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Acid-catalyzed Rearrangement of 2-Substituted and 2,4-Disubstituted 8H-3-oxaheptalen-8-ones to 1-Acyl-6-hydroxyazulenes

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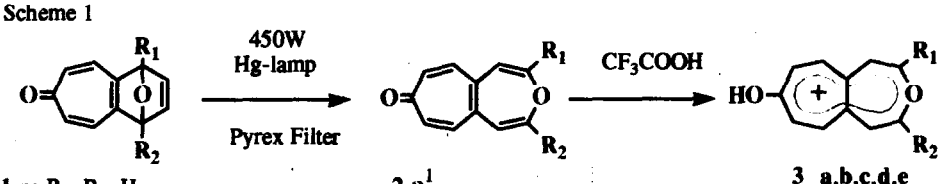
Abstract: It was found that in trifluroacetic acid, 2-methyl-8H-3-oxaheptalen-8-one was transformed into 2-hydroxy-3-methyl-7H-benzocyclohepten-7-one and 1-formyl-6-hydoxy-2-methylazulene, whereas 2,4-dimethyl-8H-3-oxaheptalen-8-one was under the same conditions converted into 1-acetyl-2-methyl-6-hydroxyazulene. 2-Phenyl- and 2,4-diphenyl-8H-3-oxaheptalen-8-on undergo the same skeletal rearrangements as those which the corresponing mono- and dimethyl derivatives suffer from, respectively.

Recently we have reported the photochemical synthesis of 8H-3-oxaheptalen-8-one **2a** from 12-oxatricyclo[7.2.1.0.^{28}]dodeca-2(8),3,6,10-tetraen-5-one **1a**. In trifluroacetic acid, **2a** underwent the protonation to give 8-hydroxy-3-oxaheptalenium ion **3a**, which suffer from the further transformation into 2-hydroxy-7H-benzocyclohepten-7-one **5a** in a few hours[1]. Here we communicate the new class of acid-catalyzed rearrangement by which 2- and 2,4-substituted derivatives **2** are converted into 1-acyl-6-hydroxyazulenes.

As for 2- and 2,4-subsutituted 8H-3-oxaheptalen-8-ones, 2-methyl (**2b**), 2,4-dimethyl (**2c**), 2-phenyl (**2d**) and 2,4-diphenyl derivative (**2e**) were synthesized on irradiation of the derivaties of **1**(**1b**, **1c**, **1d** and

Scheme 1



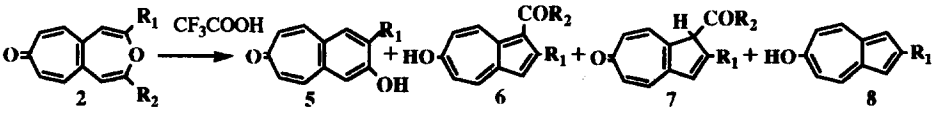
1 a: R_1=R_2=H
b: R_1=CH_3, R_2=H
c: R_1=R_2=CH_3
d: R_1=C_6H_5, R_2=H
e: R_1=R_2=C_6H_5

2 a[1]
b: Yield 58 %
c: 65 %
d: 82 %
e: 24 %

3 a,b,c,d,e

4

Scheme 2



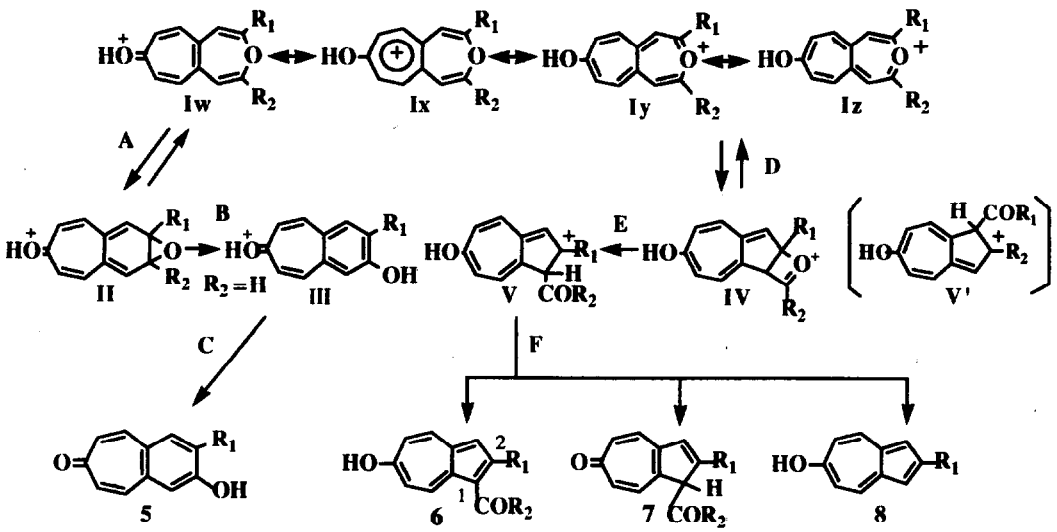
	5	6	7	8
a: R_1=R_2=H	95 % [1]	--	--	--
b: R_1=CH_3, R=H	70 %	23 %	--	--
c: R_1=R_2=CH_3	--	51 %	--	--
d: R_1=C_6H_5, R_2=H	15 %	85 %	--	--
e: R_1=R_2=C_6H_5	--	37 %	35 %	23 %

1e) with 450W Hg lamp through Pyrex filter in a mixture of benzene and ethanol (23:2 v/v) for **1b** and **1c** or in ethanol for **1d** and **1e** in moderate yields. ^{1}H NMR spectra of **2b** and **2c** in trifluoroacetic acid show the distinct downfield shifts for all the skeletal protons, indicating that both compounds underwent the protonation to give the substituted 8-hydroxy-3-oxaheptalenium ions **3b** and **3c**.[2] Chemical shift differences between protons attached to tropone skeltons in the neutral and protonated forms of **2b** and **2c** (0.93 ppm and 0.95 ppm, respectively) are smaller as compared with those of a 4,5-dialkyltropone, tricyclo[7.2.1.$0^{2,8}$]dodeca-2(8),3,6,10-tetraen-5-one **4** (1.27-1.47 ppm),[3] indicating that the positive charge are delocarized over the whole parts of molecules, as we have already reported for **1a**.[1] Upon standing the solution at room temperature for 1h, the ions underwent the subsequent skeletal rearrangements. Both the monophenyl and diphenyl derivatives **2d** and **2e** suffered from similar skeletral rearrangements so rapidly (in less than 5 min) that the corresponding ions **3d** and **3e** were not observed.

After usual workup of the trifluoroacetic acid solutions, the products were separated. Interestingly, the monosubstituted derivatives **2b** and **2d** were found to be transformed not only into 2-hydroxy-7H-benzocyclohepten-7-ones **5b** and **5d** but also into 6-hydroxy-1-acylazulenes **6b** and **6d**, respectively. In the case of disubstituted derivatives **2c** and **2e**, none of the products **5** were isolated. Instead the azulenoid products **6c** and **6e**, **7e**, and **8e** were produced from **2c** and **2e**, respectively. The yields of the products are shown in scheme 2.[4,5] In trifluoroacetic acid, **7e** was converted into **6e** and **8e** in 20 and 20% yield, respectively, whereas **6e** was stable. The fact indicates that **8e** is the secondary product through **7e**.

Plausible reaction pathways are drawn in sheme 3. 8-Hydroxy-3-oxaheptalenium ion **3** could be depicted as the resonance hydrid of contributing structure **Iw**, **Ix**, **Iy** and **Iz**. Two intramolecular electrocyclizations are allowed for **I**. One is 6π electrocyclization of **I** to produce the protonated species of 2,3-epoxy-7H-benzocycloheptene-7-one **II** (step A).[6] The other is 10π electrocyclization of **I** to form 2a,8a-dihydro-1-oxoniacyclobut[a]azulene **IV** (step D).[7] Since step A and D are considered to be reversible, the steps following them should determine product distribution. As in the case of **2a**[1], monosubstituted **2b** and **2d** are allowed to isomerize to **5b** and **5d**, respectively, through the reaction sequence including acid-catalyzed ring opening of the epoxide of **II** (step B) and deprotonation of **III** (step C).[6] For the disubstituted **2c** and **2e**, however, the step B is suppressed since the step B for **2c** and **2e** involves unfavorable demethylation or dephenylation process.[8] The reaction leading to the azulenoid products proceeds further by opening of the oxoniacyclobutene ring of **IV** resulting in formation of 1-acyl-1H-azulenium ion **V** (step E), from which 2-substituted 1-acyl-6-hydroxyazulene **6**, its tautomer **7**, and 2-subsutituted-6-hydroxyazulene **8** (step F) are produced. Furthermore,

Scheme 3



following facts concerning the product distribution and the reaction rate shoud be noted. 1) The parent compound **2a** is transformed only into **5** through step A, B and C, whereas the reaction proceeding through step D, E and F is enhanced for the subsutituted **I** from **2b** ~ **2e**. 2) The substitutent R_1 in monosubstituted **I** generated from **2b** and **2d** locates at C_2 of the products **6**, which are derived from **V**. 3) For monosubstituted **I**, which suffer from two types of the rearrangements descrived above, main product from **2b** is troponoid **5b**, whereas that from **2d** is azulenoid **6d**. 4) For disubstituted **I** from **2c** and **2e**, the phenyl groups increase the rate of the rearrangement as compared with the methyl groups. These findings of 1) - 4) could be rationalized in terms of the facile and irreversible ring opening of **IV** due to the substituent, since the cationic intermediate **V** is stabilized by the substituent at C_2 whose effect is in the order of C_6H_5 > CH_3 > H. The increased stability of **V** would discriminate the pathway shown in Scheme 3 from the pathway involving the less stable alternative **V'**.

As descrived above, we have found the acid-catalyzed rearrangement of 2-substituted and 2,4-disubstituted 8H-3-oxaheptalen-8-one to 1-acyl-6-hydroxyazulenes, which is of interest from the view point of not only reaction mechanism but also the products inaccessible otherwise.

References and Notes

1. Nakazawa, T.; Ishihara, M.; Jinguji, M.; Yamaguchi, M.; Yamochi, H. and Murata, I. *Chem. Lett.*, 1647 (1988).
2. **2b**: ^{1}H NMR ($CDCl_3$) δ 1.98 (s, CH_3), 5.56 (s, H-1), 5.63 (d, J= 6.0 Hz, H-5), 6.15 (d, J=6.0 Hz, H-4), 6.75 (s-like, H-6,7,9,10). **3b**: ^{1}H NMR (CF_3COOH) δ 1.98 (s, CH_3), 5.52 (d, J=7.4 Hz, H-5), 5.61 (s, H-1), 7.68 (s-like, H-6,7,9,10). **2c**: ^{1}H NMR ($CDCl_3$) δ 1.99 (s, CH_3), 5.63 (s, H-1,5), 6.80 (s-like, H-6,7,9,10). **3c**: ^{1}H NMR (CF_3COOH) δ 2.07 (s, CH_3), 5.82 (s, H-1,5), 7.75 (s-like, H-6,7,9,10).
3. Nakazawa, T.; Niimoto, Y. and Murata, I. unpublished results.
4. Due to the labitity of the products **5** and **6** in air, the hydroxy groups were converted into methoxy groups by the treatment with CH_2N_2 and the structures were further determined. Selected NMR data of the products

are descrived below. Methyl ether of **5b**: ^{1}H NMR ($CDCl_3$) δ 2.33 (s, CH_3), 3.95 (s, OCH_3), 6.73 (dd, J=12.5, 2.8 Hz, H-6), 6.80 (dd, J=12.6, 2.8 Hz, H-8), 7.02 (s, H-1), 7.38 (d, J=12.5 Hz, H-5), 7.41 (d, J=12.5 Hz, H-9), 7.44 (s, H-4). Methy ether of **6b**: ^{1}H NMR ($CDCl_3$) δ 2.77 (s, CH_3), 3.98 (s, OCH_3), 6.97 (s, H-3), 7.12 (dd, J=11.2, 2.7 Hz, H-5), 7.13 (dd, J=11.2, 2.7 Hz, H-7), 8.17 (d, J=11.2 Hz, H- 4), 9.37 (d, J=11.2 Hz, H-8), 10.4 (s, CHO). **7e**: ^{1}H NMR (DMSO-d_6) δ 5.50 (s, H-3), 5.85 (s, H-1), 6.83 (dd, J=12.1, 2.7 Hz, H-5), 6.93 (dd, J=12.1, 2.7 Hz, H-7), 7.04 (d, J=12.1 Hz, H-4), 7.30 (d, J=12.1 Hz, H-8), 7.20-7.28 (m, 5H of C_6H_5 and COC_6H_5), 7.42 (d, J=7.2 Hz, 2H of COC_6H_5), 7.46 (dd, J=7.5, 7.3 Hz, 1H of C_6H_5), 7.52 (d, J=7.2 Hz, 2H of C_6H_5). ^{13}C NMR (DMSO-d_6) δ 68.7 (-CH), 125.0, 126.6, 127.7, 127.8, 128.2, 132.4, 135.1, 136.8, 138.7, 140.2 (=CH), 137.7, 144.0, 146.7, 147.1 (=C-), 186.4, 197.5 (C=O). Methyl ether of **8e**: ^{1}H NMR (DMSO-d_6) δ 3.95 (s, OCH_3), 6.80 (d, J=11.1 Hz, H-5,7), 7.29 (t-like, J=7.3 Hz, H-4' of C_6H_5), 7.43 (t-like, J=7.3 Hz, H-3',5' of C_6H_5), 7.57 (s, H-1,3), 7.90 (dd, J=7.1, 1.3 Hz, H-2',6' of C_6H_5), 8.15 (dt, J=11.1, 1.3 Hz, H-4,8).

5. **5**, **6** and 1-acyl-1,6-dihydroazulen-6-one **7** are isomeric with the corresponding **2**. **7e** was isomerized to **6e** quantitatively on treatment with KOH in ethanol.
6. For oxepines, oxepine-benzene oxide tautomerism and acid-catalyzed isomerizations of oxepines to phenols were reported. Vogel, E. and Gunther, H. *Angew. Chem. Int. Ed. Eng.*, **1967**, *6*, 385.
7. It was reported that several substituted heptalenes were pyrolyzed to yield azulenes and acetylenes. In the reactions, 10π electrocyclizations of the heptalenes to give 2a,8a-dihydrocyclobut[a]azulenes were postulated as most reasonable pathways. Zeller, K. -P.: Azulene. In *Carbocyclische π-Elektronen Systeme. Houben-Weyl, Bd V/2c*,; Kropf, H. Eds.; Georg Thieme Verlag : Stuttgart·New York, 1985; pp.127-416. Hogrefe, F.. Dissertation, Universitat Köln, 1978. Diehl, H.. Dissertation, Technische Hochshule Darmstadt, 1976.
8. 2,7-Dialkyloxepines isomerize to cyclohexadienones or phenols through migration of an alkyl group.[6] Such a rearrangement was not observed for **2c** and **2e**.

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