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A new entry to carbocycles: synthesis of cyclopentene and cyclohexene derivatives through *endo*-mode ring closure of allenyl sulfones

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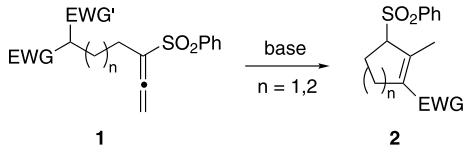
Abstract—Treatment of dimethyl 4-(phenylsulfonyl)-4,5-hexadiene-1,1-dicarboxylate with potassium *tert*-butoxide in *tert*-butanol at room temperature effected successive *endo*-mode ring closure at the *sp*-hybridized carbon center and demethoxycarbonylation of the resulting malonate derivative leading to the exclusive formation of methyl 2-methyl-3-(phenylsulfonyl)-1-cyclopentenecarboxylate. An additional seven allenyl sulfones having a 1,3-dicarbonyl functionality gave the corresponding cyclopentene or cyclohexene derivatives in high yields.

The construction of five- and six-membered carbocycles is a fundamental process in synthesis, and enormous procedures have been developed for preparing them. The classical intramolecular Michael-type conjugate addition[1] of carbanionic organometallic species to activated alkenes and alkynes with an electron-withdrawing group (i.e. Michael acceptors) is still one of the most frequently used methods, although recent progress in the field of organotransition metal chemistry has enabled the efficient metal-catalyzed intramolecular addition of enolates, derived from active methine derivatives, to unactivated alkynes[2] and allenes[3] as well. In contrast to the many examples of intramolecular conjugate addition of carbanion species to alkenes and alkynes[1] having an electron-withdrawing group, relatively few examples of the corresponding allene derivatives[4] have been reported. During our own studies[5] toward the development of a convenient and efficient procedure for the preparation of oxacycles, we were able to show that the *endo*-mode intramolecular ring closure of allenes[6] having a phenylsulfonyl functionality with a terminal hydroxyl group proceeded very efficiently. This letter describes our preliminary results on the novel intramolecular ring closure reaction of the allenyl sulfones **1** with suitable internal carbon nucleophiles[7] in an *endo*-mode manner[8] leading to the intriguing direct formation of the 1,2,3-trisubstituted-cyclopentene and cyclohexene derivatives **2** (Scheme 1). Thus, to the best of our knowledge, this would be the first example dealing with the *endo*-mode intramolecular Michael-type reaction of allenes with the active methine moiety.



1 **2**

Scheme 1.

The required starting allenes **7** and **8** for the ring closure reaction were prepared by conventional means in a straightforward manner as depicted in Scheme 2. Condensation of the iodo derivatives **3**[9] and **4**[10] with the active methine species under basic conditions was followed by acid hydrolysis to give the condensed products **5** and **6** with a propargyl alcohol moiety. Exposure of the methine derivatives **5** and **6** to benzenesulfenyl chloride[11] in THF in the presence of triethylamine effected successive sulfenic ester formation and the [2,3]-sigmatropic rearrangement to afford the corresponding sulfoxides, which were subsequently oxidized with *m*CPBA to furnish the sulfone derivatives **7** and **8**.

Keywords: carbocycle; *endo*-mode ring closure; allenyl sulfone; carbon nucleophile; Michael-type reaction.

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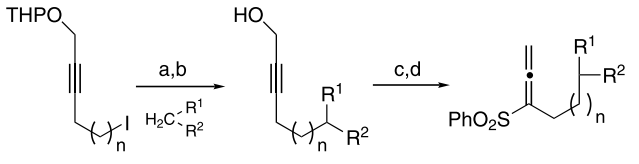


3 : n = 1
4 : n = 2

5 : n = 1
6 : n = 2

7 : n = 1
8 : n = 2

a : $R^1 = R^2 = CO_2Me$, **b** : $R^1 = R^2 = CO_2Et$, **c** : $R^1 = CO_2Et$, $R_2 = COPh$, **d** : $R^1 = SO_2Ph$, $R^2 = CO_2Me$

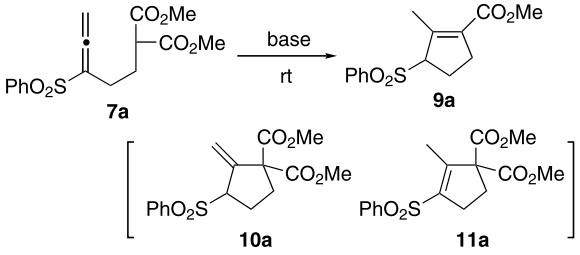
Scheme 2. *Reagents and conditions*: (a) NaH, DMF, 0°C–rt; (b) *p*-TsOH, MeOH, rt, **5a** (86%), **5b** (86%), **5c** (34%), **5d** (90%), **6a** (88%), **6b** (83%), **6c** (41%), **6d** (98%); (c) PhSCl, Et_3N, THF, −78°C; (d) *m*CPBA, CH_2Cl_2, 0°C, **7a** (85%), **7b** (81%), **7c** (77%), **7d** (50%), **8a** (91%), **8b** (74%), **8c** (66%), **8d** (88%).

At the beginning of this study, we investigated the transformation of **7a** to the corresponding ring-closed products. Treatment of the allenyl sulfone **7a** with sodium methoxide in MeOH at room temperature immediately led to complete consumption of the starting material as well as production of three new spots on TLC, which needed a prolonged reaction time (26 h) to converge into one product. The isolated product from the reaction mixture was the cyclopentenecarboxylate derivative **9a**[12] (96%) instead of the expected cyclopentene-1,1-dicarboxylate derivatives **10a** and/or **11a** (Table 1, entry 1). A similar result was observed when **7a** was exposed to potassium methoxide in MeOH for a shorter reaction time (2 h) (entry 2). In contrast to these two cases, rapid conversion of **7a** into **9a** (84%) was realized within 5 min upon treatment with potassium *tert*-butoxide in ^{t}BuOH at room temperature (entry 3). The ring closure of **7a** with potassium hydroxide in THF also furnished **9a** in 67% yield (entry 4).[14] These results are summarized in Table 1.

The fascinating formation of **9a** from **7a** can tentatively be rationalized in terms of the intermediacy of the products **10a** and/or **11a**, which would collapse to **9a** through demethoxycarbonylation.[15] In order to obtain more information on the mechanism of this transformation, several experiments were carried out (Scheme 3). Treatment of **7a** with triethylamine in CH_2Cl_2 at room temperature for 2 h provided **10a** and **11a** in 69% and 24% yield, respectively. Compound **10a** was isomerized to **11a** in 15% yield when it exposed to triethylamine at room temperature for 48 h along with starting **10a** (68%). However, **11a** was found to be stable under the same conditions and no isomerization to **10a** could be detected. It turned out that these malonate derivatives **10a** and **11a** easily underwent demethoxycarbonylation with alkoxides to provide **9a**. Thus, independent treatment of **10a** and **11a** with potassium *tert*-butoxide in ^{t}BuOH at room temperature for 5 min furnished **9a** in 79% and 63% yield, respectively. On the basis of these experiments, it could be concluded that the Michael-type ring closure of **7a** under the basic conditions first occurred at the *sp*-hybridized carbon center of the allenyl moiety in an *endo*-mode manner, as anticipated, resulting in the formation of **10a**, which might be in part susceptible to the base-catalyzed isomerization to **11a**. The final step of this transformation must be the demethoxycarbonylation of **10a** and/or **11a** with the alkoxide species leading to the production of **9a**, although the exact mechanism of the demethoxycarbonylation is so far unclear.[16]

The next phase of this program involved the application of this newly developed procedure to the con-

Table 1. Ring closure reaction of **7a**[a]



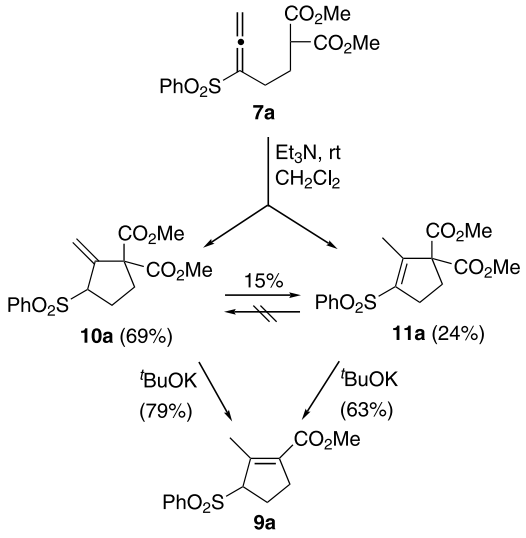
7a **9a**

10a **11a**

entry	base	equiv.	solvent	time	yield (%)
1	MeONa	4.5[b]	MeOH	26 h[c]	96
2	MeOK	4.5[b]	MeOh	2 h[c]	95
3	^{t}BuOK	1.5	^{t}BuOH	5 min[d]	84
4	aq. KOH	1.5	THF	6 h[c]	67

>>67

[a] Reaction was monitored by TLC. Complete consumption of **7a** was observed within 5 min in each case.
[b] It took more prolonged reaction time when 1.5 equiv. of base was used.
[c] Three new spots gradually converged to **9a**.
[d] No other products could be detected on TLC.



Scheme 3.

struction of other carbocycles. We chose potassium *tert*-butoxide in ^{t}BuOH (Table 1, entry 3) for further investigation, since rapid conversion involving dealkoxycarbonylation would be anticipated. The results obtained from the reactions of **7b–d** and **8a–d** under standard conditions, in combination with the result of **7a**, are summarized in Table 2. There are several features that should be pointed out. (i) All reactions, except for entries 3 and 7, afforded the corresponding cyclized-products accompanied with dealkoxycarbonylation in high yields. (ii) Contrary to our prediction, **7c** and **8c** produced **9b** and **12b**, respectively, via debenzoylation instead of deethoxycarbonylation (entries 3 and 7). This observation might provide additional information concerning the mechanism.[16,17] (iii) In the case of **7d** and **8d**, longer time as well as higher temperature (60°C) were required to complete the reaction, although rapid consumption of the starting materials was observed within 5 min (entries 4 and 8).

In summary, we have developed a simple and convenient procedure for the preparation of the cyclopentene and cyclohexene frameworks having three distinguishable functionalities via the *endo*-mode ring closure of the allenyl sulfone derivatives. Application of this interesting method to the construction of other carbocycles, like cycloheptene and cyclooctene skeletons, as well as further investigation on the mechanism of the decarbonylation process is now in progress.

Acknowledgements

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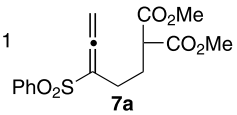
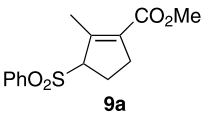
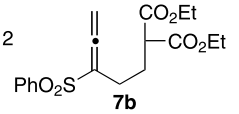
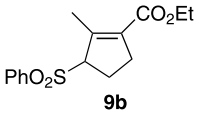
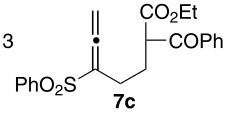
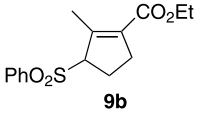
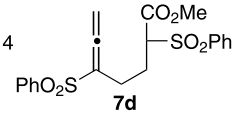
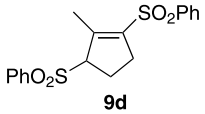
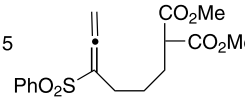
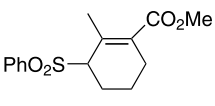
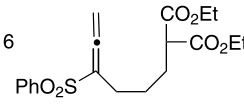
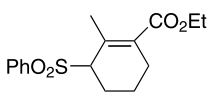
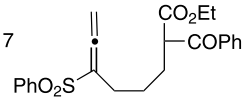
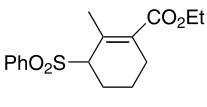
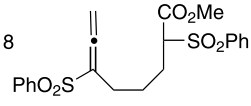
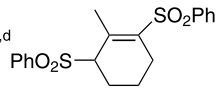
Table 2. Ring closure reaction of **7** and **8** with ^{t}BuOK in ^{t}BuOH[a]

entry	allene	time	product	yield (%)
1	 **7a**	5 min	 **9a**	84
2	 **7b**	5 min	 **9b**	93
3	 **7c**	5 min	 **9b**	93
4	 **7d**	3 h[b,c]	 **9d**	98
5	 **8a**	5 min	 **12a**	92
6	 **8b**	5 min	 **12b**	72
7	 **8c**	5 min	 **12b**	83
8	 **8d**	15 h[b,d]	 **12d**	80

[a] Allenes **7**, **8** were treated with ^{t}BuOK (1.5 equiv.) in ^{t}BuOH at rt. [b] Reaction was carried out in a combined solvent of ^{t}BuOH and THF (1:1) at 60°C. [c] When **7d** was treated with aq.KOH in THF at rt for 5 min, methyl 1,3-bis(phenylsulfonyl)-2-methylenecyclopentanecarboxylate was obtained in 83% yield. [d] When **8d** was treated with aq.KOH in THF at rt for 5 min, methyl 1,3-bis(phenylsulfonyl)-2-methylenecyclohexanecarboxylate was obtained in 98% yield.

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Cruciani, P.; Aubert, C.; Malacria, M. *Tetrahedron Lett*. **1994**, *35*, 6677; (e) McDonald, F. E.; Olson, T. C. *Tetrahedron Lett*. **1997**, *38*, 7691; (f) Tsukada, N.; Yamamoto, Y. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 2477. (g) Kitagawa, O.; Suzuki, T.; Inoue, T.; Taguchi, T. *Tetrahedron Lett*. **1998**, *39*, 7357; (h) Kadota, I.; Shibuya, A.; Gyoung, Y.; Yamamoto, Y. *J. Am. Chem. Soc*. **1998**, *120*, 10262; (i) Kitagawa, O.; Suzuki, T.; Inoue, T.; Watanabe, Y.; Taguchi, T. *J. Org. Chem*. **1998**, *63*, 9470; (j) Bouyssi, D.; Monteiro, N.; Balme, G. *Tetrahedron Lett*. **1999**, *40*, 1297; (k) Kitagawa, O.; Suzuki, T.; Fujiwara, H.; Fujita, M.; Taguchi, T. *Tetrahedron Lett*. **1999**, *40*, 4585; (l) Kitagawa, O.; Fujiwara, H.; Suzuki, T.; Taguchi, T.; Shiro, M. *J. Org. Chem*. **2000**, *65*, 6819, and references cited therein.

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10. The iodo derivative **4** was prepared according to the procedure described in Ref. 9.
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12. The structure of **9a** was unambiguously established on the basis of its spectral evidence. In particular, the IR spectrum of **9a** showed a carbonyl absorption band at 1712 cm^{-1}, which is in good accordance with that of ethyl 1-cyclopentenecarboxylate (1710 cm^{-1}) rather than that of its regioisomer, ethyl 2-cyclopentenecarboxylate (1730 cm^{-1}).[13]
13. Scharf, H.-D.; Korte, F. *Chem. Ber*. **1964**, *97*, 2425.
14. Other bases such as ^{t}BuOLi, MeOLi and aq. NaOH were also examined, but were found to be inferior to the ones listed in Table 1.
15. Similar demethoxycarbonylation was reported by Balme and co-workers[2b] during their investigation on the palladium-catalyzed *exo*-mode cyclization of dimethyl 5-hexyne-1,1-dicarboxylate and its analogues in the presence of ^{t}BuOK.
16. The simple explanation for demethoxycarbonylation of **10a** and **11a** might involve nucleophilic attack of the alkoxide on the cationic carbonyl center. However, the fact that a more sterically hindered *tert*-butoxide reacted much faster than methoxide and hydroxide can not be rationalized by the above assumption.
17. Debenzoylation preferentially occurred over deethoxycarbonylation (entries 3 and 7). Therefore, the other plausible mechanism for decarbonylation of the 1,3-dicarbonyl functionality, which would involve the attack of the alkoxide on the alkyl group of the ester functionality with liberation of carbon monoxide, can be ruled out. In addition, preferential deacetylation over demethoxycarbonylation was also reported under the palladium-catalyzed *exo*-mode cyclization of alkyne derivatives in the presence of ^{t}BuOK.[2b]