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The Reactions of 4,5-Dehydrotropone with 4-Phenyloxazols

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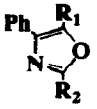
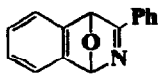
Abstract: 4,5-Dehydrotropone reacted with 4-phenyl-, 5-methyl-4-phenyl-, and 2,5-dimethyl-4-phenyloxazol to give, involving facile loss of benzonitrile from the corresponding Diels-Alder adducts, furo[3,4-d]tropone and its 1-methyl and 1,3-dimethyl derivative, respectively. Protonation of furo[3,4-d]tropones yielded delocalized 6-hydroxy-3-oxaazulenium ions.

Acetylenic dienophiles react with oxazols to give substituted furans with facile loss of nitriles.[1a] Dehydrobenzene **1**, generated under the Reddy-Batt condition (anthranilic acid + RONO, 101 °C)[2], reacts with 4-phenyloxazol **2a** to give the 2 : 1 adduct **4**. The formation of **4** results from the extrusion of benzonitrile from the corresponding Diels-Alder adduct **3** and the following addition of a second molecule of **1** to the intermediate isobenzofuran.[3a] On the other hand, **1**, generated under the Campbell-Rees condition (1-aminobenzotriazol + $Pb(OAc)_4$, 0 °C)[4] undergoes the same reaction to give the isolable adduct **3** in essentially quantitative yield.[3b] We have studied the reactivities of 4,5-dehydrotropone **5** and synthesized novel aromatic compounds containing seven-membered rings by the application of the high reactivities of **5**.[5] Here we report the reaction of **5** with 4-phenyloxazols **2**, leading to the facile synthesis of furo[3,4-d]tropones.



2a: R_1=R_2=H
2b: R_1=CH_3, R_2=H
2c: R_1=R_2=CH_3



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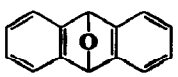

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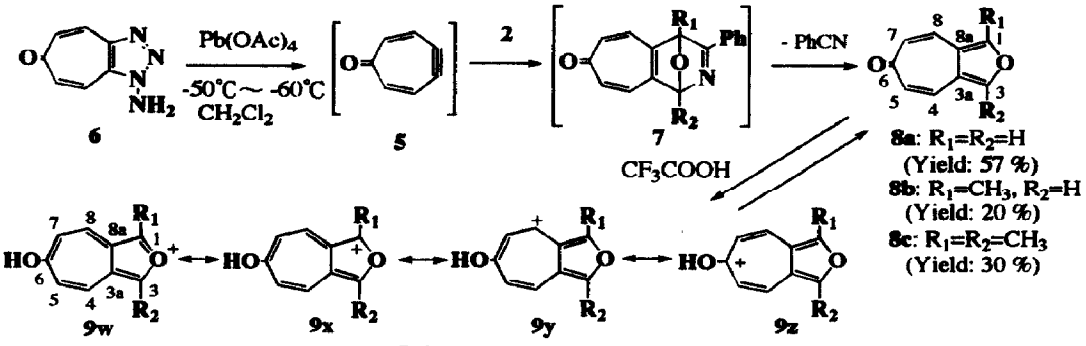
1-Aminocycloheptatriazol-6-one **6** was allowed to react with equal mols of lead tetraacetate in anhydrous dichloromethane in the presence of a large excess of 4-phenyloxazol **2a** or those having methyl substituents **2b** or **2c** at −50 ~ −60 °C. The resulting solution was rapidly chromatographed through a short alumina column to remove acetic acid and lead oxide originating from lead tetraacetate and then was treated in an usual manner to yield furo[3,4-d]tropone **8a**, **8b**, and **8c**, respectively, as shown in Scheme 1. The structure of **8a** was identified by comparison of its spectroscopic data with those which have already been reported.[6] The structures of **8b** and **8c** were determined from their spectroscopic data.[7]

Like **8a**,[6] **8b** and **8c** are protonated in strongly acidic solvents. Thus, NMR and UV and VIS spectra of **8** in strongly acidic solvents confirm the structures of protonated forms **9**. In ^{13}C NMR spectra of **8a** and **8c**, as shown in Table 1, considerable deshieldings (*ca.* 6 ~ 20 ppm) of skeletal carbons C-1,3 and C-4,8 in



Scheme 1

CF_3COOD, compared with those in $CDCl_3$, are observed. This result proves that **9a**, **9b**, and **9c** are delocalized 6-hydroxy-2-oxaazulenium ions. This finding is also deduced from ^1H NMR data, that is, downfield chemical shifts (0.7 ~ 1.3 ppm) of tropone ring protons and decreases in $J_{H4,H5}$ values (10.8 Hz for **9a**, 11.4 Hz for **9b**, and 11.3 Hz for **9c**; 12.0 Hz for **8a** and **8c**, 11.9 Hz for **8b**) in comparison of the spectra in CF_3COOD with those in $CDCl_3$[8]. UV and VIS spectra of **9** in 9M H_2SO_4, as shown in Fig. 1, consist of three absorption bands, the pattern of which is similar to that of 6-hydroxyazulene chromophore.[9] These spectroscopic results, described above, suggest that the structure of **9** could be expressed by the formula to which polar structures **9w**, **9x**, **9y**, and **9z** are contributed. Furthermore, the band at longest wavelength exhibits a bathochromic shift by introduction of a methyl group at 1 or 3 position of **9** (**9a**: 462 nm, **9b**: 505 nm, **9c**: 545 nm), which is comparable to the shift of 6-hydroxyazulenes (6-hydroxyazulene: 526 nm,[9] 6-hydroxy-1-methylazulene: 554 nm in $CHCl_3$[10]). These data reveal that, on the electronic transitions of **9**, electron transfer from 5-membered ring to 7-membered ring takes place.

Table 1. ^{13}C NMR Spectra of furo[3,4-d]tropones **8a** and **8c** (δ: ppm)

	C-1,3	C-3a,8a	C-4,8	C-5,7	C-6	CH_3	Solvent
8a	144.6	123.6	129.4	131.5	190.2		$CDCl_3$
9a	151.4	126.8	147.9	126.6	193.7		CF_3COOD
Δδ (**9a** - **8a**)	6.8	3.2	18.5	-4.9	3.5		
8c	115.6	119.0	130.4	129.1	190.6	11.6	$CDCl_3$
9c	161.7	123.6	150.9	122.4	191.1	12.4	CF_3COOD
Δδ (**9c** - **8c**)	10.1	4.6	20.5	-6.7	0.5	0.8	

It is worth noting that the adduct **3**, isolated under the reaction conditions at 0°C, is relatively stable among the adducts formed by the addition reactions of oxazols with acetylenic dienophiles.[1,11] In contrast, the adduct **7**, which could not be isolated under the comparable conditions, is more labile than **3**. This finding indicates that the ring condensed with 7-oxa-2-azabicyclo[2.2.1]heptadiene system affect its stabilities.

As to the reaction mechanisms leading to furotropones **8**, the possible ways are benzonitrile elimination catalyzed by acetic acid by way of protonated intermediate **10** and **11** [pathway A] and retro-Diels-Alder

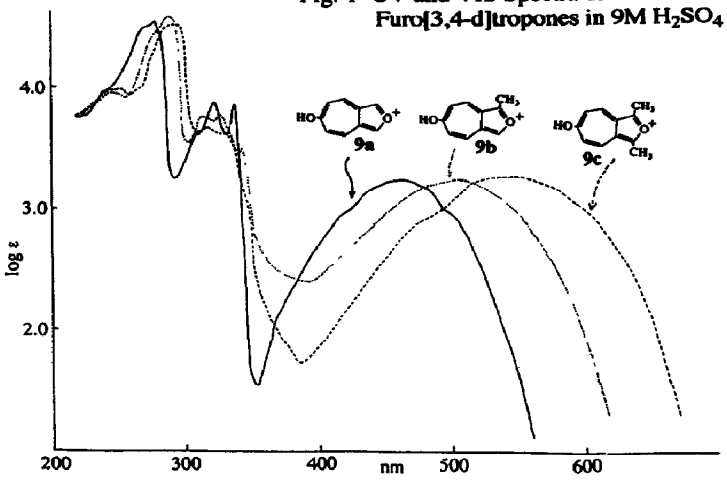
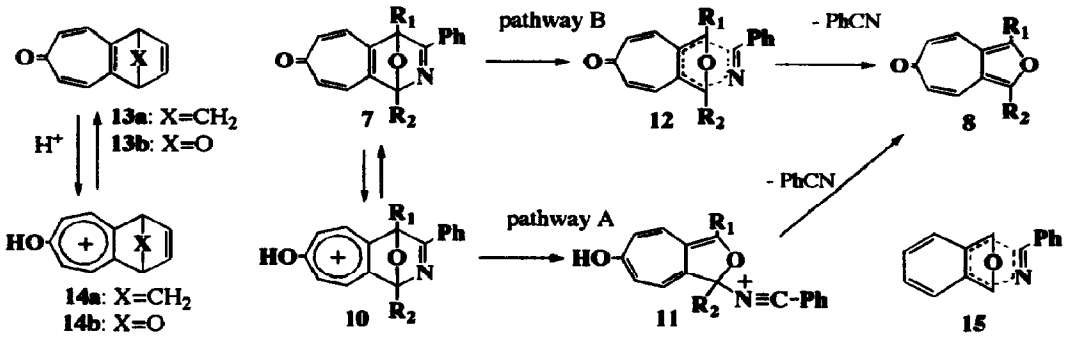


Fig. 1 UV and VIS Spectra of Furo[3,4-d]tropones in 9M H_2SO_4

reaction involving cycloreversion transition state **12** [pathway B], as shown in Scheme 2. Bridged tropones **13** are protonated with CF_3COOH, HCl, and H_2SO_4 to give tropylium ions **14**.[5a,12] The acidity of conjugate acid **14a** is determined to be pKa = 1.4 at 25 ℃.[13] With respect to pathway A, the adduct **7** should be a weak base like **13b** and accordingly acetic acid could not function as an acid catalyst because of its weak acid strength and its minute presence in the reaction mixture. Pathway A could not be, therefore, rationalized. The activation parameters for retro-Diels-Alder reaction of **3** yielding isobenzofuran were reported as follows: $\Delta H^{\neq}$= 28.1 kcal/mol, $\Delta S^{\neq}$= 5 kcal/mol·deg. Authors said that this small activation entropy was typical of many retro-Diels-Alder reactions and expulsion of a nitrile from **3** was not extraordinry.[3b] Thus, the transition state for the reaction is considered to be **15**. Assuming that 1) both the transition states **12** from **7** in pathway B and **15** from **3** are similarly polyolefinic and lack aromatic stabilization and, therefore, 2) the difference in $\Delta H^{\neq}$for the reactions **7** → **12** and **3** → **15** is mainly due to that in π–stabilization energies of **3** and **7** [π–stabilization energy: 20 ~ 40 kcal/mol for benzene, 3kcal/mol for tropone[14]], $\Delta H^{\neq}$for pathway B can be roughly estimated to be less than *ca.* 11kcal/mol.[15] Thus, pathway B could account for facile loss of a nitrile from the adduct **7** and the labile adducts formed from oxazols and acetylenic dienophiles.[1a]



Scheme 2

As described above, furo[3,4-d]tropones **8** are available in one step from oxazols by employing dehydrotropone **5**. Usefulness of **5** for synthesis of novel aromatic compounds has been further demonstrated.

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7. **8b**: ^{1}H NMR ($CDCl_3$) δ 2.48(s, CH_3), 6.28(d, J=11.9 Hz, H-7), 6.30(d, J=11.9 Hz, H-5), 7.07(d, J=11.9 Hz, H-8), 7.10(d, J=11.9 Hz, H-4), 7.69(s, H-3). **8c**: ^{1}H NMR ($CDCl_3$) δ 2.45 (s, CH_3), 6.23 (d, J=12.0 Hz, H-5,7), 7.02(d, J=12.0 Hz, H-4,8).
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15. According to the assumption on the transition state **12** and **15**, $\Delta H^{\neq}$ for pathway B should be obtained by subtracting the difference in π–stabilization energy between benzene and tropone from $\Delta H^{\neq}$ for the reaction **3** → **15** : 28 kcal/mol − [(20 ~ 40 kcal/mol) − 3 kcal/mol].

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