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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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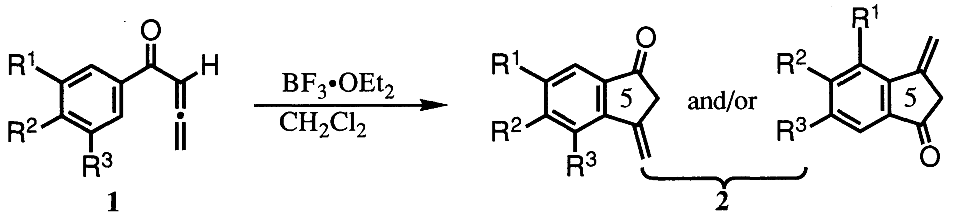
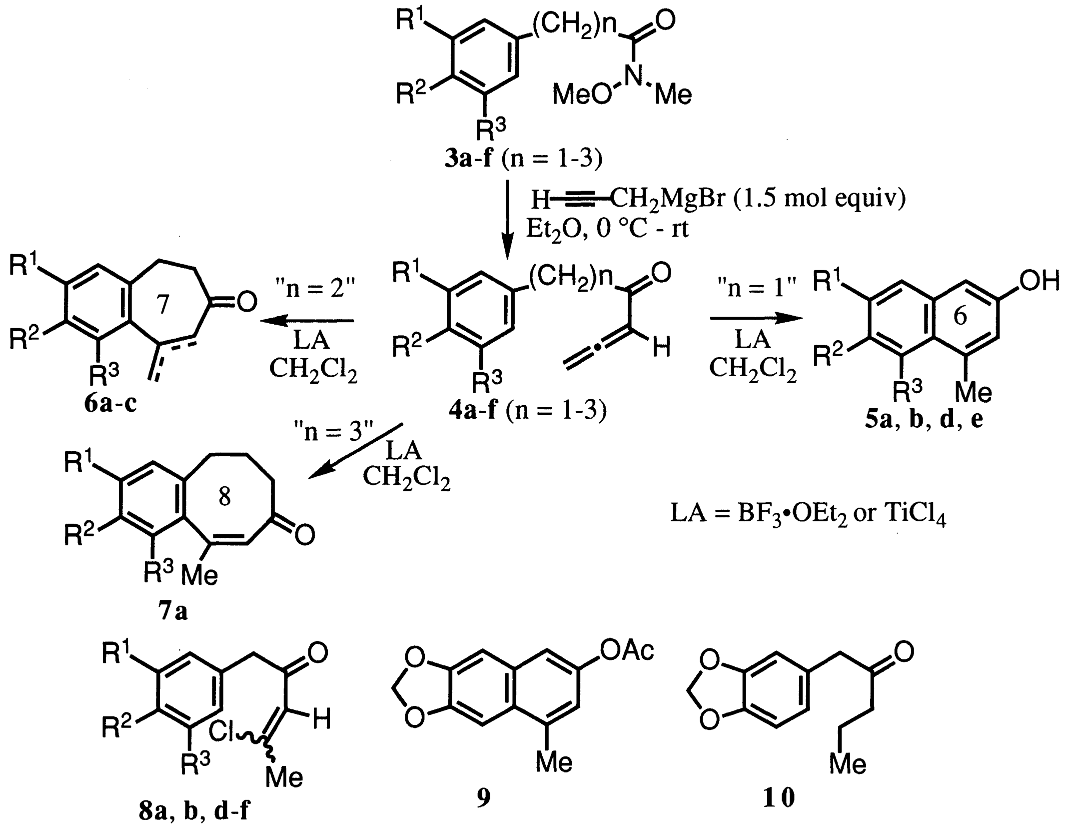
Several allenyl ketones possessing an aryl group were submitted to a new intramolecular endo-mode cyclization with BF_3•OEt_2 or $TiCl_4$ in CH_2Cl_2 to afford the corresponding 6-, 7-, and 8-membered carbocyclic products.

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 reaction[2)] with an ether solution of propargylmagnesium bromide onto *N*-methoxy-*N*-methylamides **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 BF_3•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 BF_3•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 determind 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**



a: $R^1 = R^2 = OMe, R^3 = H$; **b** : $R^1 = R^2 = OCH_2O, R^3 = H$;
c: $R^1 = R^3 = OMe, R^2 = H$; **d** : $R^1 = OMe, R^2 = R^3 = H$;
e: $R^1 = R^2 = Me, R^3 = H$ **f** : $R^1 = Cl, R^2 = R^3 = H$

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

Compd **4**	Reaction conditions LA[a)]	Temp/ °C	Time/ min	Product **5-7**	Yield[b)]/ %	mp/ °C
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 = $BF_3•OEt_2$, T = $TiCl_4$ b) Isolated. c) Each chloline 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 BF_3•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

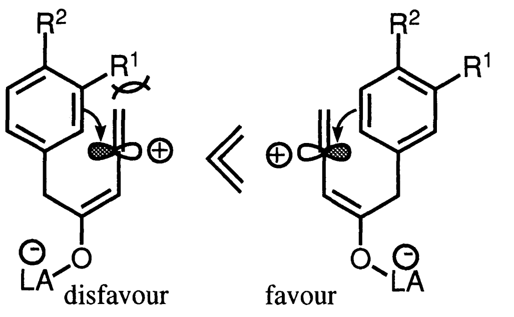


Fig.1. Predominant orientation for 6-endo-mode cyclization.

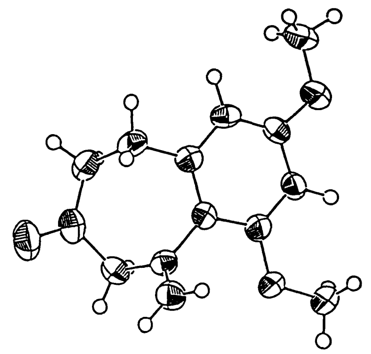
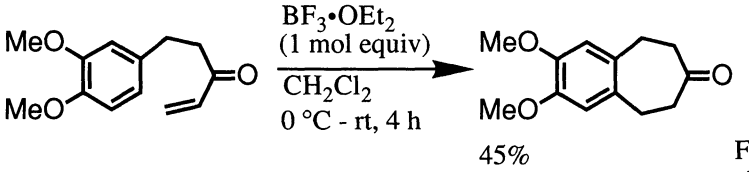


Fig.2. Perspective view of the crystallographic structure of exo-**6c**.

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 BF_3•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 cyclization[5] of vinyl ketone **11** was performed in the presence of 1 mol equiv of BF_3•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 exo-methylene double bond.



11 **12**

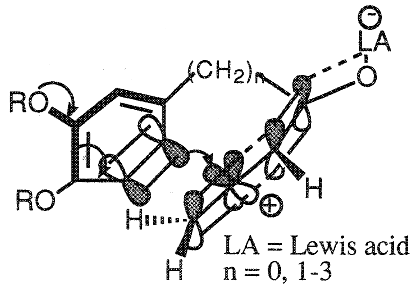


Fig. 3. Plausible transition state for ring closure of the allenyl ketones.

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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.
$C_{14}H_{16}O_3$, M = 232.28, monoclinic, P21/n, a = 10.225(7)Å, b = 7.751(9)Å, c = 15.579(6)Å, β = 101.27(4)°, V = 1210(1)$Å^3$, z = 4, Dcalc = 1.274 g cm-3, R = 0.043

4) ^{1}H NMR (400 MHz, CDCl3) 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) ^{1}H NMR (200 MHz, CDCl3) 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 resonable 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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