A Highly Convenient, One-Pot Synthesis of 3-Bromo-1,5- and -1,7-Azulenequinones by Polybromination of Azulene[1]

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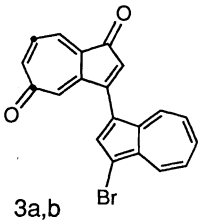
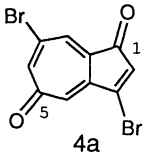
A very convenient, one-pot synthesis (in ca. 80% yield) of 3-Bromo-1,5- and -1,7-azulenequinones which can be used as synthones has been developed by polybromination of azulenes. Zink dust reduction and reductive acetylation of these azulenequinones were studied, and possible pathways for the present synthesis are briefly discussed.

Quinones are generally believed to constitute one of the oldest known and the most interesting class of compounds in all of the chemistry but most of them belonged to benzenoid compounds.[2,3] Some azulenequinones were synthesized by Morita et al.,[3] and one of the authors (T.N.) and his coworkers.[3] In 1980, Scott, Houk, Fukunaga, Hafner, and their coworkers[2] published a joint paper, describing all sixteen possible structures of azulenequinones together with their predicted physical properties such as UV spectra, magnetic susceptibility, redox potential and stability based on the theoretical calculation. Then fact, Scott et al. obtained unstable 1,4- and 1,6-azulenequinones as Diels-Alder adducts,[2] and stable 1,5-and 1,7- azulenequinones as predicted.[2] However, the synthetic method was not general in scope and unsuitable for a large scale production of azulenequinones. We now wish to describe a more convenient, one-pot synthesis of azulenequinones **2a** and **2b**, which can be used as synthones.[4]

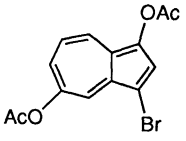
To a stirred solution of 300 mg of azulene (**1a**) in 70 ml of 5-20% aqueous THF was added 4.3 equiv. of bromine in 12 ml of acetic acid during 3 min at 5-10 °C, then 60 ml of water was added. After having been kept at room temperature overnight, the solution was extracted with dichloromethane. The combined organic layers were evaporated in vacuo, and the residue was separated by alumina gel column chromatography to give 3-bromo-1,5-azulenequinone (**2a**,[5] light yellow needles; mp 135 °C dec, 58% yield) and 3-bromo-1,7-azulenequinone (**2b**,[6] pale yellow needles; mp 142 °C dec, 20% yield), together with a small amount of 3,7-dibromo-1,5-azulenequinone (**4a**,[7] light yellow needles; mp 138 °C dec), 3,5-dibromo-1,7-azulenequinone (**4b**,[8] pale yellow needles; mp 153 °C dec) and other bromo compounds.



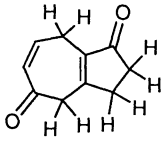
3a,b



4a



6a



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Addition of water to the above bromination reactants and an immediate separation of the precipiates afforded a 1:1 mixture of tribromoazulenones **5a,b**[9] (colorless needles), which, upon quenching with water, gave a mixture of **2a** and **2b** in 85% yield. On the other hand, when **1a** was treated with 3.4 equiv. of bromine at 5 to 10 °C in 25% aqueous acetic acid, **2a** (38% yield) and **2b** (12% yield) were obtained together with unidentified dark precipitates (50% yield). The precipitates, soluble in chloroform, showed three reddish violet spots on silica gel TLC, the top spot containing 3-(3-bromo-1-azulenyl)-1,5-azulenequinone (**3a**, reddish violet needles, mp >300 °C) and 3-(3-bromo-1-azulenyl)-1,7-azulenequinone (**3b**, reddish violet needles, mp >300 °C) formed by a nucleophilic substitution[4] of **2a,b** with **1a** followed by bromination with bromine in aqueous acetic acid. A repeated rebromination of these dark precipitates with 1 equiv. of bromine in aqueous acetic acid also afforded **2a,b** (80% total yield) along with 10% yield of **4a** and **4b**, and other bromo compounds.

The pure bromoazulenequinones are stable even on being left standing in the air or at a high temperature of 150 °C, but easily blacken with alkaline agents. On reductive acetylation, compounds **2a,b** afforded 1,5-diacetoxy-3-bromoazulene (**6a**,[10] green needles; mp 123-124 °C, 45% yield) and its 1,7-diacetoxy isomer (**6b**,[11] green needles; mp 86-87 °C, 48% yield), respectively, together with other reduced products. Compound **2a** gave enedione **7**[12] (colorless needles; mp 104-105 °C) with Zink dust in acetic acid at room temperature. We have not yet obtained parent azulenequinone itself from **2a** or **2b** by conventional methods.

Because of the facile formation of bromoazulenequinones **2a,b** also from **1b** with bromine, as well as from the result of theoretical calculations,[13] a key intermediate for these azulenequinone formation should be 1,1,3-tribromoazulenium ion **8**, which equilibrates with its conjugate base **9** and will easily be oxidized by bromine to give **2a,b** via a mixture of tribromoazulenone **5a,b** as shown in Scheme 1. More detailed discussions of the reaction path will be published later.

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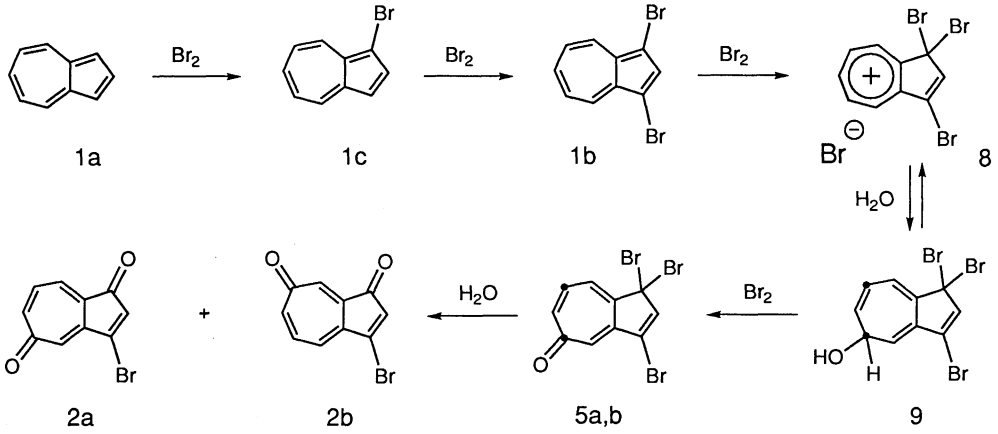
References and Notes

1 A part of the results has been presented: H. Wakabayashi, K. Shindo, S. Ishikawa, and T. Nozoe, The 69th National Meeting of the Chemical Society of Japan, March 1993, Tokyo, Abstr. 1A717; T. Nozoe, 24th Symposium on Structural Organic Chemistry, August 1993, Kiryu, Abstr. 1A07; H. Wakabayashi, K. Shindo, S. Ishikawa, M.



Scheme 1.

Kageyama, and T. Nozoe, 24th Symposium on Structural Organic Chemistry, August 1993, Kiryu, Abstr. P05.

2 L. T. Scott, M. D. Roseboom, K. N. Houk, T. Fukunaga, M. T. Lindner, and K. Hafner, *J. Am. Chem. Soc.*, **102**, 5169 (1980); L.T. Scott, P. Grütter, and R.E. Chamberlain, III, *J. Am. Chem. Soc.*, **106**, 4852 (1984); L.T. Scott and C.M. Adams, *J. Am. Chem. Soc.*, **106**, 4857 (1984).

3 T.Morita and K.Takase, *Chem, Lett.*, **1977**, 513; T.Morita, M. Karasawa, and K. Takase, *Chem, Lett.*, **1980**, 197; T. Morita, T. Ise, and K. Takase, *Chem, Lett.*, **1982**, 1303; Y. Matsubara, H. Yamamoto, and T. Nozoe in "Studies on Natural Products Chemistry", ed by Atta-ur-Rahman, Elsevier, Amsterdam, 1994, 14, pp. 313-354.

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5 **2a**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.87 (1H, d, J=0.7 Hz, H-2), 7.02 (1H, ddd, J=12.1, 2.4, 1.5 Hz, H-6), 7.11 (1H, dt, J=2.4, 0.7 Hz, H-4), 7.17 (1H, dd, J=12.1, 8.0 Hz, H-7), 7.31 (1H, ddd, J=8.0, 1.5, 0.7 Hz, H-8); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 127.55 (d, C-8), 133.59 (d, C-4), 134.46 (d, C-7), 134.90 (s, C-8a), 136.47 (d, C-2), 144.05 (d, C-6), 144.27 (s, C-3a), 152.71 (s, C-3), 186.28 (s, C-5), 189.67 (s, C-1).

6 **2b**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.81 (1H, s, H-2), 6.91 (1H, ddd, J=12.2, 2.7, 0.8 Hz, H-6), 7.05 (1H, ddd, J=8.2, 0.8, 0.5 Hz, H-4), 7.17 (1H, dd, J=12.2, 8.2 Hz, H-5), 7.24 (1H, dd, J=2.7, 0.5 Hz, H-8); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 127.19 (d, C-4), 132.82 (d, C-8), 134.06 (d, C-2), 134.73 (d, C-5), 135.61 (s, C-8a), 141.22 (d, C-6), 142.28 (s, C-3a), 153.61 (s, C-3), 187.40 (s, C-7), 190.46 (s, C-1).

7 **4a**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.89 (1H, d, J=0.6 Hz, H-2), 7.06 (1H, ddd, J=2.1, 0.8, 0.6 Hz, H-4), 7.48 (1H, dd, J=2.3, 0.8 Hz, H-8), 7.50 (1H, dd, J=2.3, 2.1 Hz, H-6).

8 **4b**:^{1}H NMR (270 MHz, $CDCl_3$) δ 6.88 (1H, s, H-2), 7.19 (1H, dd, J=2.6, 0.7 Hz, H-4), 7.25 (1H, dd, J=2.3, 0.7 Hz, H-8), 7.42 (1H, dd, J=2.6, 2.3 Hz, H-6).

9 **5a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (1H, ddd, J=12.0, 2.4, 1.0 Hz, H-6), 7.07 (1H, ddd, J=2.4, 0.5, 0.5 Hz, H-4), 7.10 (1H, d, J=0.5 Hz, H-2), 7.19 (1H, dd, J=12.0, 8.5 Hz, H-7), 7.59 (1H, ddd, J=8.5, 1.0, 0.5 Hz, H-8); **5b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (1H, ddd, J=11.9, 2.6, 1.0 Hz, H-6), 7.07 (1H, ddd, J=8.3, 1.0, 0.5 Hz, H-4), 7.03 (1H, d, J=0.5 Hz, H-2), 7.21 (1H, dd, J=11.9, 8.3 Hz, H-5), 7.68 (1H, dd, J=2.6, 0.5 Hz, H-8).

10 **6a**: ^{1}H NMR (270 MHz, benzene-d_6) δ 1.71 (3H, s, $COCH_3$), 1.78 (3H, s, $COCH_3$), 6.42 (1H, dd, J=10.8, 9.6 Hz, H-7), 7.00 (1H, ddd, J=10.8, 2.5, 1.2 Hz, H-6), 7.81 (1H, dd, J=9.6, 1.2 Hz, H-8), 7.93 (1H, s, H-2), 8.23 (1H, d, J=2.5 Hz, H-4).

11 **6b**: ^{1}H NMR (270 MHz, benzene-d_6) δ 1.69 (3H, s, $COCH_3$), 1.74 (3H, s, $COCH_3$), 6.43 (1H, dd, J=10.7, 9.8 Hz, H-5), 6.94 (1H, ddd, J=10.7, 2.8, 0.8 Hz, H-6), 7.98 (1H, dd, J=9.8, 0.8 Hz, H-4), 8.02 (1H, s, H-2), 8.05 (1H, d, J=2.8 Hz, H-8).

12 **7**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.56 (2H, m, H-2), 2.72 (2H, m, H-3), 3.22 (2H, m, J=6.1, 1.0 Hz, H-8), 3.52 (2H, s, H-4), 5.92 (1H, dt, J=10.5, 6.1 Hz, H-7), 6.52 (1H, dt, J=10.5, 1.0 Hz, H-6); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 31.00 (t, CH_2), 34.89 (t, CH_2), 45.68 (t, CH_2), 48.78 (t, CH_2), 122.36 (d), 124.86 (d), 138.73 (s), 165.06 (s), 203.53 (s, C=O), 206.31 (s, C=O).

13 The molecular orbitals of **1a-c** and **8** were calculated by the MNDO method. J.J.Stewart, MOPAC Version 6.0, QCPE No. 455, Chemistry Department, Indiana University, Bloomington, IN, 1987; T.Hirano, MOPAC Version 6.01, *JCPE Newslett.*, **2**, 26 (1991). HOMO coefficients for the **1b**: -0.516, -0.031, 0.374, 0.270, 0.048, -0.326, -0.172, 0.347, 0.280, and, 0.327 for the positions, 1,2,3,3a,4,5,6, 7,8, and 8a, respectively; LUMO coefficients for the **8**: -0.036, -0.202, -0.132, 0.429, -0.233, -0.457, 0.390, 0.378, -0.388, and 0.180 for the positions, 1,2,3,3a,4,5,6, 7,8, and 8a, respectively.