Preparation of Various Azulenequinone Derivatives by a Nucleophilic Substitution of 3-Bromoazulenequinone Synthones[1]

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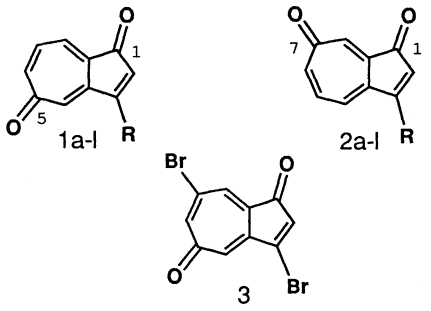
3-Bromo derivatives of 1,5- and 1,7-azulenequinones easily react with various nucleophiles to give 3-methoxy, phenoxy, *p*-nitrophenoxy, butylthio, butylamino, *p*-tolylamino, dimethylamino, 2-hydroxyethylamino, azulenyl, and guaiazulenyl derivatives of the respective azulenequinones almost quantitatively. 3-Bromo-1,5- and -1,7-azulenequinones afford the 2,3-bisbutylthio derivatives under basic conditions.

In the preceding communication we reported a highly convenient one-pot synthesis of 3-bromo-1,5-azulenequinone (**1a**: R=Br) and 1,7-isomer (**2a**: R=Br) together with dibromoazulenequinones **3** and **4** by polybromination of azulene.[2] In this communication we wish to describe the utility of 3-bromo-1,5- (**1a**) and -1,7-azulenequinones (**2a**) as very useful synthones.



When **1a** was treated with 2.5 equivalents of sodium methoxide in dry MeOH at room temperature, 3-methoxy-1,5-azulenequinone[3] (**1b**) was formed in 92% yield. Similarly, **1a** and **2a** were treated with nucleophilies such as phenol, *p*-nitrophenol, butanethiol, butylamine, *p*-toluidine, dimethylamine, ethanolamine, azulene, and guaiazulene to give the corresponding 3-substituted 1,5-azulenequinones **1b-k** and its 1,7-isomers **2b-k**. The structures, properties, and isolated yields of the azulenequinones obtained by this method are shown in Table 1.

Interestingly, the reaction of **1a** or **2a** with butanethiol in the presence of sodium methoxide at room temperature, respectively

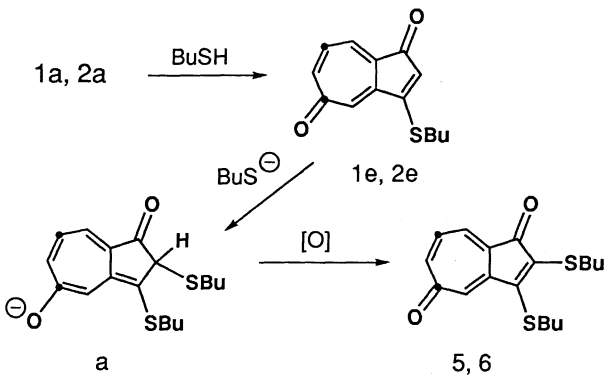
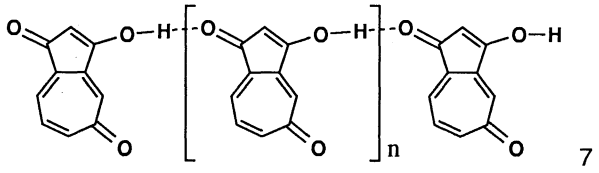


Table 1. Synthesis of Azulenequinone Derivatives by the Reaction of **1a** or **2a** with Various Nucleophiles.

Reagent Material		Azulenequinone Derivatives[3-12]		Color / Form	mp (℃)	Yield/%*
1a	Sodium methoxide	**1b**[3]	R=methoxy	light yellow needles	215 (dec)	92
2a	Sodium methoxide	**2b**	R=methoxy	pale yellow needles	206-207	89
1a	Phenol	**1c**[4]	R=phenoxy	light yellow needles	163-165	80
2a	Phenol	**2c**	R=phenoxy	pale yellow needles	173-175	84
1a	*p*-Nitrophenol	**1d**[5]	R=*p*-nitrophenoxy	light yellow needles	251-252	95
2a	*p*-Nitrophenol	**2d**	R=*p*-nitrophenoxy	pale yellow needles	273-274	90
1a	Butanethiol	**1e**	R=butylthio	yellow needles	136-138	70
2a	Butanethiol	**2e**[6]	R=butylthio	yellow needles	68-70	76
1a	Butylamine	**1f**	R=butylamino	yellow prisms	202-204	90
2a	Butylamine	**2f**[7]	R=butylamino	yellow needles	178-180	89
1a	*p*-Toluidine	**1g**[8]	R=*p*-tolylamino	yellow prisms	291 (dec)	97
2a	*p*-Toluidine	**2g**	R=*p*-tolylamino	yellow prisms	282 (dec)	98
1a	Dimethylamine	**1h**	R=dimethylamino	yellow needles	160-162	85
2a	Dimethylamine	**2h**[9]	R=dimethylamino	yellow needles	199-201	80
1a	Ethanolamine	**1i**	R=2-hydroxyethylamino	yellow needles	240 (dec)	90
2a	Ethanolamine	**2i**[10]	R=2-hydroxyethylamino	yellow needles	195 (dec)	95
1a	Azulene	**1j**[11]	R=1-azulenyl	reddish violet needles	>300	60
2a	Azulene	**2j**	R=1-azulenyl	reddish violet needles	>300	65
1a	Guaiazulene	**1k**[12]	R=3-guaiazulenyl	blue violet needles	>300	96
2a	Guaiazulene	**2k**	R=3-guaiazulenyl	blue violet needles	>300	75

* Isolated yields



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afforded 2,3-bisbutylthio-1,5-azulenequinone (**5**,[13] orange prisms, mp 69-70 °C, 45% yield) and 1,7-isomer (**6**,[14] orange prisms, mp 54-56 °C, 50% yield), presumably via the addition intermediate **a** followed by oxidation.

With alkali or acid, or even on heating with 1:1 dioxane-water at 80 °C, **1a** was readily hydrolized to give a dark brown or almost black insoluble solid, which is presumed to be a linear oligomer **7** of 3-hydroxy-1,5-azulenequinone (**1l**: R=OH) on the basis of the elemental analysis as well as by a negative test with silver nitrate.

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References and Notes

1 Partially presented: H.Wakabayashi, K.Shindo, S.Ishikawa, and T. Nozoe, 65th National Meeting of the Chemical Society of Japan, Tokyo, March 1993, Abstr. 1A717; T.Nozoe, 24th Symposium on Structual Organic Chemistry, Kiryu, October 1993, Abstr. 1A07; H. Wakabayashi, K.Shindo, S. Ishikawa, M. Kageyama and T. Nozoe, 24th Symposium on Structual Organic Chemistry, Kiryu, October 1993, Abstr. P05.

2 T. Nozoe, H. Wakabayashi, K. Shindo, T. Kurihara, S. Ishikawa, and M. Kageyama, *Chem.Lett.*, preceding paper.

3 **1b**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.06 (3H, s, OCH_3), 5.73 (1H, d, J=0.8 Hz, H-2), 6.95 (1H, ddd, J=12.1, 2.6, 1.1 Hz, H-6), 7.06 (1H, dt, J=2.6, 0.8 Hz, H-4), 7.14 (1H, dd, J=12.1, 7.8 Hz, H-7), 7.29 (1H, ddd, J=7.8, 1.1, 0.8 Hz, H-8).

4 **1c**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.50 (1H, s, H-2), 7.02 (1H, ddd, J=12.3, 2.7, 1.0 Hz, H-6), 7.18 (1H, dd, J=12.3, 8.0 Hz, H-7), 7.19 (2H, m, J=8.0 Hz, H-2',6'), 7.21 (1H, dd, J=8.0, 1.0 Hz, H-8), 7.32 (1H, d, J=2.7 Hz, H-4), 7.35 (1H, m, J=8.0 Hz, H-4'), 7.48 (2H, m, J=8.0 Hz, H-3',5').

5 **1d**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.58 (1H, d, J=0.5 Hz, H-2), 7.03 (1H, ddd, J=12.2, 2.6, 1.0 Hz, H-6), 7.21 (1H, dd, J=12.2, 8.0 Hz, H-7), 7.28 (1H, ddd, J=2.6, 0.5, 0.5 Hz, H-4), 7.38 (1H, ddd, J=8.0, 1.0, 0.5 Hz, H-8), 7.42 (2H, m, H-2',6'), 8.40 (2H, m, H-3',5').

6 **2e**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.00 (3H, t, J=7.3 Hz, CH_3), 1.52 (2H, m, CH_2), 1.80 (2H, m, CH_2), 3.08 (2H, t, J=7.3 Hz, SCH_2), 6.33 (1H, s, H-2), 6.89 (1H, dd, J=8.0, 0.8 Hz, H-4), 6.90 (1H, ddd, J=12.4, 2.8, 0.8 Hz, H-6), 7.10 (1H, dd, J=12.4, 8.0 Hz, H-5), 7.28 (1H, d, J=2.8 Hz, H-8).

7 **2f**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.99 (3H, t, J=7.3 Hz, CH_3), 1.46 (2H, m, CH_2), 1.72 (2H, m, CH_2), 3.38 (2H, m, NCH_2), 5.56 (1H, s, H-2), 5.61 (1H, br, NH), 6.72 (1H, dd, J=8.1, 0.8 Hz, H-4), 6.89 (1H, ddd, J=12.2, 2.7, 0.8 Hz, H-6), 7.05 (1H, dd, J=12.2, 8.1 Hz, H-5), 7.26 (1H, d, J=2.7 Hz, H-8).

8 **1g**:^{1}H NMR (270 MHz, DMSO-d_6) δ 2.22 (3H, s, CH_3), 5.82 (1H, s, H-2), 6.88 (1H, ddd, J=11.6, 2.6, 0.8 Hz, H-6), 7.17 (1H, dd, J=7.8, 0.8 Hz, H-8), 7.28 (4H, m, H-2', 3', 5', 6'), 7.33 (1H, dd, J=11.6, 7.8 Hz, H-7), 7.57 (1H, d, J=2.6 Hz, H-4), 9.81 (1H, br, NH).

9 **2h**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.32 (6H, s, CH_3), 5.58 (1H, s, H-2), 6.84 (1H, ddd, J=10.8, 2.8, 2.4 Hz, H-6), 7.05 (1H, dd, J=10.8, 8.3 Hz, H-5), 7.11 (1H, dd, J=8.3, 2.4 Hz, H-4), 7.20 (1H, d, J=2.8 Hz, H-8).

10 **2i**: ^{1}H NMR (270 MHz, CD_3OD) δ 3.52 (2H, t, J=5.5Hz, NCH_2), 3.79 (2H, t, J=5.5Hz, OCH_2), 5.64 (1H, s, H-2), 6.90 (1H, ddd, J=12.2, 2.5, 1.0 Hz, H-6), 7.19 (1H, d, J=2.5 Hz, H-4), 7.20 (1H, dd, J=8.1, 1.0 Hz, H-8), 7.32 (1H, dd, J=12.2, 8.1 Hz, H-7).

11 **1j**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.71 (1H, s, H-2), 7.01 (1H, ddd, J=11.9, 2.6, 1.5 Hz, H-6), 7.21 (1H, dd, J=11.9, 7.9 Hz, H-7), 7.27 (1H, d, J=2.6 Hz, H-4), 7.38-7.46 (3H, m, H-8,5',7'), 7.52 (1H, d, J=4.0 Hz, H-3'), 7.79 (1H, t, J=9.8 Hz, H-6'), 8.10 (1H, d, J=4.0 Hz, H-2'), 8.48 (1H, d, J=9.8 Hz, H-4'), 8.58 (1H, d, J=9.8 Hz, H-8').

12 **1k**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.41 (6H, d, J=6.7 Hz, iPr-CH_3), 2.64 (3H, s, CH_3), 2.69 (3H, s, CH_3), 3.14 (1H, m, J=6.7 Hz, iPr-CH), 6.39 (1H, s, H-2), 6.83 (1H, d, J=2.4 Hz, H-4), 6.97 (1H, ddd, J=12.2, 2.4, 1.0 Hz, H-6), 7.16 (1H, d, J=10.7 Hz, H-5'), 7.19 (1H, dd, J=12.2, 8.0 Hz, H-7), 7.38 (1H, d, J=8.0 Hz, H-8), 7.54 (1H, dd, J=10.7, 1.8 Hz, H-6'), 7.57 (1H, s, H-2'), 8.25 (1H, d, J=1.8 Hz, H-8').

13 **5**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.93 (6H, t, J=7.3 Hz, CH_3), 1.38 (2H, m, CH_2), 1.42 (2H, m, CH_2), 1.62 (2H, m, CH_2), 1.65 (2H, m, CH_2), 3.29 (2H, t, J=7.3 Hz, SCH_2), 3.35 (2H, t, J=7.3 Hz, SCH_2), 6.89 (1H, ddd, J=11.9, 2.6, 1.0 Hz, H-6), 7.06 (1H, dd, J=11.9, 8.0 Hz, H-7), 7.09 (1H, dd, J=2.6, 0.5 Hz, H-4), 7.17 (1H, ddd, J=8.0, 1.0, 0.5 Hz, H-8).

14 **6**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (3H, t, J=7.0 Hz, CH_3), 0.95 (3H, t, J=7.0 Hz, CH_3), 1.44 (2H, m, CH_2), 1.48 (2H, m, CH_2), 1.59 (2H, m, CH_2), 1.64 (2H, m, CH_2), 3.32 (2H, t, J=7.2 Hz, SCH_2), 3.37 (2H, t, J=7.2 Hz, SCH_2), 6.78 (1H, ddd, J=12.1, 2.6, 1.2 Hz, H-6), 6.98 (1H, dd, J=8.5, 1.2 Hz, H-4), 7.07 (1H, dd, J=12.1, 8.5 Hz, H-5), 7.16 (1H, d, J=2.6 Hz, H-8).