Stereocontrolled Synthesis of 3-Acyl-4-alkoxy-5-aryl-1,2,4(*E*)-pentatrienes and Their Subsequent Electrocyclization to Naphthalenes

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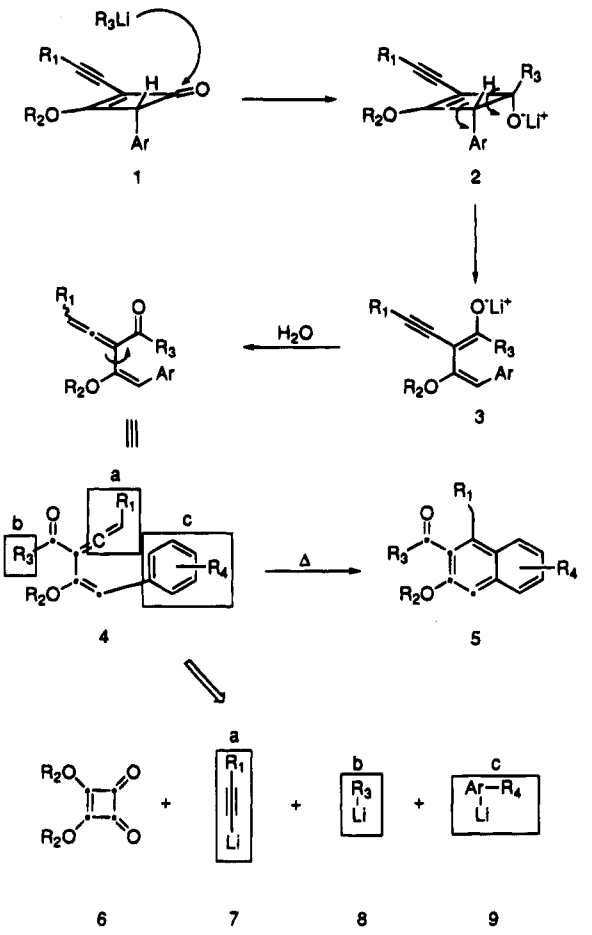
Reported herein is a stereocontrolled synthesis of 3-acyl-4-alkoxy-5-aryl-1,2,4(*E*)-pentatrienes (conjugated allenes) from 2-alkynyl-4-arylcyclobutenones and their subsequent, thermally induced, electrocyclization to naphthalenes.[1] This method is of synthetic and mechanistic importance and adds to the emerging efforts in the regiospecific construction of annulation precursors to highly substituted aromatic systems. The reaction specifically demonstrates that squaric acid derivatives are a valuable component in the synthetic arsenal and that this value stems from the circumvention of difficulties in convergency and regiochemistry control found in conventional electrophilic and nucleophilic substitution reactions.[2,3]

The generalized reactions are envisioned to proceed through the following sequence (Scheme 1): (1) facial selective addition of a lithium reagent to 2-alkynyl-4-arylcyclobutenones **1** results in a lithium alkoxide **2** that undergoes a low temperature oxy-anion accelerated conrotatory electrocyclic ring opening with outward rotation of the alkoxide oxygen;[4,5] (2) protonation at the alkynyl terminus of the resulting enolate **3** results in the isolable arylenylallene **4**;[6] (3) the *E*-stereochemistry of the arylalkene component allows a 6π electrocyclization to afford the corresponding naphthalene **5**, upon mild thermolysis and subsequent tautomerization. Overall, the naphthalenes and/or allenes translate to a dialkylsquarate **6** and

Scheme 1



the alkynyl-, alkyl-, and aryllithium reagents, respectively, **7**, , **8**, and **9**.

The above transformations stem from 3-alkoxy-4-alkynylcyclobutenediones **10**, which are readily accessible from dialkylsquarates (e.g., diisopropylsquarate) by previously reported methods.[7] Regiospecific addition of aryllithium reagents to cyclobutendiones **10** resulted in 4-aryl-4-hydroxycyclobutenones **11.** The initial study of the ring opening reaction was limited to the reduced form of the hydroxycyclobutenones **11**, which were selectively reduced with triethylsilane in the presence of Lewis acids to give the cyclobutenones **1** in good yields (67–90%) (Scheme 2).[8] Conversion to the corresponding allenes **4** was realized upon addition of an organolithium reagent (R_2Li, 1.1 equiv) at ca. −78 °C in THF.

The electronically and stereochemically predisposed conjugated allenes **4** undergo facile electrocyclic ring closure to naphthalenes **5** when heated in refluxing toluene or *p*-xylenes (Scheme 3). Stereochemical factors favoring cyclization have already been noted, however, the electronic factors merit further comment. An electron deficient allene component is likely required and is provided by the appended acyl group. Complementing this electron deficiency is an electron rich arylethenyl

(1) For other syntheses of dienylallenes and their synthetic applications see: (a) Bross, H.; Schneider, R.; Hopf, H. *Tetrahedron Lett.* **1979**, *23*, 2129–2132. (b) Balme, G.; Malacria, M.; Gore, J. *Tetrahedron Lett.* **1979**, *1*, 7–10. (c) Andemichael, Y. W.; Wang, K. K. *J. Org. Chem.* **1992**, *57*, 796–798. (d) Ezcurra, J. E.; Pham, C.; Moore, H. W. *J. Org. Chem.* **1992**, *57*, 4787–4789.

(2) For reviews and selected examples of aromatic annulation reactions see: (a) Bamfield, P.; Gordon, P. F. *Chem. Soc. Rev.*, **1984**, *13*, 441. (b) Wedenmeyer, K. F. in *Methoden der Organischen Chemie (Houben-Weyl);* Muller, E., Ed.; George Theime: Stuttgart, 1976; Vol. 6/1c, pp 853–924. (c) Snowden, R. L.; Wust, M. *Tetrahedron Lett.*, **1986**, *27*, 703. (d) Boger, D. L.; Mullican, M. D. *Org. Synth.* **1987**, *65*, 98. (e) Ziegler, T.; Layh, M.; Effenberger, F. *Chem. Ber.* **1987**, *120*, 1347. (f) Tius, M. A.; Gomez-Galeno, J. *Tetrahedron Lett.* **1986**, *27*, 2571. (g) Chan, T. H.; Prasad, C. V. C. *J. Org. Chem.* **1986**, *51*, 3012. (h) Volhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539. (i) Dotz, K. H.; Fischer, H.; Hofmann, P.; Kriessel, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlog Chemie International: Deerfield Beach, FL, 1984. (j) Dotz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587. (k) Wulff, W. D. In *Advances in Metal-Organic Chemistry*, Liebeskind, L. S., Ed.; JAI Press Inc.: Greenwich, CT, 1989; Vol. 1.

(3) For reviews on the ring expansions of cyclobutenones see: (a) Moore, H. W.; Yerxa, B. R. *Chemtracts* **1992**, *5*, 273. (b) Moore, H. W.; Decker, O. H. W. *Chem. Rev.* **1986**, *86*, 821. (c) Liebeskind, L. S. *Tetrahedron* **1989**, *45*, 3053. (d) Bellus, D.; Ernst, B. *Angew Chem.* **1988**, *100*, 820.

(4) For an example of an oxy-anion accelerated ring opening of a cyclobutenone see: Negri, J. T.; Morwick, T.; Doyon, J.; Wilson, P. D., Hickey, E. R.; Paquette, L.A. *J. Am. Chem. Soc.* **1993**, *115*, 12189–12190.

(5) Rodan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2099–2111.

(6) For an example of an α-oxo-ketene generated from a homoacetylenic ketone see: Covey, D. F.; Robinson, C. H. *J. Am. Chem. Soc.* **1976**, *98*, 5038.

(7) (a) Perri, S. T.; Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1986**, *51*, 3067. (b) Liebeskind, L. S.; Jewell, C. F.; Iyer, S. *J. Org. Chem.* **1986**, *51*, 3065. (c) Perri, S. T.; Moore, H. W. *J. Am. Chem. Soc.* **1988**, *53*, 996. (d) Liebeskind, L. S; Fengl, R. W.; Wirtz, K. R.; Shawe, T. T. *J. Org. Chem.* **1988**, *53*, 2482–2488.

(8) The inability of the alkyne to stabilize an α cation in the cyclobutenyl cation intermediate allows for selective hydride capture at the benzylic site. Turnbull, P.; Moore, H. W. *J. Org. Chem.* **1995**, *60*, 644–649.

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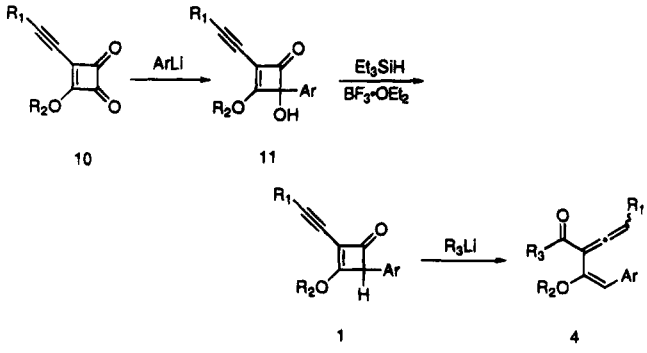
Scheme 2



entry	R_1	R_2	Ar	R_3Li	product	yield%
1	*n*-Bu	*i*-Pr	Ph	*n*-BuLi	4a	80
2	*n*-Bu	*i*-Pr	Ph	PhLi	4b	65
3	CH_2OMe	*i*-Pr	Ph	*n*-BuLi	4c	62
4	*n*-Bu	Me	3,4-dimethoxy	*n*-BuLi	4d	88
5	*n*-Bu	*i*-Pr	2,4-dimethoxy	*n*-BuLi	4e	84
6	*n*-Bu	*i*-Pr	2,5-dimethoxy	*n*-BuLi	4f	80

group whose alkoxy substituent provides electron donation to the aryl substituent. In agreement with these favorable features is the observation that those cumulenes bearing electron rich aryl groups cyclize at lower temperatures in the same amount of time (refluxing toluene [111 °C], 10–20 min, entries 4–6) than those bearing an unsubstituted phenyl group (refluxing *p*-xylene [138 °C], 10–30 min, entries 1–3).

In summary, an efficient method has been described that further demonstrates the synthetic viability of squaric acid derivatives as precursors to a wealth of highly substituted aromatic systems. The ability to synthesize cyclobutenones hosting a variety of functional groups allows for further exploitation of the ring expansions outlined here. Details of these studies are forthcoming.

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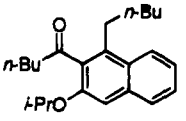
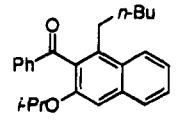
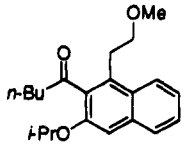
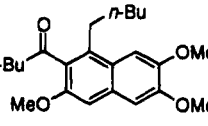
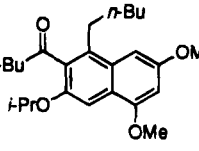
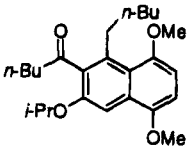
Scheme 3

entry	allene	product	yield%
1	5a		88
2	5b		63
3	5c		61
4	5d		89
5	5e		75
6	5f		75

Supplementary Material Available: General experimental procedures and characterization data are given (9 pages).

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