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THE REGIOCHEMISTRY OF THE *o*-CLAISEN REARRANGEMENT OF *BIS*-(ALLOXY)POLYCYCLIC AROMATICS[§]

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Abstract – The *o*-Claisen rearrangement of *bis*-(allyloxy) naphthalenes, anthracenes and phenanthrenes is regiospecific and is consistent with resonance theory and molecular orbital calculations.

While the *o*-Claisen rearrangement of allyl phenyl ethers has been rigorously studied,[1] the rearrangement of *bis*-allyl aryl ethers has been limited to the ethers of hydroquinone (**1**),[2] resorcinol (**2**),[3] and 2,6-dihydroxynaphthalene (**3**).[4] As shown in Scheme 1, the rearrangement of *bis*-1,4-(allyloxy)benzene (**1**) gives two isomeric *o*-Claisen rearrangement products, whereas the rearrangements of *bis*-1,3-(allyloxy)benzene (**2**) and *bis*-2,6-(allyloxy)naphthalene (**3**) give single products (an asterisk indicates an available *ortho* position). Because we required various allyl substituted anthracenes and phenanthrenes for other projects, the rearrangement of the *bis*-allyl ethers of sixteen polycyclic aromatic compounds was investigated.

Scheme 1

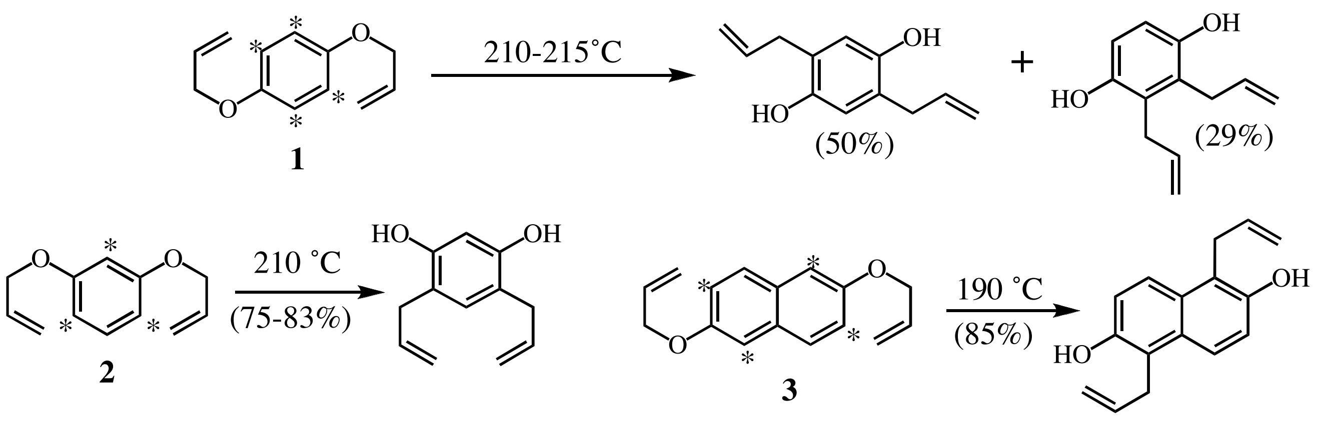
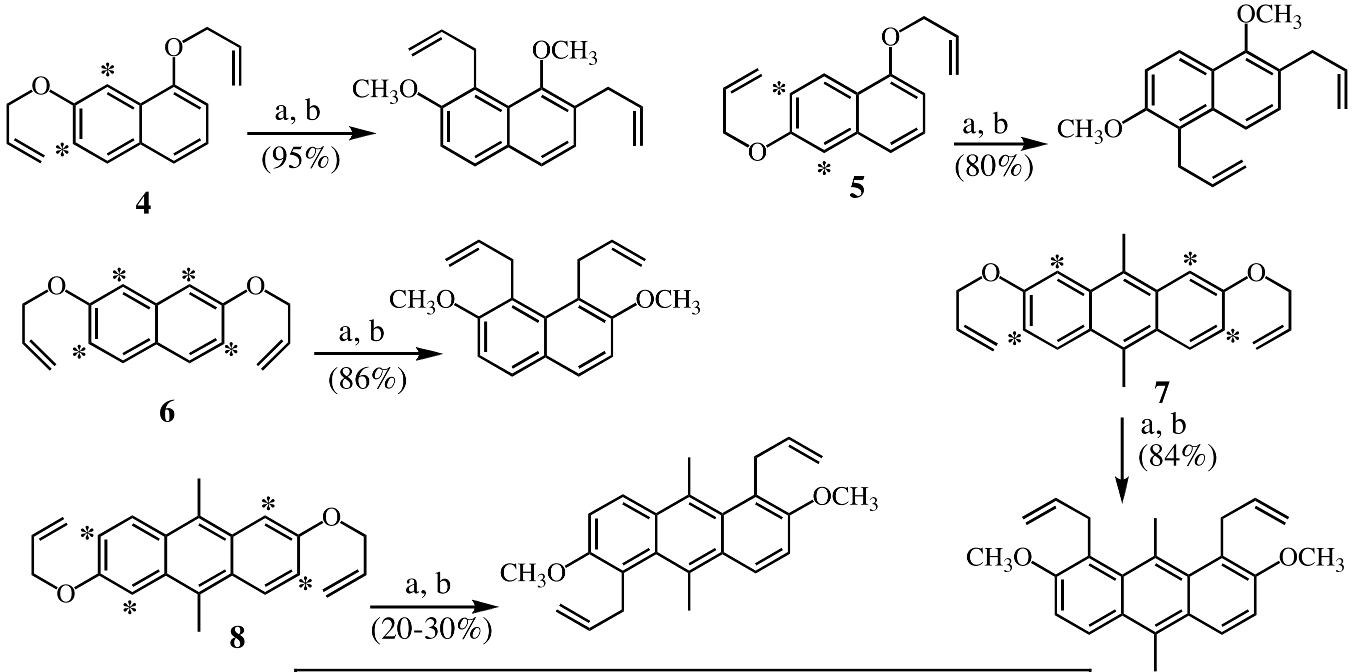


Chart 1 presents the results obtained from the thermolysis of three *bis*-(allyloxy)naphthalene derivatives and two *bis*-(allyloxy)anthracene derivatives. In order to preclude decomposition, the crude rearrangement product was methylated prior to isolation and characterization.[5-8] Please note that ethers **4** and **5** can give rise to two isomeric products, while substrates **6**, **7** and **8** can rearrange to any of three isomeric products. Nevertheless, the sigmatropic rearrangement of each *bis*-ether shown produced a single rearranged product. Unfortunately, the rearranged product of *bis*-ether **8** decomposes under the reaction conditions required for rearrangement;[9] this low yield contrasts with the high overall yield obtained for each of the other rearrangements.

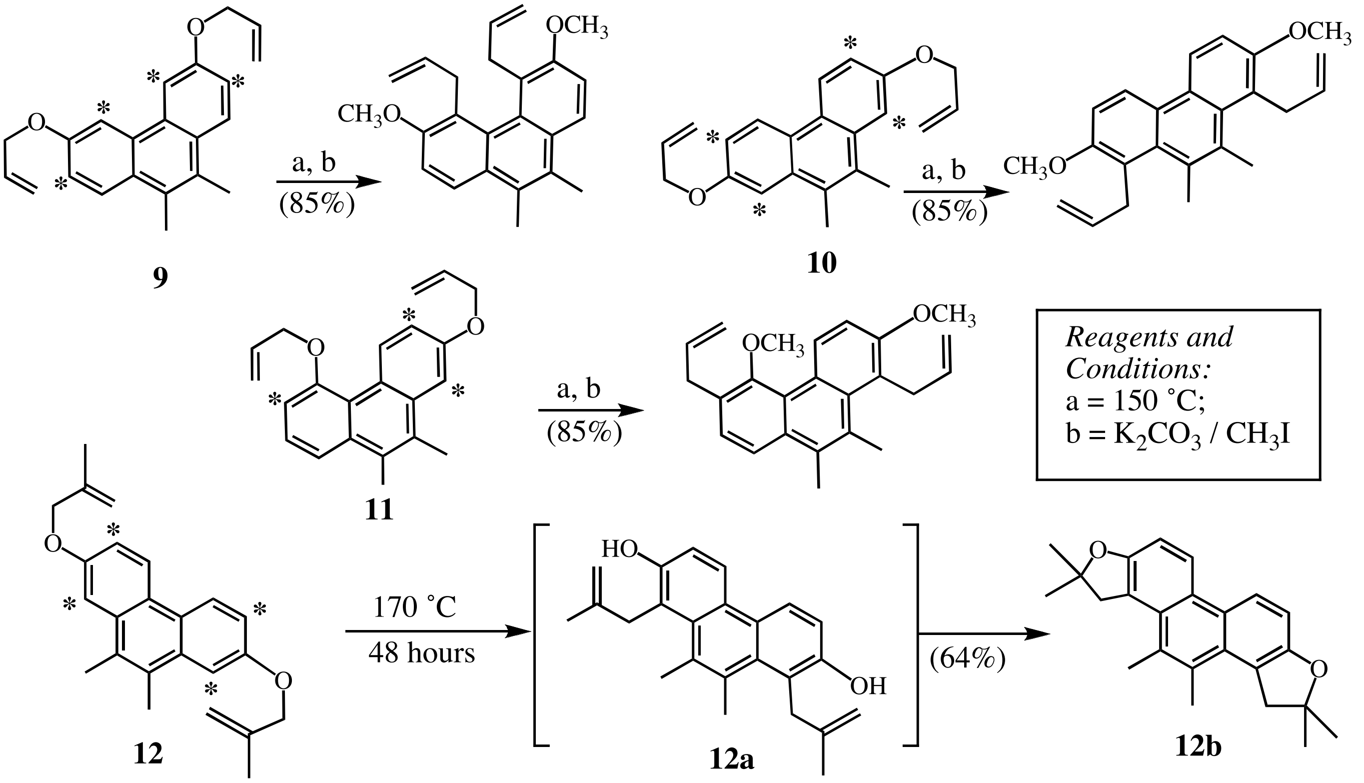
Chart 1



Reagents and Conditions: a = 150 °C; b = K_2CO_3 / CH_3I

The *o*-Claisen rearrangement of phenanthrene-based *bis*-allyl ethers was also studied (Chart 2). Although several possible phenanthrene derivatives can be envisioned, *bis*-allyl ethers **9**-**12** were the focus of our study.[10] The regiospecific rearrangement of *bis*-ether **9** is particularly interesting since both benzylic sites are extremely crowded. In order to expand the scope of these rearrangements, a more substituted allyl ether, i.e. **12**, was synthesized. However, under the lengthy reaction conditions employed and despite the presence of a base in the reaction medium, the rearrangement of *bis*-ether **12** gave a single *bis*-dihydrofuran (cf. **12b**), formed by protonation of the disubstituted double bonds present in rearranged product **12a**, followed by ring closure. We speculated that shorter reaction times might minimize the formation of the dihydrofuran products. However, heating of naphthalene ethers **13** and **14** for only

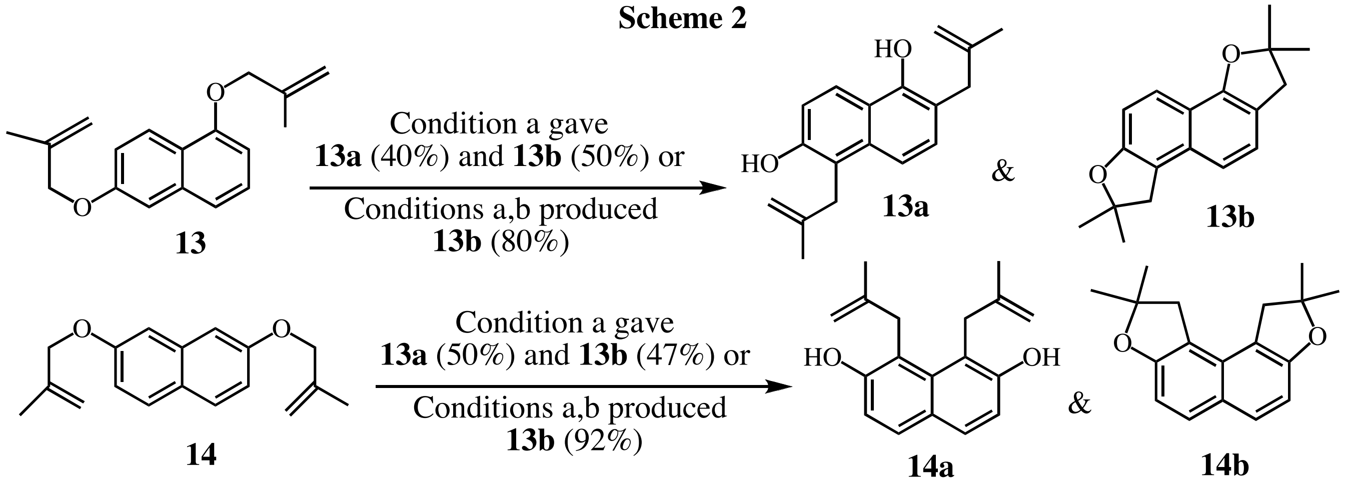
Chart 2



Reagents and Conditions:
a = 150 ˚C;
b = K_2CO_3 / CH_3I

twenty-four hours produced heterocycles **13b** and **14b** in 50% yield, and 40-50% yield of the rearranged products **13a** and **14a** (Scheme 2). The yield for the formation of the heterocycles was improved by simply treating the crude rearrangement product with mild acid and mild warming.

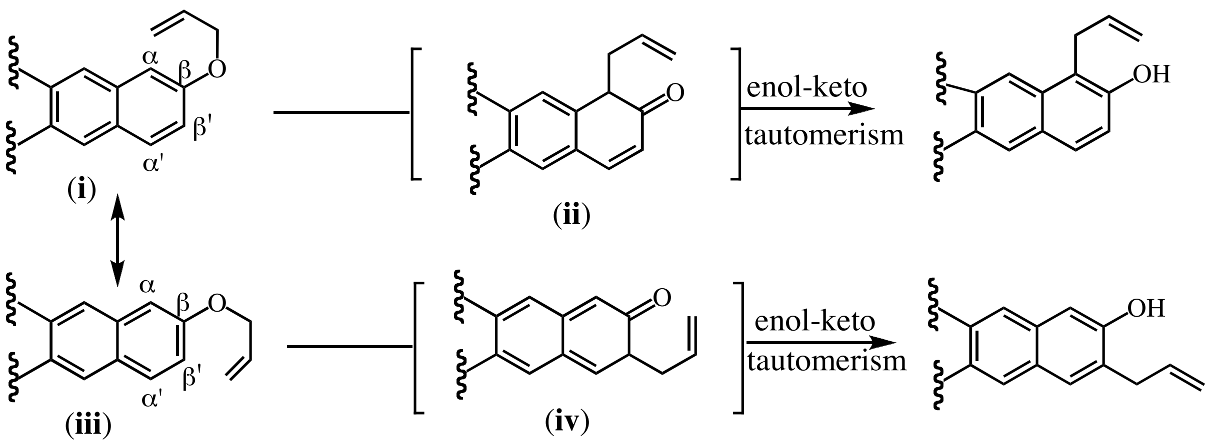
Scheme 2



Reagents and Conditions: a = 170 ˚C, 24 hours; b = TsOH, benzene, reflux 30 minutes

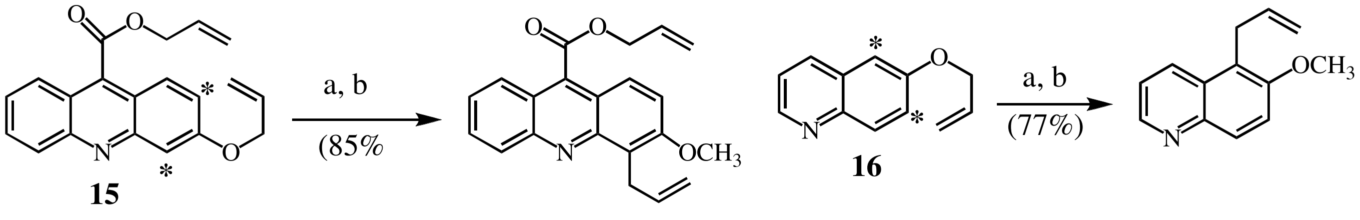
The above results indicate that when there is a choice between two unsubstituted *ortho* positions, the rearrangement always occurs at the α-position. This regioselectivity can be explained by considering the aromaticity of the ketone intermediate that is generated *in situ* (Scheme 3). For example, rearrangement towards the α-position (cf. **ii**) preserves the aromaticity in the fused ring, whereas rearrangement towards the β'-position generates a non-aromatic initial ketone (cf. **iv**), making this a higher energy intermediate and therefore a less likely reaction pathway. Alternatively, *ab inito* calculations show bond orders of 1.724 and 1.603 for the α,β- and β,β'- bonds of naphthalene, respectively,[10] thus indicating that the α,β-bond (cf. **i**) has more double bond character than does the β, β'-bond (cf. **iii**).

Scheme 3



The regioselectivity of the *o*-Claisen rearrangement of allyl ethers of heterocyclic polycyclic aromatics such as substrates **15** and **16** is consistent with this analysis (Scheme 4). The synthetic utility of this work is forthcoming.

Scheme 4



Reagents and Conditions: a = 150 °C; b = K_2CO_3 / CH_3I

ACKNOWLEDGEMENTS

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REFERENCES AND NOTES

§ Dedicated to Professor Yoshito Kishi on the occasion of his 70th birthday

† Taken in part from the MS thesis of Scott H. Allen, the *University of Georgia* (1997) and from the

Ph.D. dissertation of Yang Li, the *University of Georgia* (2006).

1. M. Hiersemann, 'The Claisen Rearrangement: Methods and Applications,' Wiley-VCH, 2007.
2. L. F. Fieser, W. P. Campbell, and E. M. Fry, *J. Am. Chem. Soc.*, 1939, **61**, 2206.
3. C. D. Hurd, H. Greengard, and F. D. Pilgrim, *J. Am. Chem. Soc.*, 1930, **52**, 1700; S. Nikiforova and S. Mel'kanovitskaya, *Zhurnal Organicheskoi Khimii*, 1966, **2**, 1240.
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5. The spectroscopic data obtained for all new compounds were fully consistent with the assigned structures. Reaction conditions have not been optimized. All yields are isolated yields.
6. The synthesis of the *bis*-allyl ethers was achieved by heating the requisite diol[7-10] with 2.50 equivalents of freshly distilled allyl chloride and 4.00 equivalents of K_2CO_3 in anhydrous DMF at 50°C overnight. The [3,3]–sigmatropic rearrangements were achieved by dissolving the *bis*-ether in an equal amount of diethylaniline; the resulting mixture was placed in a sealed tube, heated for 12h, cooled, and then subjected to standard ethereal workup. The crude phenolic product was methylated using a standard procedure, see: A. R. Mackenzie, C. J. Moody, and C. W. Rees, *Tetrahedron*, 1986, **42**, 3259.
7. For the preparation of 1,7-naphthalenediol (cf. *bis*-ether **4**) see: C. G. Sims and D. Wege, *Aust. J. Chem.*, 1992, **45**, 1983. 1,6- and 2,7-Naphthalenediol (cf. *bis*-ethers **5** and **6**) are commercially available.
8. For the preparation of 2,7-dihydroxy-9,10-dimethylanthracene (cf. *bis*-ether **7**) see: J. Hall and A. G. Perkin, *J. Chem. Soc., Perkin*, 1923, **1237**, 2029. 2,6-Dihydroxy-9,10-dimethylanthracene was prepared from anthraflavic acid using the same synthetic route.
9. All attempts to produce 2,6-dihydroanthracene by reducing the carbonyls of anthraflavic acid, followed by reductive aromatization using aluminium amalgam, failed due to the thermal instability of the product, see: M. A. Petti, T. J. Shepodd, R. E. Barrans, Jr., and D. A. Dougherty, *J. Am. Chem. Soc.,* 1988, **110**, 6825.
10. *p*-Methoxyactophenone was converted in three steps into 3,6-dihydroxy-9,10-dimethylphenanthrene (cf. *bis*-ether **9**), see: J. Leimner and P. Weyerstahl, *Chem. Ber.*, 1982, **115**, 3697; M. R. Schnerder and C. D. Schiller, *Arch. Pharm. (Weinheim, Germany)*, 1987, **320**, 159; T. D. Doyle, N. Filipescu, W. R. Benson, and D. Banes, *J. Am. Chem. Soc.,* 1970, **92**, 6371. Applying the same set of reactions to 3-methoxyacetophenone gave a 1:4 mixture of 2,7- (cf. *bis*-ether **10**) and 2,5-dimethoxy-9,10-dimethylphenanthrene (cf. *bis*-ether **11**), respectively, which were separated by chromatography. Deprotection of the methyl ethers, followed by protection with excess of allyl chloride, gave *bis*-allyl ethers **10** and **11**.
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