

New Six- to Eight-Membered-Ring Formation Based on the Intramolecular Endo- Mode
Ring Closure of Allenyl (Substituted Phenyl)alkyl Ketones

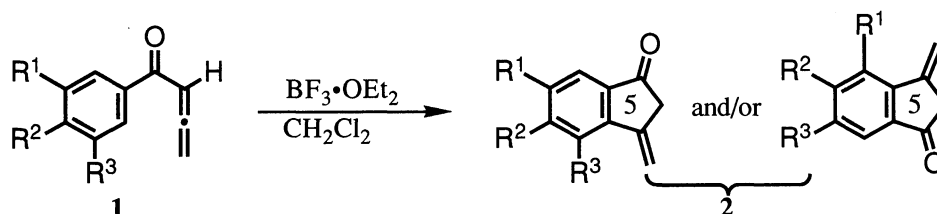
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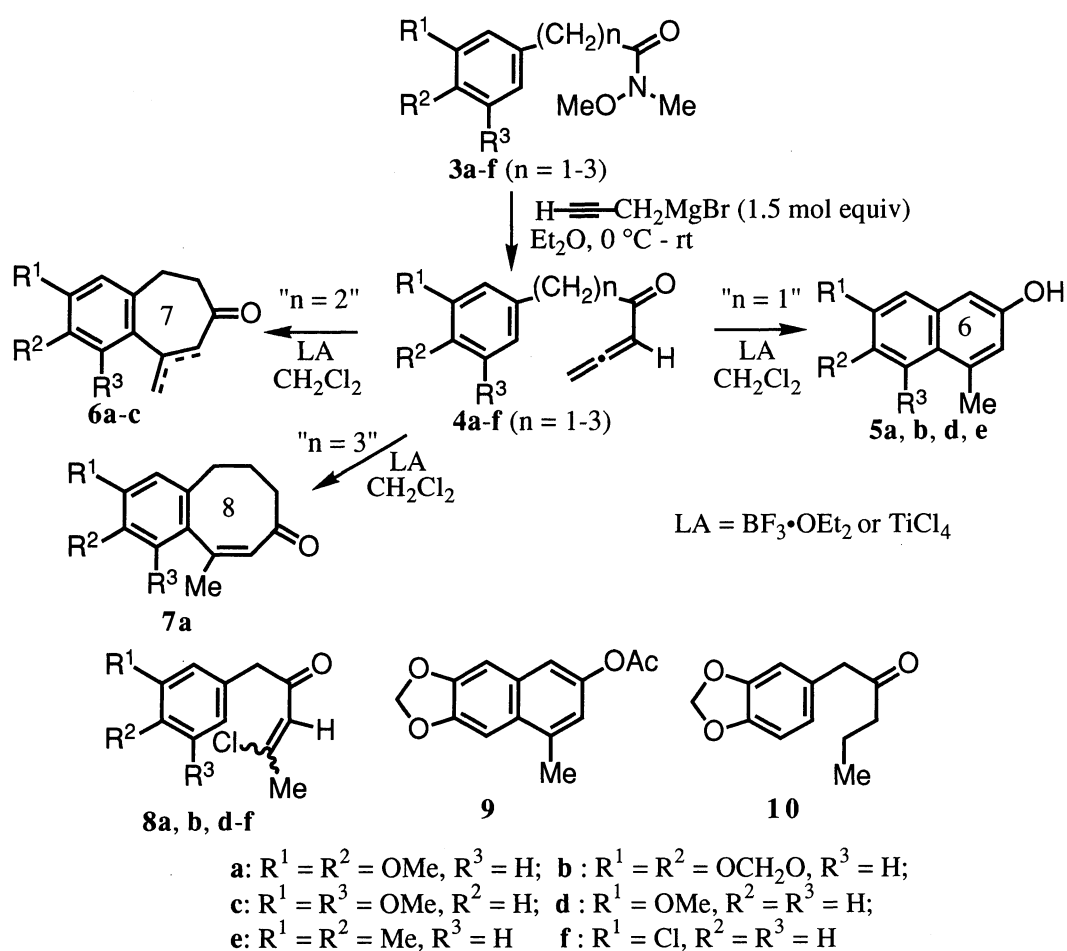
Several allenyl ketones possessing an aryl group were submitted to a new intramolecular endo-mode cyclization with $\text{BF}_3 \cdot \text{OEt}_2$ or TiCl_4 in CH_2Cl_2 to afford the corresponding 6-, 7-, and 8-membered carbocyclic products.

Recently, we disclosed a new intramolecular 5-endo-mode ring closure (**1**→**2**) at the sp carbon atom of the allenic moiety of allenyl aryl ketones.¹⁾ It should be attractive to expand this endo-mode cyclization toward larger ring compounds than 5-membered-ring ones.



Thus, various allenyl (substituted phenyl)alkyl ketones **4a-f** ($n = 1-3$) were prepared in 65-94% yields by the Weinreb-modified Grignard reaction²⁾ with an ether solution of propargylmagnesium bromide onto *N*-methoxy-*N*-methanilamides **3a-f** ($n = 1-3$) obtained by the usual method.¹⁾ The same direct formation of the allenyl ketone moiety proceeded also smoothly as the case of allenyl ketones **1**.¹⁾ The structure of all oily products was determined on the basis of their characteristic spectroscopic data.¹⁾

First of all, a six-membered-ring formation reaction of compound **4b** ($n = 1$) was attempted in the presence of 1 mol equiv of $\text{BF}_3 \cdot \text{OEt}_2$ in anhydrous CH_2Cl_2 at 0 °C for 30 min. However, the reaction almost resulted in decomposition of the starting compound. Hence, compound **4b** ($n = 1$) was treated with 1 mol equiv of TiCl_4 in CH_2Cl_2 at -78 °C for 8 min to give a β -naphthol **5b** in 54% yield and a trace amount of chlorine atom adduct **8b**, respectively. Other allenyl ketones **4a,d-f** ($n = 1$) were similarly treated with 1 mol equiv of TiCl_4 to furnish the corresponding β -naphthols **5a** (trace), **5d** (trace), **5e** (52%), and **5f** (0%) together with the chlorine atom adducts **8a** (47%), **8d** (56%), **8e** (40%), and **8f** (55%), respectively as shown in Table 1. On treatment with 1 mol equiv of $\text{BF}_3 \cdot \text{OEt}_2$, compound **4a** ($n = 1$) was effectively converted to the desired β -naphthol **5a** in 53% yield. The structure of all β -naphthol products was determined by their IR [KBr and CHCl_3 : no carbonyl absorption, ν 3191-3324 cm^{-1} (naphthol OH)], ^1H NMR [200 MHz, CDCl_3 : δ 6.81-7.83 (5H or 4H, aromatic protons)], and Mass (M^+ ion peak) spectrum data. Compound **5b** was converted to its acetyl derivative **9**

Table 1. Endo-Mode Cyclization of Allenyl Ketones **4**

Compd 4	Reaction conditions			Product 5-7	Yield ^{b)} / %	mp/ °C
	LA ^{a)}	Temp/ °C	Time/ min			
n = 1						
4a	B	-2	25	5a	53	194-195
4b	T	-78	8	5b ^{c)}	54	130
4d	◇	◇	10	5d ^{c)}	trace	108
4e	◇	◇	15	5e ^{c)}	52	113
4f	◇	◇	◇	5f ^{c)}	0	—
n = 2						
4a	B	-3 - 0	30	6a	100 ^{d)}	94-94.5 (endo) 74.5 (exo)
4b	◇	-3 - rt	150	6b	70 ^{d)}	72-73 (exo) 72.5 (endo)
4c	◇	-78 - rt	50	6c	86 ^{d)}	103 (exo) 97.5-98 (endo)
n = 3						
4a	◇	0 - 60	30	7a	31	87-88

a) LA: Lewis acid. B = $\text{BF}_3 \cdot \text{OEt}_2$, T = TiCl_4 b) Isolated. c) Each chlorine atom adduct **8b, d, e, f** was also obtained (see Text). d) Total yield of a mixture of exo- and endo-olefinic products [**6a** (1 : 4.5), **6b** (1 : 6.6), and **6c** (1 : 3.3)].

(mp 124-125 °C) by the usual acetylation method. The structure of chlorine atom adducts **8a,b,d-f** was confirmed by their IR [neat and CHCl_3 : ν 1685-1692 cm^{-1} (α , β -unsaturated ketone)], ^1H NMR [200 MHz, CDCl_3 : δ ca. 6.45 (1H, olefinic proton), 6.61-7.28 (3H or 4H, aromatic protons), and ca. 2.55 (3H, vinyl-Me)] and characteristic Mass (M^+ due to ^{35}Cl and $M^+ + 2$ due to ^{37}Cl) spectrum data and their positive Beilstein test. Catalytic hydrogenation of **8b** and compound **4b** ($n = 1$) gave the same product **10**. Each compound **8a, b, d-f** should be pure from the viewpoint of the ^1H NMR analysis but its geometry has not been established yet. Interestingly, this 6-membered-ring formation using compounds **4d,e** ($n = 1$) afforded the ring-closure product at the *para* position to R^1 group, while a mixture of *ortho* and *para* products was obtained in the case of 5-membered-ring formation (**1**→**2**).¹⁾ This outcome can be rationalized in terms of severe steric repulsion between terminal methylene protons and the substituent group of the aromatic moiety in the transition state (Fig.1) of 6-endo-mode ring closure.

Allenyl ketones **4a-c** ($n = 2$) were allowed to react with 1 mol equiv of $\text{BF}_3 \cdot \text{OEt}_2$ in CH_2Cl_2 as shown in Table 1. Surprisingly, their 7-membered-ring formation proceeded quite readily to afford a mixture of *exo*- and *endo*-olefinic cyclized products **6a-c** in excellent yields (70-100%). These mixed products can be separated on a silica gel plate (Merck Kieselgel 60 F254) to give each pure compound as crystals (Table 1). The structure was undoubtedly determined on the basis of their characteristic spectroscopic data {[for *exo*-olefinic compound: IR (KBr) ν 1697-1719 cm^{-1} (carbonyl); ^1H NMR (200 MHz, CDCl_3) δ 5.11-5.17, 5.19-5.48 (each s like, each 1H, *exo*-methylene protons) and 6.38-6.88 (each s or d, 2H aromatic protons)] [for *endo*-olefinic compounds: IR (KBr) ν 1644-1658 cm^{-1} (α , β -unsaturated carbonyl); ^1H NMR (200 MHz, CDCl_3) δ 2.28-2.33 (s, 3H, olefin-Me), 6.13-6.23 (s, 1H, olefinic proton), and 6.40-6.98 (each s or d, 2H, aromatic protons)]}. The structure of *exo*-olefinic compound **6c** was clarified by its X-ray analysis as illustrated in Fig. 2.³⁾ All

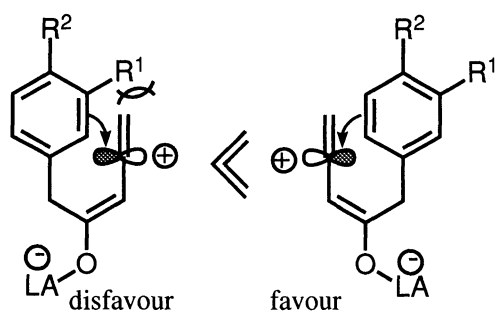


Fig.1. Predominant orientation for 6-endo-mode cyclization.

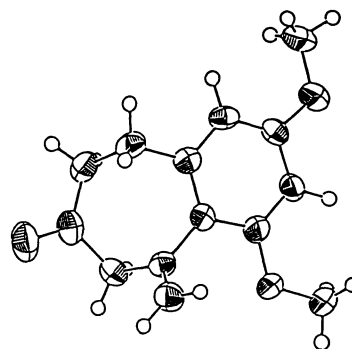


Fig.2. Perspective view of the crystallographic structure of *exo*-**6c**.

exo-olefinic compounds **6a-c** were perfectly converted to the corresponding *endo*-olefinic compounds (conjugated enones) under the basic conditions (NaH , THF, 0 °C- rt, 2.5 h). This easy double bond shift is quite usual vs. the case of 5-membered-ring compounds **2**. Eight-endo-mode ring closure seems to be somewhat difficult. Similar treatment of compound **4a** ($n = 3$) with $\text{BF}_3 \cdot \text{OEt}_2$ gave 31% of cyclized product **7a** after warming at 60 °C for 30 min. The *endo*-olefinic structure of **7a** was determined by its spectroscopic analyses.⁴⁾ In comparison with successful 7-endo-mode cyclization of the allenyl ketones, 7-endo-trigonal cyclization⁵⁾ of vinyl ketone **11** was performed in the presence of 1 mol equiv of $\text{BF}_3 \cdot \text{OEt}_2$ in CH_2Cl_2 at 0 °C to room temperature. The desired reaction proceeded but took much more time (4 h) to give a cyclized product **12**⁶⁾ in a lower yield (45%) than those (30 min, 100% yield) of compound **4a** ($n = 2$). Thus, this characteristic

reactivity of the various allenyl ketones vs. that of the α,β -unsaturated ketones may be explained in terms of a plausible transition state (Fig. 3)^{7,8)} where the cationic sp carbon formed by Lewis acid-promoted enolization must be fairly reactive to the aryl group because of enough conjugation of the resultant enolate with exomethylene double bond.

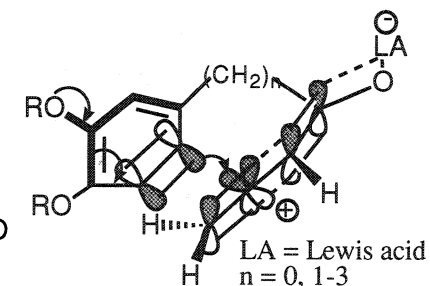
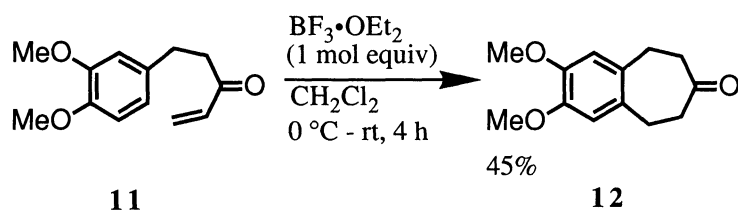


Fig. 3. Plausible transition state for ring closure of the allenyl ketones.

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References

- 1) Y. Nagao, W.-S. Lee, and K. Kim, *Chem. Lett.*, **1994**, 389.
- 2) S. Nahm and S. M. Weinreb, *Tetrahedron Lett.*, **22**, 3815 (1981).
- 3) The crystallographic data of exo- **6c** are as follows.
 $\text{C}_{14}\text{H}_{16}\text{O}_3$, $M = 232.28$, monoclinic, $P2_1/n$, $a = 10.225(7)\text{\AA}$, $b = 7.751(9)\text{\AA}$, $c = 15.579(6)\text{\AA}$, $\beta = 101.27(4)^\circ$, $V = 1210(1)\text{\AA}^3$, $z = 4$, $D_{\text{calc}} = 1.274 \text{ g cm}^{-3}$, $R = 0.043$
- 4) ^1H NMR (400 MHz, CDCl_3) of compound **7a**: δ 1.80 (m, 2H), 2.13-2.31 (m, 2H), 2.26 (s, 3H), 2.62- 2.82 (m, 2H), 3.88 (s, 3H), 3.91 (s, 3H), 6.25 (s, 1H), 6.71 (s, 1H), and 6.86 (s, 1H).
- 5) The 7-endo-trigonal cyclization should be favorable on the basis of the Baldwin rule for ring closure. J. E. Baldwin, *J. Chem. Soc., Chem. Commun.* **1976**, 734.
- 6) ^1H NMR (200 MHz, CDCl_3) of compound **12**: δ 2.59 (m, 4H), 2.85 (m, 4H), 3.88 (s, 6H), and 6.75 (s, 2H).
- 7) We adopted an sp-linear vinyl cation which must be 45-65 kcal/mol more stable than the sp^2 -bent one.⁸⁾ This is reasonable from the viewpoint of *para*-selective 6-endo-mode cyclization of compounds **4d,e** ($n = 1$).
- 8) R. H. Summerville and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **95**, 1110 (1974).

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