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Communication

Formation of Azulenequinone Derivatives from Variously Functionalized Azulenes by Bromine-oxidation[1]

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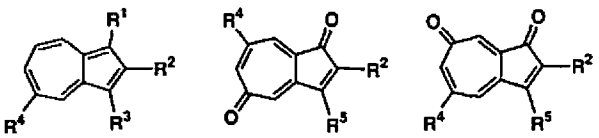
Variously functionalized 1,5- and 1,7-azulenequinones were easily derived in one-pot in 30-50% yield from the bromine-oxidation of 2-methoxyazulene and 2-methyl derivatives of 1-cyano-, 1-methoxycarbonyl- and its 7-isopropyl derivatives, while 1-methoxycarbonylazulene afforded several unstable products from which we could not isolate any azulenequinones. 1-Acetylazulene afforded 3-bromo-1,5- and -1,7-azulenequinones via side-chain brominated intermediates in high yield. 1,3-Dichloroazulene afforded a mixture of 3-chloro-1,5- and -1,7-azulenequinones, while 1-fluoro- and 1,3-diiodoazulene gave a mixture of 3-bromoazulenequinones. Analogous oxidation of 1,3-difluoroazulene produced 3-fluoroazulenequinones, but we could not isolate them due to its instability. Hydroxy group of 2-(3-hydroxypropyl)azulene was intact during this quinone formation reaction.

We have reported the formation of various 1,5- and 1,7-azulenequinones by the oxidation of azulene[2] and its alkyl and phenyl derivatives in aqueous THF.[3] In this paper we wish to describe azulenequinone formation from variously functionalized azulene to see the effect of kind and position on the functional groups.

Using our usual method of oxidation with slight excess of required bromine (in acetic acid) in 25% aqueous THF at 0-5 °C afforded a mixture of 1,5-azulenequinones (**2a-k**) and its 1,7-isomers (**3a-k**) as shown below: A mixture of **2a** (yellow needles; mp 168-170 °C) and **3a** (yellow needles; mp 143-145 °C) in 25% yield (9:1 ratio) from 2-methoxyazulene[4] (**1a**); 50% (8:1 ratio) of **2b**[5] (yellow needles; mp 92-94 °C) and **3b**[6] (yellow solid) from 1-methoxycarbonyl-2-methylazulene[7] (**1b**), 50% of **3c**[8] (yellow oil) from 1-methoxycarbonyl-2-methyl-7-isopropylazulene[7] (**1c**), and **2d**[9] (yellow needles; mp 121-123 °C) and **3d**[10] (yellow needles; mp 108-110 °C) from 1-cyano-2-methylazulene[7] (**1d**) in 45% yield (3:1 ratio).

On the other hand, 1-methoxycarbonylazulene[7] (**1e**) gave a mixture of yellow or orange unstable complex mixture without any azulenequinones.

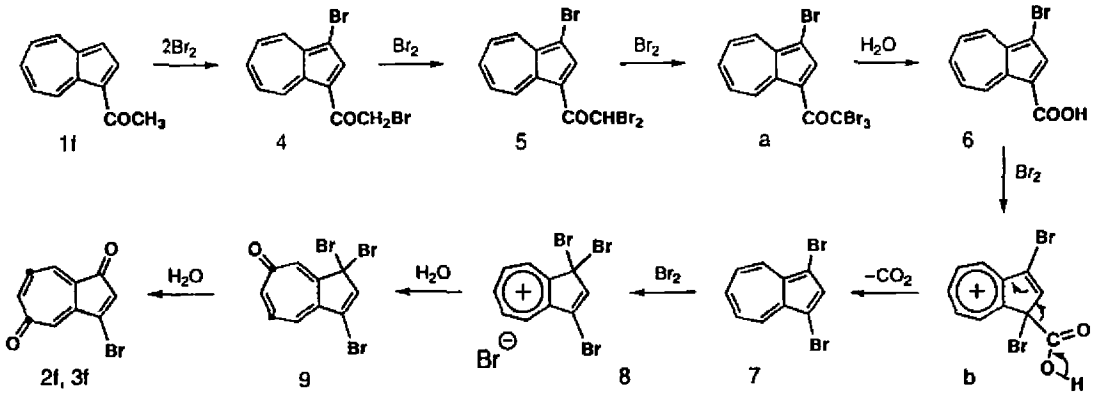
1-Acetylazulene (**1f**) afforded a mixture of 3-bromo-1,5- (**2f**) and -1,7-azulenequinones[2] (**3f**) in 73% yield (13:1 ratio) by extruding brominated side-chain. As mentioned earlier,[3] azulene-1-carboxylic acid and its 2-methyl, 5- and 6-isopropyl derivatives afforded azulenequinones (without carboxylic group) in high yield, while azulene-1-carboxylic acids having alkyl group at C-1 position gave a mixture of unidentified products.



a: $R^1=R^3=R^4=H$, $R^2=OMe$, $R^5=Br$
b: $R^1=R^5=COOMe$, $R^2=Me$, $R^3=R^4=H$
c: $R^1=H$, $R^3=R^5=COOMe$, $R^2=Me$, $R^4=iPr$
d: $R^1=R^5=CN$, $R^2=Me$, $R^3=R^4=H$
e: $R^1=COOMe$, $R^2=R^3=R^4=H$
f: $R^1=COMe$, $R^2=R^3=R^4=H$, $R^5=Br$
g: $R^1=R^3=R^4=H$, $R^2=(CH_2)_3OH$, $R^5=Br$
h: $R^1=R^3=R^5=Cl$, $R^2=R^4=H$
i: $R^1=F$, $R^2=R^3=R^4=H$, $R^5=Br$
j: $R^1=R^3=I$, $R^2=R^4=H$, $R^5=Br$
k: $R^1=R^3=R^5=F$, $R^2=R^4=H$

As one of our preliminary experiments **1f** was oxidized in acetonitril by $KMnO_4$ and HBr, and we found 3-bromo-1-bromoacetyl- (**4**) and 3-bromo-1-dibromoacetylazulene (**5**) were produced in good yield, showing the acetyl group was easily brominated than 7-membered moiety. Considering the above mentioned experimental evidence,

Scheme I



we propose the possible path-ways for the easy formation of **2f** and **3f** from **1f** as Scheme I.

As on example of azulene having a primary alcohol group on a side-chain, we examined the similar oxidation of 2-(3-hydroxypropyl)azulenes (**1g**) and obtained **2g**[11] (light yellow needles, mp 101-103 °C) and **3g**[12] (pale yellow needles, mp 120 °C dec.) in 43% yield (3:1 ratio).

Similar treatment of 1,3-dichloro- (**1h**) afforded a mixture of 3-chloro-1,5-azulenequinone (**2h**,[13] light yellow needles, mp 140 °C dec.) and its 1,7-isomer (**3h**,[14] pale yellow needles, mp 148 °C dec.) in 80% yield (3:1), while 1-fluoro- (**1i**) and 1,3-diiodoazulenes (**1j**) afforded a mixture of 3-bromo-1,5- (**2f**) and -1,7-azulenequinones[2] (**3f**) in 60% and 55% yield (3:1 ratio), respectively. 1,3-Difluoroazulene[15] (**1k**) afforded an unstable mixture of pale yellow monofluoro-1,5- and 1,7-azulenequinones (**2k**, **3k**; *m/z* 176, trace) which easily changed on alumina column chromatography to a dark brown compound, presumably an H-bonded 3-hydroxy-1,5-azulenequinone polymer[16] produced by hydrolysis.

So far, our one-pot azulenequinone synthesis bromine-oxidation in aqueous THF has proved to be very convenient method for the preparation of various 1,5- and 1,7-azulenequinone derivatives. Although, azulenes having alkoxycarbonyl or alkyl groups at C-1 position did not afford corresponding quinones, their 2-methyl derivatives did, suggesting that some modification of the reaction conditions would give corresponding azulenequinones without extruding substituent at C-1.

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Key Words

Variously functionalized azulenequinones; Bromine-oxidation; Azulenes; One-pot synthesis.

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5. **2b**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.23 (3H, s, CH_3), 3.39 (3H, s, $COOCH_3$), 6.97 (1H, ddd, J = 12.2, 2.5, 1.3 Hz, H-6), 7.12 (1H, dd, J = 12.2, 8.0 Hz, H-7), 7.39 (1H, ddd, J = 8.0, 1.3, 0.8 Hz, H-8), 7.43 (1H, dd, J = 2.5, 0.8 Hz, H-4).
6. **3b**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.23 (3H, s, CH_3),

4.00 (3H, s, $COOCH_3$), 6.84 (1H, ddd, J = 12.2, 2.8, 0.8 Hz, H-6), 7.11 (1H, dd, J = 12.2, 8.5 Hz, H-5), 7.33 (1H, dd, J = 2.8, 0.5 Hz, H-8), 7.45 (1H, ddd, J = 8.5, 0.8, 0.5 Hz, H-4).

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8. **3c**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.24 (6H, d, J = 6.7 Hz, iPr-CH_3), 2.21 (3H, s, CH_3), 2.76 (1H, septet, J = 6.7 Hz, iPr-CH), 4.01 (3H, s, $COOCH_3$), 6.79 (1H, dd, J = 2.6, 1.0 Hz, H-6), 7.29 (1H, d, J = 2.6 Hz, H-8), 7.45 (1H, d, J = 1.0 Hz, H-4).
9. **2d**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.29 (3H, s, CH_3), 7.01 (1H, ddd, J = 11.9, 2.6, 1.2 Hz, H-6), 7.05 (1H, dd, J = 2.6, 0.5 Hz, H-4), 7.15 (1H, dd, J = 11.9, 8.0 Hz, H-7), 7.42 (1H, ddd, J = 8.0, 1.2, 0.5 Hz, H-8).
10. **3d**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.28 (3H, s, CH_3), 6.90 (1H, ddd, J = 12.2, 2.5, 0.5 Hz, H-6), 6.99 (1H, dd, J = 8.0, 0.5 Hz, H-4), 7.15 (1H, dd, J = 12.2, 8.0 Hz, H-5), 7.32 (1H, dd, J = 2.5, 0.5 Hz, H-8).
11. **2g**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.84 (2H, m, CH_2), 2.62 (2H, t, J = 7.2 Hz, CH2), 3.62 (2H, t, J = 6.0 Hz, CH_2), 6.96 (1H, ddd, J = 12.2, 2.8, 1.2 Hz, H-6), 7.04 (1H, dd, J = 2.8, 0.8 Hz, H-4), 7.14 (1H, dd, J = 12.2, 7.8 Hz, H-7), 7.30 (1H, ddd, J = 7.8, 1.2, 0.8 Hz, H-8).
12. **3g**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.00 (2H, m, CH_2), 2.44 (2H, t, J = 6.1 Hz, CH2), 4.44 (2H, t, J = 5.2 Hz, CH_2), 6.80 (1H, ddd, J = 12.2, 2.8, 0.8 Hz, H-6), 6.86 (1H, ddd, J = 8.4, 0.8, 0.5 Hz, H-4), 7.06 (1H, dd, J = 12.2, 8.4 Hz, H-5), 7.23 (1H, dd, J = 2.8, 0.5 Hz, H-8).
13. **2h**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.67 (1H, d, J = 0.5 Hz. H-2), 7.01 (1H, ddd, J = 12.2, 2.5, 0.8 Hz, H-6), 7.14 (1H, dd, J = 2.5, 0.5 Hz, H-4), 7.17 (1H, dd, J = 12.2, 8.0 Hz, H-7), 7.33 (1H, dd, J = 8.0, 0.8 Hz, H-8).
14. **3h**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.62 (1H, s, H-2), 6.92 (1H, ddd, J = 12.2, 2.6, 1.0 Hz, H-6), 7.09 (1H, dd, J = 8.2, 1.0 Hz, H-4), 7.16 (1H, dd, J = 12.2, 8.2 Hz, H-5), 7.27 (1H, d, J = 2.6 Hz, H-8).
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