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Novel Metal-Free Hydrogenation of the Carbon–Carbon Double Bond in Azulenoid Enones by Use of Cycloheptatriene and Protic Acid

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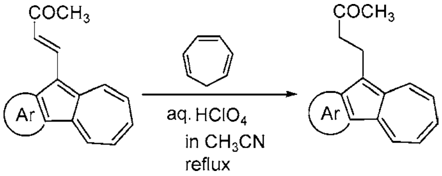
ABSTRACT



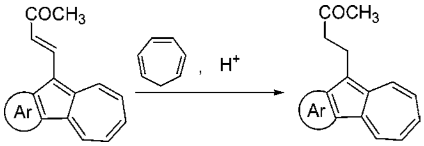
An efficient method for the hydrogenation of the carbon–carbon double bond in azulenoid and aromatic fused azulenoid enones without the use of hydrogen and a metal catalyst is reported. Treatment of a variety of azulenoid enones with cycloheptatriene and a protic acid in acetonitrile gave the corresponding *β*-azulenyl ketone derivatives in excellent to moderate yield. In this reaction, cycloheptatriene acts as a hydride donor.

The selective reduction of the carbon−carbon double bond of α,*β*-unsaturated carbonyl compounds is an important step in both industrial and laboratory synthesis. Catalytic hydrogenation by use of hydrogen and transition-metal catalysts is a widely applicable technique for the conversion of benzenoid enones, such as benzalacetone and chalcone, to the corresponding saturated ketones.[1] However, it cannot be applied for the azulenoid enones because azulene nuclei are easily reduced to octahydro or decahydro moieties.[2] In the course of our studies on the developments of a synthesis of aromatic fused azulenes having enone groups,[3] a novel and convenient method for the conversion of azulenoid and aromatic fused azulenoid enones to the corresponding saturated ketones was found.

Herein, we report a novel and convenient method for the conversion of azulenoid and aromatic fused azulenoid enones to the corresponding saturated ketones.

In a general method of hydrogenation, the mixture of the azulenoid enone **1**, 20 M equiv of cycloheptatriene, and 15 M equiv of aqueous perchloric acid (60%) or tetrafluoroboric acid (42%) in acetonitrile was refluxed for a few hours (Scheme 1).

Scheme 1. Hydrogenation of Azulenoid Enones



In a typical case, a mixture of 4-(10-benz[*a*]azulenyl)-3-butene-2-one (**1a**)[3d] (100 mg, 0.41 mmol), cycloheptatriene (760 mg, 8.2 mmol), and perchloric acid (60% aqueous

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[1] (a) Hudlický, M. In *Reductions in Organic Chemistry*; John Willey & Sons: New York, 1984; p 120. (b) Harmon, R. E.; Parsons, J. L.; Cooke, D. W.; Gupta, S. K.; Schoolenberg, J. *J. Org. Chem.* **1969**, *34*, 3684. (c) Djerassi, C.; Guntzwiller, J. *J. Am. Chem. Soc.* **1966**, *88*, 4527. (d) Breitner, E.; Roginski, E.; Rylander, P. N. *J. Org. Chem.* **1959**, *24*, 1855. (e) Adams, R.; Kern, J. W.; Shriner, R. E. *Org. Syn. Coll. Vol. 1* **1932**, 101.

[2] Melville, J. *J. Am. Chem. Soc.* **1933**, *55*, 3288.

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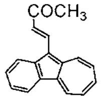
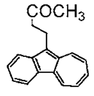
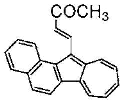
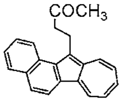
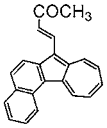
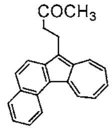
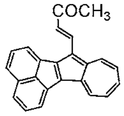
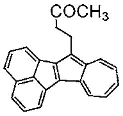
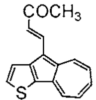
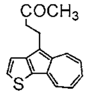
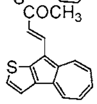
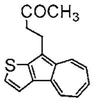
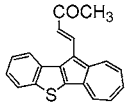
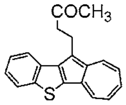
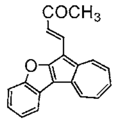
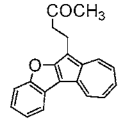
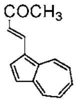
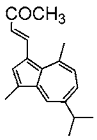
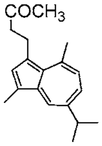
solution, 2.5 mL, 6.15 mmol) in 30 mL of acetonitrile was refluxed for 2 h. The resulting mixture was poured into 50 mL of water and 60 mL of toluene. The organic layer was separated and concentrated in vacuo. The residue was purified by column chromatography over silica gel using toluene as eluent to give **2a** in 78.1% yield.

The results are listed in Table 1. The yields listed in Table 1 are of isolated and purified products.[4] It is seen from Table 1 that a benzene-fused azulene derivative (**1a**) (Table 1, entry 1) and naphthalene-fused azulene derivatives (**1b** and **1c**) (Table 1, entries 2 and 3) were reduced to the corresponding saturated ketones in excellent to moderate yields. With an acenaphthalene-fused azulene derivative (**1d**) (Table 1, entry 4), the yield was slightly lower. The lower yield is attributed to the lack of stability of the saturated ketone **2d**. Heteroaromatic fused azulene derivatives (**1e**∼**1h**) (Table 1, entries 5∼8) were also reduced to the corresponding saturated ketones in excellent to moderate yields. With 4-(1-azulenyl)-2-but-3-ene-2-one (**1i**), a complex mixture was obtained instead of the expected saturated ketone, 4-(1-azulenyl)-2-butanone. Presumably, this is attributed to the high reactivity of the 1(3)-position of the azulene ring toward protic acid and electrophiles. In fact, 4-(1-guaiazulenyl)but-3-ene-2-one (**1j**) whose 3-position is blocked by the methyl group was reduced smoothly to the corresponding saturated ketone **2j**.

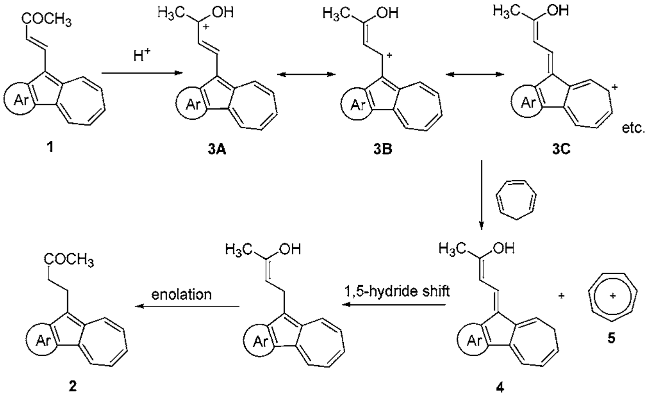
Table 1. Metal-Free Hydrogenation of the Azulenoid Enones

entry	azulenoid enone (**1**)		saturated ketone (**2**)		time/h	yield/%
1		(**1a**)		(**2a**)	2	78.1
2		(**1b**)		(**2b**)	1	71.1
3		(**1c**)		(**2c**)	1	80.5
4		(**1d**)		(**2d**)	4	59.2
5		(**1e**)		(**2e**)	4	63.0
6		(**1f**)		(**2f**)	2	65.9
7		(**1g**)		(**2g**)	2	76.4
8		(**1h**)		(**2h**)	2	77.0
9		(**1i**)	————		(20)	——
10		(**1j**)		(**2j**)	4	50.4

To our knowledge, this is the first example of metal-free hydrogenation of a carbon−carbon double bond in α,β-unsaturated ketones[5] which is brought about by a hydrocarbon and protic acid. When this novel hydrogenation was applied to benzenoid enones such as benzalacetone and 2,4-dimethylbenzalacetone, the starting materials were recovered unchanged even after a prolonged reaction time.

Although the reaction mechanism of this novel hydrogenation by cycloheptatriene and protic acid is not clear at present, the following reaction mechanism, which involves the addition of a proton and subsequent hydride abstraction from cycloheptatriene, can be postulated. As outlined in Scheme 2, addition of a proton to the oxygen atom of the carbonyl group in **1** generates the cation **3**, in which contribution of 3C is thought to be fairly large because it includes the stable

Scheme 2. Reaction Mechanism of Metal-Free Hydrogenation of the Azulenoid Enones



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(3) (a) Yamamura, K.; Kawabata, S.; Kimura, T.; Eda, K.; Hashimoto, M. *J. Org. Chem.* **2005**, *70*, 8902. (b) Yamamura, K.; Houda, Y.; Hashimoto, M.; Kimura, T.; Kamezawa, M.; Otani, T. *Org. Biomol. Chem*. **2004**, *2*, 1413. (c) Yamamura, K.; Kusuhara, N.; Kondou, A.; Hashimoto, M. *Tetrahedron* **2002**, *58*, 7653. (d) Sasabe, M.; Houda, Y.; Takagi, H.; Bo, X.; Yamamura, K. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3786.

(4) All new compounds were fully characterized by mass, ^{1}H NMR, and ^{13}C NMR spectra as well as elemental analyses. Selected data for **2a**: green oil; *m/z* 248 (M$^+$). Anal. calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49. Found: C, 87.12; H, 6.35. ^{1}H NMR (500 MHz, CDCl3) δ: 2.08 (3H, s, methyl), 2.80 (2H, t, J = 7.8 Hz, methylene), 3.35 (2H, t, J = 7.8 Hz, methylene), 6.75 (1H, dd, J = 11.1, 8.3 Hz, seven-membered ring), 6.89 (1H, dd, J = 11.1, 8.3 Hz, seven-membered ring), 7.06 (1H, dd, J = 11.0, 8.5 Hz, seven-membered ring), 7.47 (1H, d, J = 7.4 Hz, six-membered ring), 7.69 (1H, d, J = 8.0 Hz, six-membered ring), 7.80 (1H, d, J = 7.9 Hz, six-membered ring), 7.85 (1H, d, J = 11.1 Hz, six-membered ring), 8.11 (1H, d, J = 8.2 Hz, seven-membered ring), 8.31 (1H, d, J = 7.9 Hz, six-membered ring). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.2, 30.2, 43.4, 118.1, 120.8, 122.3, 123.3, 125.3, 125.5, 126.8, 128.5, 130.8, 132.6, 133.9, 134.4, 141.0, 141.8, 208.4.

tropylium ion moiety. Hydride abstraction from cycloheptatriene gives **4**, which undergoes rearrangement by a 1,5-sigmatropic shift, followed by enolation, to furnish **2**. The formation of the tropylium ion (**5**) was determined by isolation. Thus, when dry ether was added to the reaction mixture which was concentrated to about a one-third volume, **5** was precipitated. When triphenylmethane or 3-ethylpentane was used as the hydride source instead of cycloheptatriene, **1** was recovered unchanged.

In conclusion, we have developed metal-free hydrogenation of the carbon−carbon double bond of azulenoid enones by cycloheptatriene and protic acid. Although benzenoid α,β-unsaturated ketones have been investigated extensively from the chemical and physical points of view, the studies of azulenoid analogues have been very sparse, and this is the first report on the selective hydrogenation of the C−C double bond in azulenoid enones. The exact reaction mechanism is still unclear and is now under study.

Acknowledgment. We thank Konan Chemical Industry Co. Ltd. for generous gifts of 1-formylazulene and 3-formylguaiazulene.

Supporting Information Available: Copies of the ^{1}H NMR and ^{13}C NMR spectra for the products **2**. Elemental analyses and MS (*m*/*e*) data for **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) Recently, a metal-free reduction of α,β-unsaturated carbonyl compounds with phenyldimethylsilane and iodine pentoxide was reported: Ruizhu, M.; Zhengang, L.; Li, Y.; Longmin, W.; Zhong, L. L. *J. Chem. Res.* **2005**, 469.