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LETTERS

Base-Promoted Ring Expansion of 2-Alkoxy-2-vinylbenzocyclobutenol into Substituted Naphthalene Derivatives

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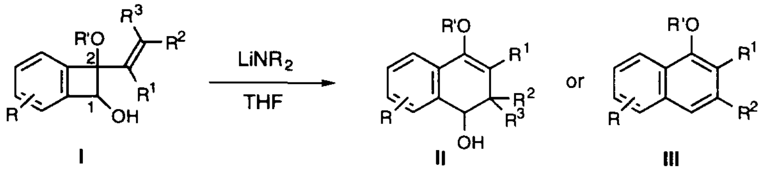
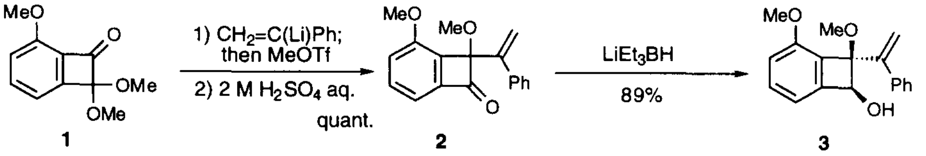
Abstract: Upon treatment with lithium dialkylamide, 2-alkoxy-2-vinylbenzocyclobutenols undergo two-carbon expansion to give substituted naphthalene derivatives.

We recently developed a flexible approach to various benzocyclobutenone/-dione derivatives via [2+2] cycloaddition of benzyne with ketene silyl acetals,[1] and became interested in exploiting the reactivities of the derived strained molecules.[2] Along these lines, we wish to report here the base-promoted ring expansion of benzocyclobutenols **I**, *i.e.* 2-vinylbenzocyclobutenols with an alkoxy group at C(2), which are easily accessible via the above method (eq. 1).[3–6]



(1)

The substrates (see Table 1) were prepared from benzocyclobutenones **1** or **8** (eqs. 2 and 3).[7,8] Addition of 1-phenylethenyllithium to **1** followed by *in-situ* trapping of the resulting alkoxide with methyl triflate (Et_2O, –78 →25 °C) and subsequent hydrolysis of the acetal gave ketone **2** quantitatively. Reduction of **2** with $LiBEt_3H$ (THF, –78 °C) proceeded in completely stereoselective manner to give alcohol **3** (eq. 2).



(2)

The cis relation with the hydroxy and the methoxy groups was assigned by an X-ray analysis.[8,9] Benzocyclobutenols **4**–**7** were obtained from **1** in a similar manner as a single isomer, respectively.[7,8] By adding 1-phenylethenyllithium to ketone **8** followed by methylation and desilylation, we prepared an

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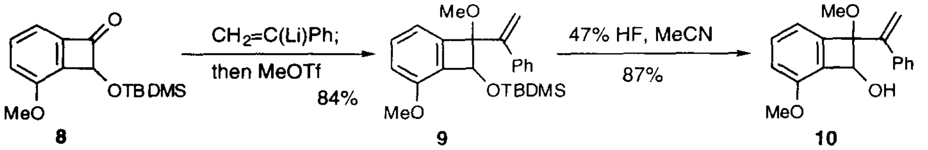
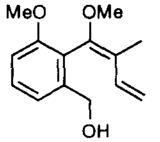
isomeric benzocyclobutenol **10** as a single stereoisomer, though the stereochemistry was not determined (eq. 3).



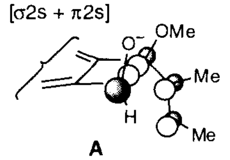
(3)

Screening of various basic conditions showed that lithium dialkylamides are quite effective in achieving the reaction mode shown in eq. 1. Upon treatment with LDA (1.2 equiv., THF, 0→25 °C), benzocyclobutenol **3** was smoothly converted to alcohol **11** in 91% yield (Table 1, run 1).[10] The alcohol **11** was much more stable than expected, allowing the isolation by silica-gel preparative TLC without dehydration. Alcohols **12–14** were also obtained in high yields by applying the similar reaction conditions to compounds **4–6** (runs 2–4).[10]

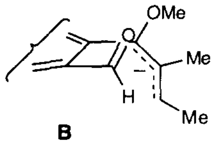
As shown in runs 3 and 4, the product composition proved different depending on the olefin geometry of the starting material. Benzocyclobutenol **5** gave *cis* alcohol **13** along with a small amount of *trans* alcohol **14**, whereas *trans* alcohol **14** was obtained as the sole product from **6**. In the latter case, a small amount (ca. 7%) of ring-opened product **17** was also obtained. These aspects gave us some insight into the mechanism. The process may be accounted by at least three mechanisms, although not discernible at present: (1) the [1,3]-sigmatropy, (2) the electrocyclic reaction via a quinodimethane, and (3) the ionic path via an allyl anion–aldehyde intermediate. Given the former two concerted paths, the stereochemistries of **13** in run 3 and **14** in run 4 are opposite to what are expected from the orbital-symmetry rule. However, it is known that an anionic substituent often facilitates the symmetrically forbidden pericyclic reactions.[11] Particularly many examples have been documented for [1,3]-sigmatropic shift that proceeds in a [σ2s + π2s] mode as shown in **A**.[5,11] The ionic mechanism may account the stereochemistry, given that the anion–aldehyde intermediate undergoes a rapid closure with keeping the geometry as shown in **B**.



17
(single isomer; the geometry undefined)

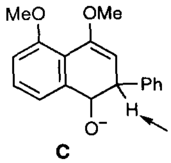


A

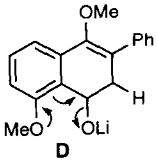


B

Under the same reaction conditions, benzocyclobutenols **7** and **10** gave the expected alcohols (not shown), which were, however, accompanied by a sizable amount of the corresponding aromatized products **15**, **16**, respectively. The formal dehydration occurs already in the basic reaction media, which could be ascribed to the oxido-elimination from the alkoxides formed (**C** for run 5, **D** for run 6), due to the enhanced acidity of the methine proton adjacent to the phenyl group in **C** or the electron donation from the *peri* methoxy group

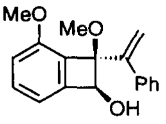
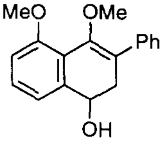
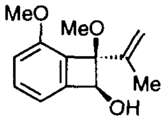
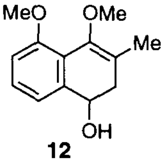
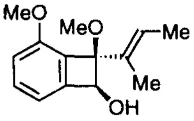
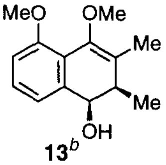
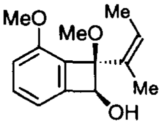
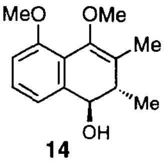
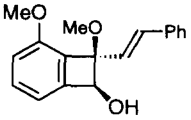
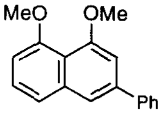
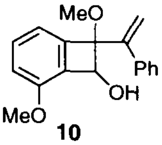
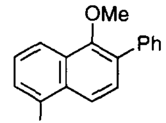


C



D

Table 1.

run	benzocyclobutenol	conditions	product	Yield/%[a]
1	 **3**	LDA, 3 h	 **11**	91
2	 **4**	LDA, 1.5 h	 **12**	74
3	 **5**	LDA, 4 h	 **13**[b]	89[c] (**13**:**14** = 14:1)
4	 **6**	LDA, 1.5 h	 **14**	78[d]
5	 **7**	LiTMP, 2.5 h	 **15**	73
6	 **10**	LiTMP, 2.5 h	 **16**	93

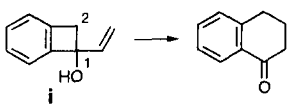
a) Isolated yield. b) The stereostructure was determined by X-ray analysis.[9] c) Combined yield of **13** and **14**. d) Single stereoisomer was detected.

in **D**.[12] As all attempts to suppress this elimination had failed, we rather sought the conditions to complete the elimination to obtain naphthalenes **15** and **16** as the products, which was achieved by using an excess amount of lithium tetramethylpiperidide (3 equiv.).

In summary, 2-vinylbenzocyclobutenol possessing a C(2) alkoxy group undergoes two-carbon expansion of the cyclobutene ring promoted by lithium dialkylamide, which permits a facile synthesis of substituted naphthalene derivatives. Further studies are currently under way in our laboratories.

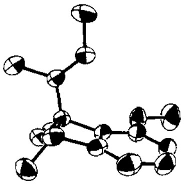
REFERENCES AND NOTES

1. Hosoya, T.; Hasegawa, T.; Kuriyama, Y.; Matsumoto, T.; Suzuki, K. *Synlett* **1995**, 177. Hosoya, T.; Hasegawa, T.; Kuriyama, Y.; Suzuki, K. *Tetrahedron Lett.* **1995**, *36*, 3377.
2. *Small Ring Compounds in Organic Synthesis I–IV*; de Meijere, A., Ed.; Topics in Current Chemistry; Springer: Berlin.
3. The rearrangement of the 1-vinyl benzocyclobutenol derivatives **i** to α-tetralones has been nicely exploited by Wallace *et al.* (a) For recent examples, see: Hickman, D. N.; Hodgetts, K. J.; Mackman, P. S.; Wallace, T. W.; Wardleworth, J. M. *Tetrahedron* **1996**, *52*, 2235. Hickman, D. N.; Wallace, T. W.; Wardleworth, J. M. *Tetrahedron Lett.* **1991**, *32*, 819. (b) For related reactions, see: Moore, H. W.; Yerxa, B. R. *Chemtracts* **1992**, *5*, 273. Swenton, J. S.; Anderson, D. K.; Jackson, D. K.; Narasimhan, L. *J. Org. Chem.* **1981**, *46*, 4825. Winters, M. P.; Stranberg, M. Moore, H. W. *J. Org. Chem.* **1994**, *59*, 7572.

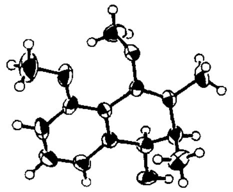


i

4. The rearrangement of the parent 2-vinylcyclobutenols, not condensed with an aromatic ring, has been well studied. (a) Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron* **1981**, *23*, 3943. (b) Cohen, T.; Bhupathy, M.; Matz, J. R. *J. Am. Chem. Soc.* **1983**, *105*, 520. Bhupathy, M.; Cohen. T. *J. Am. Chem. Soc.* **1983**, *105*, 6978. (c) Snider, B. B.; Niwa, M. *Tetrahedron Lett.* **1988**, *29*, 3175.
5. For recent reviews on charge-accelerated rearrangements, see: Wilson, S. R. *Org. React.* (N. Y.) **1993**, *43*, 93. Bronson, J. J.; Danheiser, R. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, p 999.
6. For examples of the mechanistically related methods, which involve this type of conversion as an elementary reaction, see: Brunet, J. J.; Essiz, M.; Caubere, P. *Tetrahedron Lett.* **1974**, 871. Sammes, P. G.; Wallace, T. W. *J. Chem. Soc., Perkin I* **1975**, 1377. Sibi, M. P.; Dankwardt, J. W.; Snieckus, V. *J. Org. Chem.* **1986**, *51*, 273.
7. Preparation of each compounds will be reported elsewhere.
8. Stereostructures of **3**, **5**, and **7** were confirmed by X-ray (for **3** and **5**) or NOE analyses (for **7**).[9] Stereostructures of **4** and **6** were deduced from these data.
9. We thank Drs. Takashi Tsuji and Kohki Ishikawa, Ajinomoto Co., and Ms. Sachiyo Kubo, Tokyo Institute of Technology, for X-ray analyses. The *ORTEP* drawings of **5** and **13** are shown below.



5



13

10. Other lithium dialkylamides gave comparable results [e.g., yields for **4**→**12**: LiNEt$_2$ (70%), LiTMP (73%)], whereas the corresponding potassium amides failed to promote the desired rearrangement.
11. Berson, J. A. *Acc. Chem. Res.* **1972**, *5*, 406, and also Carpenter, B. K. *Tetrahedron* **1978**, 1877.
12. Mechanistic details of this "formal dehydration" will be discussed in a full account.