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Dienone-phenol Rearrangement of C-9 Oxygenated Decalinic Dienone and Analogs through B-Ring Cleavage

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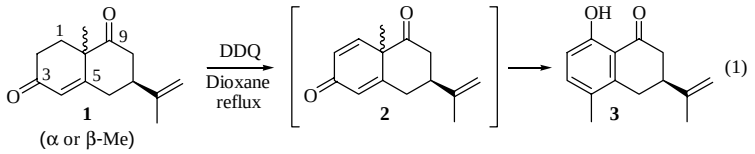
Abstract: Dehydrogenation of 9-hydroxy decalinic enones and analogs with DDQ resulted in a formal dienone-phenol type rearrangement *via* B-ring cleavage, while the corresponding dienone acetates underwent base-catalyzed formal dienone-phenol type rearrangement analogously.

Keywords: Dienone-phenol rearrangement, decalinic dienone, dehydrogenation, DDQ.

In our previous synthetic studies on the eudesmane-type sesquiterpene natural products, we have observed a skeletal rearrangement of decalinic enone intermediate **1** during the attempt on dehydrogenation by 2, 3-dichloro-5, 6-dicyano-1, 4-benzoquinone (DDQ) leading to phenolic compound **3** as major product (**eq. 1**)[1]. The reaction was assumed to proceed *via* a dienone intermediate **2** catalyzed by acid, which is formally characterized as dienone-phenol rearrangement[2]. Detailed mechanistic studies by Waring and co-workers[3] suggested that the unstable dienones of type **2** undergo readily dienone-phenol rearrangement *via* intramolecular acyl migration under mild acidic condition or B-ring cleavage in reaction with nucleophile to afford aromatized phenolic products.



1 (α or β-Me) **2** **3**

To investigate the effect of C-9 oxygenated functions and substituents bearing on the ring system, we prepared[4] some of the C-9 hydroxylated analogs of decalinic enone **1** with different substituents and B-ring fusion, which were subjected to the dehydrogenation reaction with DDQ[5]. The results are summarized in **Table 1**. In contrast to Waring's previous report[6], the starting hydroxyl enones were consumed slowly in refluxing dioxane and the phenolic compounds were isolated as major isolable products in low to moderate yields. The initial B-ring cleavage is obvious in all

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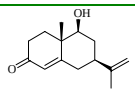
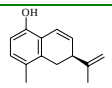
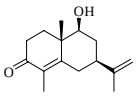
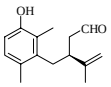
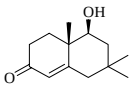
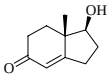
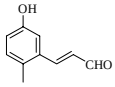
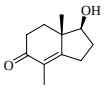
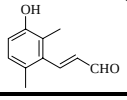
examples[7]. Substituent at C-4 (*i.e.* methyl) prohibited reforming of B-ring in products to give phenolic aldehydes (entry 2). Five-membered B-ring analogs of enone **1** afforded B-ring cleavage products α, β-unsaturated phenolic aldehydes by further dehydrogenation with DDQ (entries 5, 6). This results imply that the formal dienone-phenol rearrangement occurred *via* the initial B-ring cleavage of the corresponding dienone intermediates through acid-catalyzed retro-aldol like process to give the phenolic aldehyde intermediates which undergo intramolecular phenolate aldol and subsequent dehydration for substrates with no substituent at C-4 position (entries 1, 3, 4).

Table 1 Dehydrogenation of 9-hydroxy decalinic enones and analogs with DDQ[a]

Entry	Enone substrate	Time (h)	Product[b]	Yield (%)[c]
1		45	 (**4**)	40
2		48		35
3		50		38
4		48		30
5		36	 (**5**)	30
6		42		40

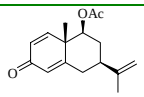
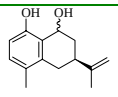
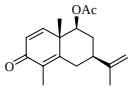
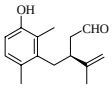
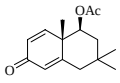
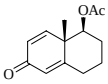
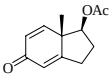
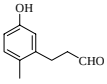
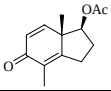
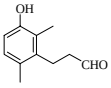
[a] The reaction were run with 1.3 equiv. of DDQ in refluxing dioxane. [b] Products were fully characterized spectroscopically.[8] [c] Isolated yield after silica gel chromatography.

Acetylation of C-9 hydroxy group of the corresponding decalinic enones and analogs listed in **Table 1** prohibited the retro-aldol type B-ring cleavage of the dienone intermediates resulting from the dehydrogenation by DDQ to give the corresponding dienone acetates in moderate to good isolated yield. Interestingly, deacetylation of the dienone acetates under mild condition (K_2CO_3, MeOH, room temperature) resulted in a fast and clean formation of rearranged phenolic compounds as major isolated products (**Table 2**), typical process of formal dienone-phenol rearrangement[9]. Apparently, this rearrangement was triggered by the release of free C-9 hydroxy group and preceded *via* a base-catalyzed retro-aldol-intramolecular phenolate aldol transformation. Similarly, the reforming of B-ring was hindered by the C-4 substituent (*i.e.* methyl) and 5-membered B-ring analogs leading to phenol aldehyde products (entries 2, 5, 6).

In conclusion, the C-9 oxygenofunctions (carbonyl or hydroxy) greatly facilitated the formal dienone-phenol type rearrangement for decalinic enones of type **1** and analogs *via* initial B-ring cleavage catalyzed either by mild acid or base through a *retro-aldol*

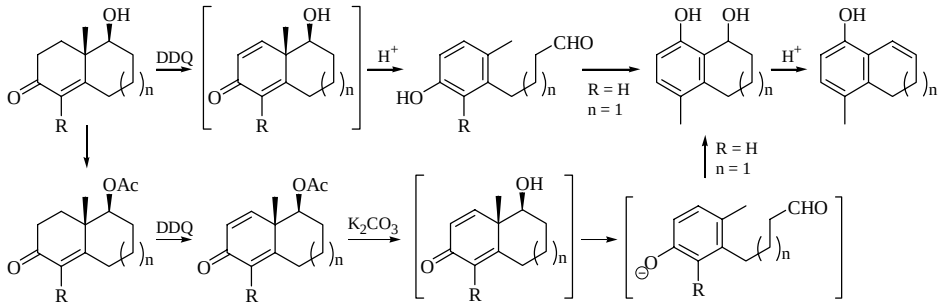
process (**Scheme 1**). The resulting phenolate aldehydes derived from decalinic enones (n = 1) readily cyclize intramolecularly in the absence of C-4 substituent.

Table 2 Mild base-catalyzed dienone-phenol rearrangement of C-9 acetoxyl decalinic dienones and analogs[a]

Entry	Dienone substrate	Time (min)	Product[b]	Yield (%)[c]
1		10	 (**6**)	75[d]
2		10		72
3		15		80
4		10		77
5		15	 (**7**)	65
6		15		67

[a] The reaction were run with 1.0 equiv. of anhydrous K_2CO_3 in methanol at room temperature. [b] Products were fully characterized spectroscopically. [8] [c] Isolated yield after silica gel chromatography. [d] Diastereomeric ratio: *syn* / *anti* 4.5 :1.

Scheme 1



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References and Notes

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8. Selected spectral data: **4**, IR (film) *v* 3413, 1587, 1485, 1384, 1272, 1023 cm^{-1}; ^{1}HNMR (200 MHz, $CDCl_3$, δ ppm): 1.80 (*s*, 3 H, CH_3), 2.12 (*s*, 3 H, CH_3), 2.71 (*dd*, 1 H, *J* = 16.0, 10.9 Hz), 2.87 (*dd*, 1 H, *J* = 16.0, 7.1 Hz), 4.85 (br d, 2 H), 5.94 (*dd*, 1 H, *J* = 9.9, 3.8 Hz), 6.54 (*d*, 1 H, *J* = 8.1 Hz), 6.82 (*dd*, 1 H, *J* = 9.9, 2.3 Hz), 6.88 (*d*, 1 H, *J* = 8.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 18.7, 20.6, 29.5, 41.3, 110.7, 112.9, 120.6, 121.1, 127.2, 129.4, 130.1, 134.5, 147.5, 149.0. **5**, IR (film) *v* 3396, 1662, 1607, 1383, 1113, 1073 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm): 2.41 (*s*, 3 H, CH_3), 6.64 (*dd*, 1 H, *J* = 8.0, 15.7 Hz), 6.86 (*dd*, 1 H, *J* = 8.0, 2.8 Hz), 7.08 (*d*, 1 H, *J* = 2.8 Hz), 7.13 (*d*, 1 H, *J* = 8.0 Hz), 7.75 (*d*, 1 H, *J* = 15.7 Hz), 9.72 (*d*, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 18.7, 112.9, 118.6, 129.5, 130.3, 132.2, 133.6, 150.3, 154.2, 194.2. **6**(*syn*), IR (film) *v* 3382, 1642, 1597, 1472, 1381, 1094 cm^{-1}; ^{1}HNMR (200 MHz, $CDCl_3$, δ ppm): 1.64-1.79 (*m*, 1 H), 1.86 (*s*, 3 H, CH_3), 2.19 (*s*, 3 H, CH_3), 2.34-2.55 (*m*, 3 H), 2.74-2.83 (*m*, 1 H), 4.85 (*m*, 2 H, $=CH_2$), 5.21 (*dd*, 1 H, *J* = 6.0, 10.4 Hz, CHOH), 6.70 (*d*, 1 H, *J* = 8.0 Hz), 7.02 (*d*, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 19.1, 20.5, 32.8, 37.8, 39.8, 70.6, 109.9, 113.8, 123.2, 127.3, 130.2, 135.9, 148.2, 154.6. **6**(*anti*), IR (film) *v* 3383, 1644, 1595, 1471, 1381, 1094 cm^{-1}; ^{1}HNMR (200 MHz, $CDCl_3$, δ ppm): 1.76-1.91 (*m*, 1 H), 1.82 (*s*, 3 H, CH_3), 2.21(*s*, 3 H, CH_3), 2.32-2.55 (*m*, 3 H), 2.84 (*brd* , 1 H, *J* = 16 Hz), 4.83 (d, 2 H, *J* = 7.8 Hz), 5.11 (*dd*, 1 H, *J* = 2.6, 7.4 Hz, CHOH), 6.72 (*d*, 1 H, *J* = 8.0 Hz), 7.04 (*d*, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 18.9, 21.0, 32.6, 36.4, 65.2, 109.6, 113.1, 123.2, 127.9, 130.1, 136.4, 148.4, 153.8. **7**, IR (film) *v* 3396, 1589, 1384, 1116, 1071 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm): 2.23 (*s*, 3 H, CH_3), 2.74 (*m*, 2 H), 2.89 (*m*, 2 H), 6.61(*dd*, 1 H, *J* = 8.0, 2.6 Hz), 6.40 (*d*, 1 H, *J* = 2.5 Hz), 7.01 (*d*, 1 H, *J* = 2.5 Hz), 9.84 (*m*, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 18.4, 25.4, 43.9, 113.2, 115.5, 127.9, 131.4, 139.8, 153.8, 201.7.
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