Chinese Chemical Letters Vol. 16, No. 8, pp 1024-1026, 2005
http://www.imm.ac.cn/journal/ccl.html

The First Total Synthesis of Triprenylquinone and Hydroquinones

Chun Hong LI, Xue Song CHEN, Guang Lian ZHOU, Zhi Xiang XIE, Ying LI*

National Laboratory of Applied Organic Chemistry, Institute of Organic Chemistry,
Lanzhou University, Lanzhou 730000

Abstract: First total synthesis of triprenylquinone and hydroquinones, three naturally occurring compound **1**, **2** and (±) **3**, have been achieved from readily available 2-bromo-5-methyl-1, 4-dimethoxybenzene **4** and geranyl bromide. The triprenylquinone and hydroquinones precursor were readily prepared with use of a Julia reaction.

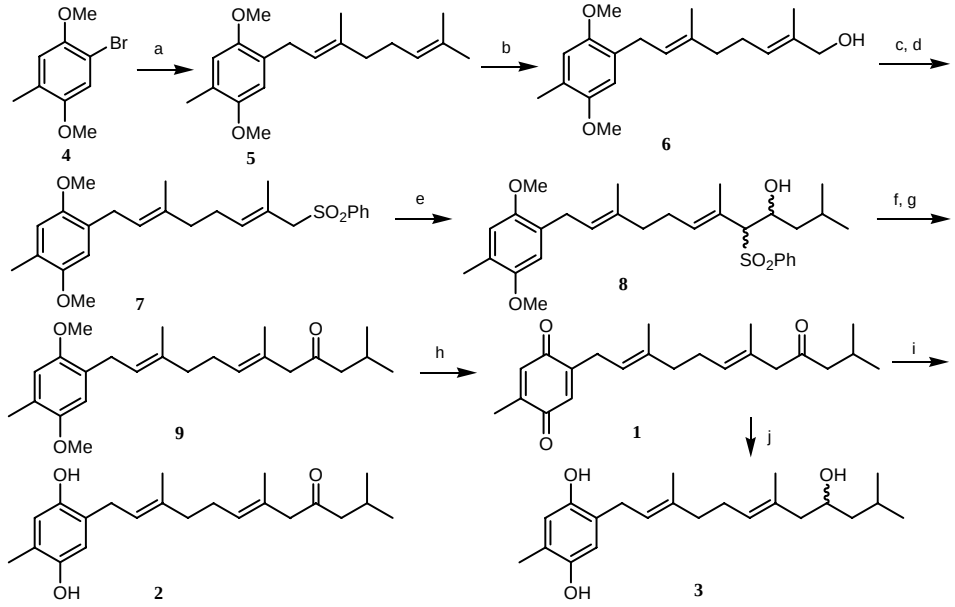
Keywords: Sesquiterpene triprenylquinones and hydroquinones, total synthesis, Julia coupling.

Marine natural products have received much attention for their attractive structural features and biological activities[1]. Since the isolation of the moritoside, about 10 related triprenylquinones and hydroquinones were isolated. Some of these natural products exhibit interesting biological effects including inhibit cell division of fertilized starfish eggs[2] and anti-HIV[3]. Triprenylquinone and hydroquinones **1**, **2** and **3** were recently isolated from endemic nudibranch *Leminda millecra* collected in Algoa Bay, South Africa by Mcphail and coworkers. Gross structure of triprenylhydroquinone **3** was determined by spectral analysis, but the absolute stereochemistry and the specific rotation are still unknown[4]. To our knowledge, no triprenyl-containing quinones and hydroquinones have been synthesized. We report herein the first total synthesis of the compounds **1**, **2** and (±) **3**.

The total synthesis of the compounds **1**, **2** and (±) **3** is detailed in **Scheme 1**. The synthesis commenced from the known bromide **4**[5]. The anisole **5** was prepared in 73% yield by reaction of 2-(5-methyl-1,4-dimethoxy)phenylmagnesium bromide with geranyl bromide using catalytic amounts of Li_2CuCl_4, with little or no Wurtz product formation[6]. Selective oxidation of the allylic methyl group to allylic alcohol of the anisole **5** with selenium dioxide-*tert*-butyl hydroperoxide afforded the alcohol **6**. Iodination of the alcohol **6** with Ph_3P, imidazole and iodine followed by treatment of $PhSO_2Na$ in DMF at room temperature provide the desired sulfone **7** in 92% yield[7]. The triprenylquinone and hydroquinone precursor **8** was prepared by Julia coupling. **7** was treated with *n*-BuLi and isovaleraldehyde at -78℃ to give a stereoisomeric mixture of hydroxy sulfone **8**. **8** was converted to ketone **9** by oxidation of the secondary alcohol followed by treatment with Na(Hg) (6%), Na_2HPO_4 in methanol for the reductive desulfonylation[8].

* E-mail: liying@lzu.edu.cn

Scheme 1



Reagents and conditions: a) Mg, Li_2CuCl_4, Geranyl bromide, THF, –78 ℃ -0 ℃, 1.5 h, 73%; b) SeO_2, *t*-BuOOH, 40%; c) Ph_3P, Imid., I_2; d) $PhSO_2Na$, DMF, r.t., 40 h, 92%, two steps; e) *n*-BuLi, THF, –78 ℃ , isovaleraldehyde, 85%; f) DMSO, $(COCl)_2$, Et_3N, –78 ℃, 78%; g) Na (Hg) (6%), Na_2HPO_4, MeOH, 80%; h) CAN, CH_3CN, 52%; i) $NaHSO_3$, THF, 71%; j) $NaBH_4$, MeOH, 68%.

With ketone **9** in hand, quinone **1** could be afforded by CAN oxidation[9]. Finally, **1** was reduced with $NaHSO_3$ to produced **2** and reduced with $NaBH_4$ to produced (±) **3**. The spectral data (^1H, ^{13}C NMR, and HRMS) of synthetic **1**[10], **2**[11] and (±) **3**[12] were identical to those of natural **1**, **2** and **3**[4].

The synthetic route presented here allows access to the other compounds of the sesquiterpene triprenylquinones and hydroquinones. The biological evaluation of the compounds **1**, **2** and (±) **3** are under going.

Acknowledgments

This research work was financially supported by the National Natural Science Foundation of China (Grant No. 20272020).

References and Notes

1. D. J. Faulkner, *J. Nat. Prod. Rep.*, **2002**, *19*, 1 and earlier reports in this series.
2. N. Fusetani, K. Yasukawa, S. Matsunaga, K. Hashimoto, *Tetrahedron Lett.*, **1985**, *26*, 6449.
3. G. J. Hooper, M. T. Davies-Coleman, *Tetrahedron Lett.*, **1995**, *36*, 3265.
4. K. L. Mcphail, M. T. Davies-Coleman, J. Starmer, *J. Nat. Prod.*, **2001**, *64*, 1183.
5. M. C. Carreno, J. L. Garcia Ruano, G. Sanz, M. A. Toledo, A. Urbano, *J. Org. Chem.*, **1995**, *60*, 5328.

6. D. H. Burns, J. D. Miller, J. Santana, *J. Org. Chem.,* **1993**, *58*, 6525.
7. J. A. Marshall, R. C. Andrews, *J. Org. Chem.,* **1985**, *50*, 1602.
8. Y. X. Jia, B. Wu, X. Li, S. K. Ren, Y. Q. Tu, *et al.*, *Org. Lett.*, **2001**, *3* (6), 847.
9. K. Sato, T. Yoshimura, M. Shindo, K. Shishido, *J. Org. Chem.,* **2001**, *66*, 309.
10. Compound **1**: ^{1}H NMR (400 M Hz, $CDCl_3$, δ ppm): 0.90 (d, 6 H, *J* = 6.6 Hz, H-12', H-13'); 1.62 (s, 3 H, H-14'); 1.63 (s, 3 H, H-15'); 2.03 (s, 3 H, H-7); 2.10~2.12 (m, 3H, H-4', H-11'); 2.16 (m, 2 H, H-5'); 2.29 (d, 2 H, *J* = 6.9 Hz, H-10'); 3.04 (s, 2H, H-8'); 3.12 (d, 2H, *J* = 7.2 Hz, H-1'); 5.17 (t, 1H, *J* = 7.2 Hz, H-2'); 5.23 (t, 1H, *J* = 6.4 Hz, H-6'); 6.50 (s, 1H, H-3); 6.60 (s, 1 H, *J* = 1 Hz, H-6); ^{13}C NMR (100 M Hz, CDCl3, δ ppm): 209.4, 188.3, 187.8, 148.3, 145.5, 139.4, 133.4, 132.3, 129.4, 128.9, 118.2, 54.3, 50.6, 39.2, 27.0, 26.6, 24.4, 22.5, 16.4, 16.0, 15.4. HRMS calcd. for $C_{22}H_{30}O_3$ ($C_{22}H_{30}O_3$-H) 341.2122, found 341.2121.
11. Compound **2**: ^{1}H NMR (400 M Hz, CDCl3, δ ppm): 0.89 (d, 6H, *J* = 6.9 Hz, H-12', H-13'); 1.62 (s, 3 H, H-14'); 1.67 (s, 3 H, H-15'); 2.11 (m, 3 H, H-4' H-11'); 2.15 (s, 3 H, H-7'); 2.18 (m, 2H, H-5'); 2.31 (d, 2 H, *J* = 6.4 Hz, H-10'); 3.04 (s, 2 H, H-8'); 3.25 (d, 2 H, *J* = 6.8 Hz, H-1'); 5.18 (t, 1 H, *J* = 6.6 Hz, H-6'); 5.27 (t, 1 H, *J* = 7.2 Hz, H-2'); 6.55 (s, 1 H, H-3); 6.56 (s, 1 H, H-6); ^{13}C NMR (100 M Hz, CDCl3, δ ppm): 211.6, 147.8, 147.0, 136.6, 128.9, 128.7, 125.3, 122.4, 122.2, 117.8, 115.7, 53.6, 51.0, 39.0, 28.2, 25.8, 24.5, 22.4, 16.9, 15.8, 15.5. HRMS calcd. for $C_{22}H_{32}O_3$ ($C_{22}H_{32}O_3$-H) 343.2279, found 343.2278.
13. Compound (±) **3**: ^{1}H NMR (300 M Hz, CDCl3, δ ppm): 0.93 (d, 6 H, *J* = 6.9 Hz, H-12', H-13'); 1.23 (m, 1 H, H-10'); 1.25 (s, 1 H, OH-9'); 1.49 (m, 1 H, H-10'); 1.65 (s, 3 H, H-14'); 1.67 (s, 3 H, H-15'); 1.82 (sept, 1 H, *J* = 6.6 Hz, H-11'); 1.96 (dd, 1 H, *J* = 3.3, 10.2 Hz, H-8'); 2.16 (s, 3 H, H-7); 2.19 (m, 3 H, H-4, H-5'); 2.23 (m, 1H, H-8'); 2.29 (m, 1 H, H-5'); 3.26 (d, 2 H, *J* = 6.9 Hz, H-1'); 3.77 (br, m, 1 H, H-9'); 5.00 (br, s, OH-1); 5.24 (m, 1 H, H-6'); 5.29 (m, 1H, H-2'); 5.98 (br, s, 1H, OH-4); 6.45 (s, 1 H, H-3); 6.58 (s, 1 H, H-6); ^{13}C NMR (100 M Hz, CDCl3, δ ppm): 148.1, 146.9, 136.6, 132.3, 128.4, 125.3, 123.1, 122.6, 118.2, 115.5, 66.5, 48.2, 45.9, 39.1, 27.9, 25.2, 24.7, 23.2, 22.3, 16.2, 15.5. HRMS calcd. for $C_{22}H_{34}O_3$ ($C_{22}H_{34}O_3$ -H) 345.2435, found 345.2441.

Received 18 October, 2004