Communications

A New Photoannulation Reaction of 2-Aryl-3-alkoxy-1,4-naphthquinones. Synthesis of Dimethylnaphthgeranine E

Thomas J. Onofrey, Dario Gomez, Michael Winters, and Harold W. Moore*

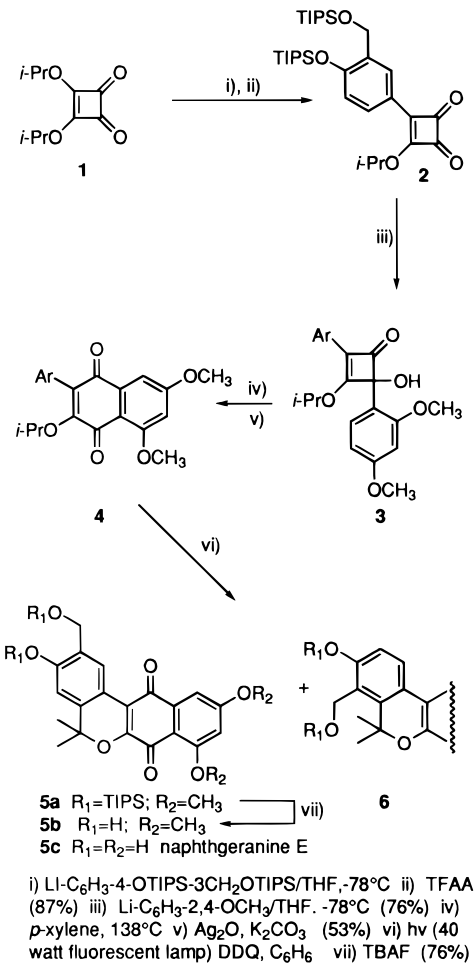
Department of Chemistry, University of California at Irvine, Irvine, California 92697

Received February 28, 1997

Reported here is the synthesis of the pyranonaphthoquinone **5b**, a dimethyl analog of naphthgeranine E (**5c**), a member of a family of bioactive naturally occurring naphthoquinones found in *Streptococcus violaceous*.[1] Key to this synthesis are the utility of the thermally induced ring expansion of 4-arylcyclobutenones for the regiospecific synthesis of 2-aryl-3-isopropoxy-1,4-naphthoquinones and a new photoannulation reaction of quinones of this structural type for the construction of the pyranonaphthoquinone nucleus.[2,3]

Cyclobutenedione **2** (87%) was prepared in a "one-pot" reaction sequence involving 1,2-addition of 5-lithio-2-(triisopropylsiloxy)benzyl triisopropylsilyl ether to diisopropyl squarate (**1**) followed by trifluoroacetic anhydride (TFAA) and aqueous workup (Scheme 1).[4] Regiospecific addition of 4-lithio-1,3-dimethoxybenzene to the more reactive carbonyl group in **2** gave cyclobutenone **3** in 76% yield. Thermolysis of **3** (*p*-xylene, 138 °C) followed by oxidation (Ag_2O) provided naphthoquinone **4** (53%). Photolysis (2 × 40 W fluorescent lamps) of a benzene solution of **4** at ambient temperature in the presence of a 5-fold excess of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave **5a** and its regioisomer **6** in 82% yield as a 1:1 mixture. Finally, desilylation of **5a** (TBAF) provided **5b** (76%).[5]

Scheme 1



The above photoannulation reaction is noteworthy since it appears to have little precedence in the literature.[3] A proposed mechanism is presented in Scheme 2 as it applies to the conversion of 3-isopropoxy-2-phenyl-1,4-naphthoquinone[6] (**7**) to the pyranonaphthoquinone **12** in 87% yield. Visible light excitation of **7** is envisaged to lead to zwitterionic (or diradical) intermediate **8**. Proton transfer from the methine carbon of the isopropoxy group to the adjacent carbonyl with concomitant aromatization would then give **9**. Intramolecular ring closure to the proposed *o*-quinone methide **10** followed by tautomerization provides hydroquinone **11**. Subsequent DDQ oxidation of **11** provides quinone **12**.[7]

The presence of excess DDQ (5 equiv) is required in order to maximize the yield of **12**. Indeed, if this high potential quinone is absent, not only do the yields of the pyranoquinone suffer, but a significant amount of the hydroquinone of **7** is realized. A reasonable pathway to account for this would involve oxidation of **11** by the starting quinone **7**. Thus, DDQ converts **11** to **12** during the course of the photolysis, thereby preventing the consumption of **7** by the nonphotolytic oxidation/reduction pathway suggested above.

The scope of the photoannulation was further probed and found to have useful generality. Specifically, alkoxyquinone analogs[6] **13a**, **13b**, **7**, and **15** give the respective annulated quinones **14a** (27%), **14b** (38%), **12** (83%), and **16** (80%) when subjected to the above reaction conditions (Scheme 3). The lower yields observed for **14a,b** as compared to **12** and **16** point to the possible importance of radical (or carbocation) stabilization of the intermediate (e.g. **9**) to the efficiency of the reaction.

In conclusion, we wish to make the following significant points: (1) For the first time, a direct analog of a member

(1) .Zeeck, A.; Wessels, P.; Gohrt, A.; Drautz, H.; Zahner, H. *J. Antibiot.* **1991**, *44*, 1013.

(2) For a review on the ring expansions of cyclobutenones see: Moore, H. W.; Yerxa, B. R. *Synthetic Utility of Cyclobutenones: Advances in Strain in Organic Chemistry*; JAI Press Inc.: Grenwich, CT, 1995; Volume 4.

(3) For a review on the photolysis of quinones see: Maruyama, K.; Osuka, A. *Chemistry of the Quinonoid Compounds*; Patai, S., Ed., Wiley: New York, 1988; Vol. II.

(4) Gayo, L. M.; Winters, M. P.; Moore, H. W. *J. Org. Chem.* **1992**, *57*, 6896.

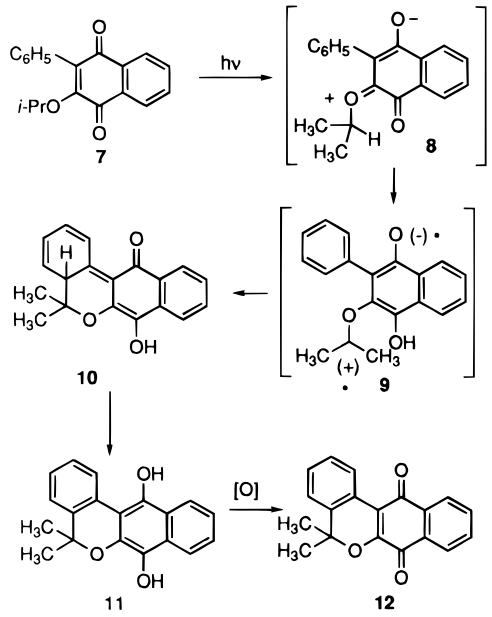
(5) The structures of the new compounds reported here are in strict agreement with their spectral and analytical properties.

(6) In direct analogy to the preparation of **4**, quinones **7**, **12a**, **12b**, and **14** were prepared from the corresponding dialkyl cyclobutenediones. Consult the Supporting Information for experimental details on **7**, **12a**, **12b**, and **14** and all intermediates.

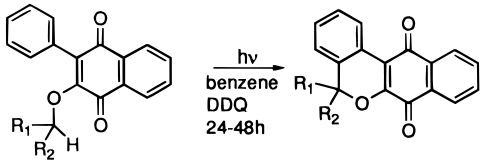
(7) Radical−radical (or ion−ion) combination is apparently more favorable than the stereoelectronically less favorable endo−trig ring closure between the carbenium ion center and the adjacent phenolic hydroxyl group.

S0022-3263(97)00385-X CCC: $14.00

Scheme 2

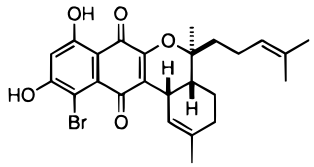


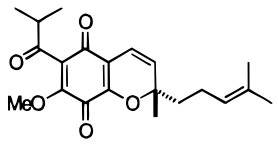
Scheme 3

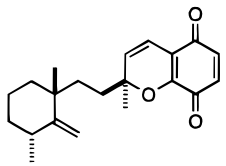


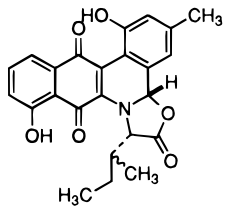
13a $R_1=R_2=H$
13b $R_1=CH_3$, $R_2=H$
7 $R_1=R_2=CH_3$
15 $R_1=CH_2Ph$, $R_2=H$
14a $R_1=R_2=H$ (27%)
14b $R_1=CH_3$, $R_2=H$ (38%)
12 $R_1=R_2=CH_3$ (83%)
16 $R_1=Ph$, $R_2=H$ (80%)

of the naphthgeranine family of natural products has been synthesized. (2) A key step in the synthetic scheme is a new and facile photoannulation reaction of 2-aryl-3-alkoxy-1,4-naphthoquinones. (3) Also, key to the synthesis is the thermal rearrangement of 4-arylcyclobutenones, thus further illustrating this ring expansion as a general, regiospecific route to highly substituted aromatic compounds.[2] (4) Finally, the synthetic strategy employing the key cyclobutenone/quinone synthesis and photoannulation reaction as outlined here can be envisaged to be applicable to the synthesis of other natural quinones as represented by marinone (**17**),[8] helinudchromene quinone(**18**),[9] metachromin E(**19**),[10] and jadomycin (**20**).[11]


marinone (**17**)


helinudchromene (**18**)


metachromin E (**19**)


jadomycin (**20**)

Acknowledgment. The authors thank the National Institutes of Health (GM-36312) for financial support of this research. We are also grateful to SmithKline Beecham for a generous sample of squaric acid.

Supporting Information Available: Experimental procedures and compound characterization data (6 pages).

JO970385C

(8) Pathirana, C.; Jensen, P. R.; Fenical, W. *Tetrahedron Lett.* **1992**, *33*, 7663.
(9) Jakupovic, J.; Kuhnke, J.; Schuster, A. *et al. Phytochemistry* **1986**, *25*, 1133.
(10) Kobayashi, J.; Haitoh, K.; Sasaki, T.; Shegemori, H. *J. Org. Chem.* **1992**, *57*, 5773.
(11) Ayer, S. W.; McInnes, G.; Thibault, P.; Walter, J. A.; Doull, J. L.; Parnell, T.; Vinning, L. C. *Tetrahedron Lett.* **1991**, *32*, 6301.