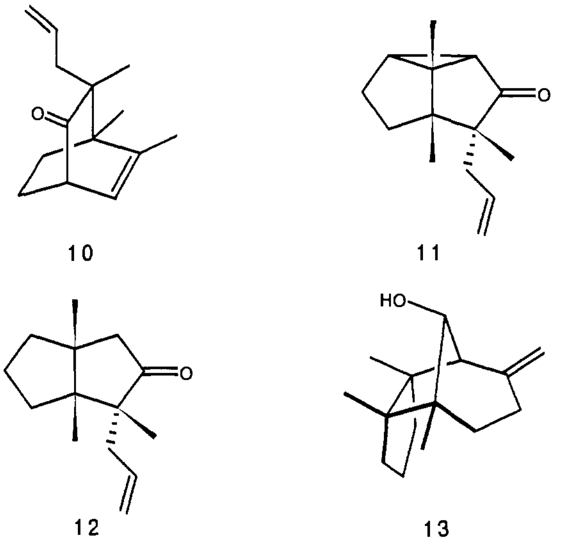
(7) Similar conversion of a 1-methoxybicyclo[2.2.2]oct-5-en-2-one into a 1-hydroxybicyclo[3.2.1]oct-3-en-2-one, see: Monti, S. A.; Dean, T. R. *J. Org. Chem.* **1982**, *47*, 2679–2681.

**Table I.** Bridgehead Substitution of 1-Methoxybicyclo[2.2.2]oct-5-en-2-ones[a]

| substrate | | | RM | product | | yield[b] (%) |
|---|---|---|---|---|---|---|
| | X | Y | | | R | |
| **5a** | Me | H | MeLi | **1a** | Me | 65 |
| **5a** | Me | H | *n*-BuLi | **1b** | *n*-Bu | 68 |
| **5a** | Me | H | *i*-PrLi[c] | **1c** | *i*-Pr | 46 |
| **5a** | Me | H | *t*-BuLi[d] | **1d** | *t*-Bu | 20 |
| **5a** | Me | H | PhLi | **1e** | Ph | 66 |
| **5a** | Me | H | DIBAH | **1f** | H | 44 |
| **5b** | H | Me | MeLi | **1g** | Me | 61 |
| **5c** | Me | Me | DIBAH | **1h** | H | 63 |
| **5d** | H | H | MeLi | **1i** | Me | 46 |

[a] All synthetic intermediates (**6**, **7**, and **8**) were used without purification. [b] Overall yields from **5**. [c] In situ generated by sonication of a mixture of *i*-PrCl and Li in THF. [d] A mixture of 4-*tert*-butyl-5-methyl-1-methoxybicyclo[3.2.1]oct-2-ones was obtained from **6a** in 47% yield.

**Chart I**



suggests that the acid-catalyzed dehydration and the bridge migration are not concerted, and a stable intermediate such as allyl cation **9** may be present. A simple model study of **9** indicates that the C-2 p atomic orbital overlaps preferentially the C-1–C-7 $\sigma$ bond (the two-carbon bridge) rather than the C-1–C-8 $\sigma$ bond (the one-carbon bridge).

The minor products, bridgehead hydroxy ketones **7** and the alcohols derived from **7**, were also useful to prepare **1** in a similar manner. In practice, the transformation of **5** to **1** was carried out without chromatographic separation of synthetic intermediates (Table I). The mode of substitution of ketones **1f** and **1h** is contrary to that of Diels–Alder 1,4-adducts derived from the corresponding 1,3-cyclohexadienes and ketene equivalents. Ketones **1b–e** are difficult to prepare selectively by means of simple Diels–Alder strategy.

The ketone **1h** has been employed as the starting material for the formal total synthesis of (±)-gymnomitrol (**13**), a unique tricyclic sesquiterpene.[8,9] Sequential treatment of **1h** with LDA, 3-iodopropene (THF–HMPA), LDA, and iodomethane (THF–HMPA) gave **10** stereoselectively in 72% overall yield.[10] The oxa-di-$\pi$-methane rearrangement of **10** proceeded efficiently in acetone to form **11** in 94% yield. Reduction of this cyclopropyl ketone by lithium in liquid ammonia gave the substituted diquinane **12** (75% yield) which had already been converted into (±)-gymnomitrol.[9c]

Thus, it is clear that this bridgehead substitution expands the utility of bridged polycyclic compounds for natural product syntheses.

**Acknowledgment.** Financial support by the Kurata Foundation is gratefully acknowledged.

**Supplementary Material Available:** Spectral (IR and $^1$H NMR) and analytical data (elemental analysis) for **6a**, **6c**, **7a**, **8a**, **1c–h**, and **10–12** (3 pages). Ordering information is given on any current masthead page.

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[8] Isolation: Connolly, J. D.; Harding, A. E.; Thornton, I. M. S. *J. Chem. Soc., Chem. Commun.* **1970**, 1320–1321; *J. Chem. Soc., Perkin Trans. 1* **1974**, 2487–2493.

[9] Synthesis: (a) Coates, R. M.; Shah, S. K.; Mason, R. W. *J. Am. Chem.* Soc. **1979**, *101*, 6765–6767; **1982**, *104*, 2198–2208. (b) Buchi, G.; Chu, P.-S. *Ibid.* **1979**, *101*, 6767–6768; *Tetrahedron* **1981**, *37*, 4509–4513. (c) Welch, S. C.; Chayabunjonglerd, S. *J. Am. Chem. Soc.* **1979**, *101*, 6768–6769. Welch, S. C.; Chayabunjonglerd, S.; Parakasa, R. *J. Org. Chem.* **1980**, *45*, 4086–4093. (d) Han, Y.-K.; Paquette, L. A. *Ibid.* **1979**, *44*, 3731–3733. Paquette, L. A.; Han, Y.-K. *J. Am. Chem. Soc.* **1981**, *103*, 1831–1835. (e) Kodama, M.; Kurihara, T.; Sasaki, J.; Ito, S. *Can. J. Chem.* **1979**, *57*, 3343–3345.

[10] The $^1$H NMR spectrum of **10** shows a singlet at $\delta$ 0.78 due to the *endo*-3-methyl protons which are shielded by the carbon–carbon double bond. Details are listed in the Supplementary Material.

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# The Role of the Product in Asymmetric C–C Bond Formation: Stoichiometric and Catalytic Enantioselective Autoinduction

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Evidence for aggregation of (alkali) metal enolates, alkoxides, and condensation products in the solid state and in solution has been rapidly accumulating in the past decade.[1] The organic moieties are mono- or bidentate ligands in these clusters prior to their liberation to monomeric products in the hydrolytic workup. Although C–C bond formation via condensation of organometallic reagents with carbonyl compounds is by far the most important synthetic procedure in organic chemistry (especially in the area of asymmetric induction with chiral auxiliary ligands), the stereochemical effect *of the product* acting as a ligand in intermediate complexes has not been systematically investigated.

We studied the effect of enriched (+)-(*R*)-1-phenyl-1-propanol-$d_1$ (+24.40),[2] **1D**, on the addition of ethyllithium to benzaldehyde:

$$\mathrm{PhCHO} \xrightarrow[\text{or: (+)-(PhC*DEtO)}_4\text{Ti/ZnEt}_2]{\text{(+)-PhC*D(OLi)Et/EtLi}} \xrightarrow{\mathrm{H_3O+}} \underset{\textbf{1D}}{\mathrm{PhC^{*}D(OH)Et}} + \underset{\textbf{1H}}{\mathrm{PhC^{*}H(OH)Et}}$$

To a solution of 2 mmol of the alkyllithium in benzene (filtered from LiBr, 5 mL, 0.402 M) was added 1 mmol of **1D** at room temperature (all operations under dry nitrogen). Ethane was evolved in an exothermic reaction. The homogeneous solution was cooled in ice, and 1 mmol of freshly distilled benzaldehyde in 1 mL of dry benzene was added within 5 min with stirring. After 10 min the reaction mixture was subjected to a hydrolytic workup with dilute HCl and ether. The product, a mixture of **1D** and **1H** (94%), was purified by molecular distillation (0.1 mm, 100 °C bath temperature, repeated until constant rotation). The use of deuterated **1D** allowed us to determine the ee of **1H** separately in the mixture. The ratio of **1D** vs **1H** (found 100:86) was determined by integration of the methine proton in **1H** at 5.1

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[1] For a recent review: Seebach, D. *Angew. Chem.* **1988**, 100, 1685.

[2] Prepared via the quinine-catalyzed addition of diethylzinc to benzaldehyde-*d* in 70% ee (according to Smaardijk, A. A.; Wynberg, H. *J. Org. Chem.* **1987**, *5*, 135). The optical properties of **1D** and **1H** are identical within experimental error. The relationship between specific rotation and various mixtures of **1D** and racemic **1H** is linear. All rotations measured at $c$ = 100, in toluene, 21 °C, 578 nm.

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