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Communication

Facile Synthesis of Cyclic Vinamidinium *p*-Toluenesulfonates

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Recently we have reported on the α-iodination reaction of some cyclic enaminones.[1] The required cyclic enaminones have been synthesized by the reaction of cyclohexane-1,3-dione and amines such as aniline in the presence of *p*-toluenesulfonic acid as the catalyst.[2] During the reaction small amounts of cyclic vinamidinium salt was isolated. From the reaction mixture we could not find and isolate any salt-free vinamidine itself. Elimination of *p*-toluenesulfonic acid from the salt could be carried out by treatment with triethylamine to afford the cyclic vinamidine (vide infra).

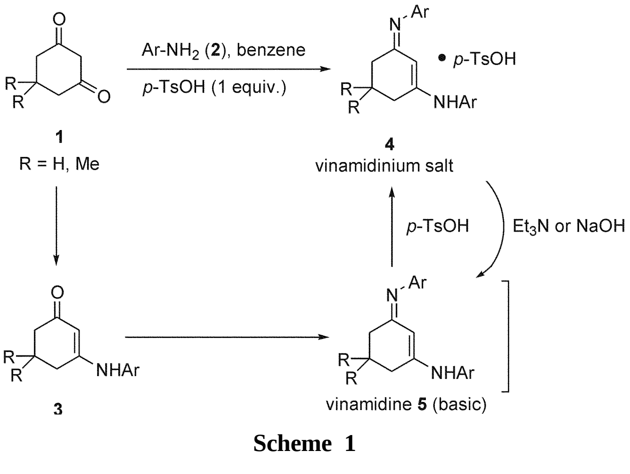
The synthesis of vinamidine in a direct method in high yield could not be achieved with excess use of aniline (up to 5 equiv.). The failure might be arised from the basic nature of vinamidine, which trap the acid catalyst and presented as its salt, namely vinamidinium salt. Electronic interactions between *p*-donor atoms (saturated nitrogen atom in this case) and π-acceptor groups (imino group in this case) through an intervening carbon-carbon double bond make vinamidine as a strong base.[3]

Vinamidinium salts have been used as versatile three-carbon building blocks in the synthesis of benzenoid, nonbenzenoid, and hetereocyclic aromatic rings.[4,5] Certain vinamidinium salts can be used as a UV absorber.[6] Thus, we intended to develop a facile preparation method of cyclic vinamidinium salt and wish to report herein the results.

As mentioned above the synthesis of vinamidine in a direct method in high yield could not be carried out with excess use of aniline. We envisioned that the problem could be solved by the use of excess amounts of acid catalyst. The acid catalyst might improve the electrophilicity of the carbonyl carbon of enaminone intermediate **3** and also act as a template for the approach of aniline toward the protonated enaminone (Scheme 1).

Thus, we examined the reaction of cyclohexane-1,3-dione (**1a**) and aniline (**2a**, 2.0 equiv.) in the presence of *p*-TsOH (1.0 equiv.). As expected the corresponding vinamidinium salt **4a** was isolated in high yield (94%, entry 2).[7] The same experiment with 0.1 equiv. of *p*-TsOH gave trace amounts of **4a** (6%) together with the enaminone **3a** (66%) as the major product. As shown in Table 1, the reaction of **1a** and 4-chloroaniline (**2b**) or 4-methoxyaniline (**2c**) showed similar pattern of reaction (entries 2 and 3). The use of dimedone (**1b**) showed same tendency as those of the cyclohexane-1,3-dione cases (entries 5 and 6). It is interesting to note that the use of picric acid instead of *p*-TsOH also produced the corresponding vinamidinium salt **4d** in moderate yield (entry 4).

As mentioned before synthesis of salt free vinamidine itself (**5a** and **5b**) could be carried out by the use of Et_3N or



Scheme 1

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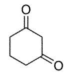
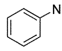
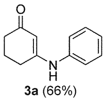
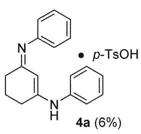
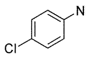
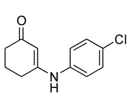
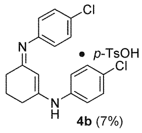
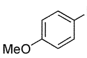
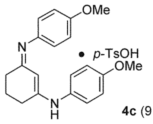
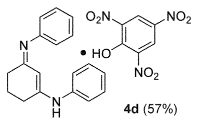
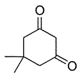
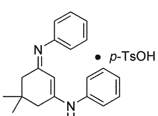
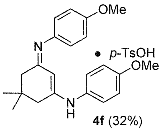
Table 1. Synthesis of vinamidinium salts **4**

Entry	Substrate	Conditions	Products (%)
1	 **1a** +  **2a**	*p*-TsOH (0.1 equiv.) benzene, reflux, 22 h **1a**:**2a** = 1:2	 **3a** (66%)  • *p*-TsOH **4a** (6%)
		p-TsOH (1 equiv.) benzene, reflux, 22 h **1a**:**2a** = 1:2	**4a** (94%)
2	**1a** +  **2b**	*p*-TsOH (0.1 equiv.) benzene, reflux, 12 h **1a**:**2b** = 1:2	 **3b** (64%)  • *p*-TsOH **4b** (7%)
		p-TsOH (1 equiv.) benzene, reflux, 10 h **1a**:**2b** = 1:2	**4b** (75%)
3	**1a** +  **2c**	*p*-TsOH (1 equiv.) benzene, reflux, 22 h **1a**:**2c** = 1:2	 • *p*-TsOH **4c** (91%)
4	**1a** + **2a**	picric acid (1.2 equiv.) benzene, reflux, 6 h **1a**:**2a** = 1:2	 **4d** (57%)
5	 **1b** + **2a**	*p*-TsOH (1 equiv.) benzene, reflux, 34 h **1b**:**2a** = 1:2	 • *p*-TsOH **4e** (81%)
6	**1b** + **2c**	*p*-TsOH (1 equiv.) benzene, reflux, 25 h **1b**:**2c** = 1:2	 • *p*-TsOH **4f** (32%)

NaOH from the corresponding vinamidinium salts **4a** and **4b**, for the removal of *p*-TsOH from **4a** could be carried out with Et_3N (52%). However, removal of *p*-TsOH from **4b** was not efficient with Et_3N, thus we used NaOH in this case (54%).

The UV spectra of some of the prepared compounds (**4a**, **4b**, **4d**, **5a**) were determined and are shown in Figure 1. Most of the compounds have strong UV absorption in the region of 320-380 nm and have relatively large molar absorptivity (26,000-37,000).[6] Further studies on the sunscreen effects of the vinamidinium salt are under progress.

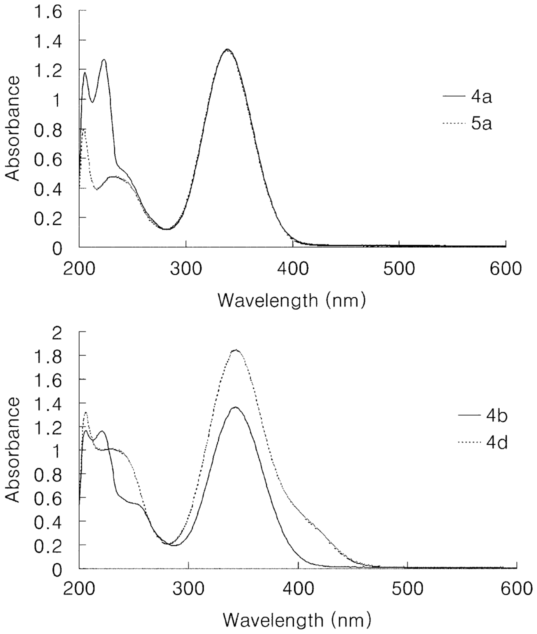


Figure 1

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References and Notes

1. Kim, J. M.; Na, J. E.; Kim, J. N. *Tetrahedron Lett.* **2003**, *44*, 6317.
2. (a) Gramain, J.-C.; Husson, H.-P.; Troin, Y. *J. Org. Chem.* **1985**, *50*, 5517. (b) Stefani, H. A.; Costa, I. M.; Silva, D. de O. *Synthesis* **2000**, 1526. (c) Elassar, A.-Z. A.; El-Khair, A. A. *Tetrahedron* **2003**, *59*, 8463.
3. Ostercamp, D. L.; Dinh, Y.; Graff, D.; Wiles, S. *J. Org. Chem.* **2003**, *68*, 3099.
4. (a) Marcoux, J.-F.; Marcotte, F.-A.; Wu, J.; Dormer, P. G.; Davies, I. W.; Hughes, D.; Reider, P. J. *J. Org. Chem.* **2001**, *66*, 4194. (b) Yamanaka, H.; Ishihara, T. *J. Fluorine Chem.* **2000**, *105*, 295. (c) Yamanaka, H.; Hisaki, K.; Kase, K.; Ishihara, T.; Gupton, J. T. *Tetrahedron Lett.* **1998**, *39*, 4355. (d) Yamanaka, H.; Takekawa, T.; Morita, K.; Ishiraha, T.; Gupton, J. T. *Tetrahedron Lett.* **1996**, *37*, 1829. (e) Yamanaka, H.; Yamashita, S.; Ishihara, T. *Tetrahedron Lett.* **1992**, *33*, 357. (f) Yamanaka, H.; Yamashita, S.; Ishihara, T. *Synlett* **1993**, 353.
5. (a) Davies, I. W.; Marcoux, J.-F.; Wu, J.; Palucki, M.; Corley, E. G.; Robbins, M. A.; Tsou, N.; Ball, R. G.; Dormer, P.; Larsen, R. D.; Reider, P. J. *J. Org. Chem.* **2000**, *65*, 4571. (b) Roll, C. P.; Donnio, B.; Guillon, D.; Weigand, W. *J. Mater. Chem.* **2003**, *13*, 1883. (c) Gupton, J. T.; Reisinger, S. W.; Shah, A. S.; Gall, J. E.; Bevirt, K. M. *J. Org. Chem.* **1991**, *56*, 976.
6. For the sunscreen effects of the vinamidinium salt and related compounds, see: (a) Chalker, B. E.; Dunlap, W. C.; Bandaranayake, W. M. AU 609125 (1991); *Chem. Abstr.* **1991**, *115*, 251161. (b) Zimmermann, T. J.; Freundel, O.; Gompper, R.; Muller, T. J. J. *Eur. J. Org. Chem.* **2000**, 3305.
7. Typical experimental procedure for the preparation of vinamidinium salt **4a**: A stirred mixture of cyclohexane-1,3-dione (112 mg, 1 mmol), aniline (186 mg, 2 mmol), and *p*-toluenesulfonic acid (190 mg, 1 mmol) in benzene (10 mL) was heated to reflux for 22 h. After cooling to room temperature and removal of solvent the residue was dissolved in CH_2Cl_2 (3-4 drops of methanol was added in order to dissolve completely). After column chromatographic purification process (CH_2Cl_2/MeOH, 5 : 1) pure product **4a** was obtained, 408 mg (94%). Other compounds were prepared analogously and the representative spectroscopic data of **4a**, **4d**, and **5a** are summarized below.
8. **4a**: 94%, brown solid; mp 182-184 °C; IR (KBr) 3444, 2970, 2927, 1523, 1489 cm^{-1}; ^1H NMR ($CDCl_3$ + few drops of DMSO-d_6) δ 1.77 (br s, 2H), 2.31 (s, 3H), 2.74 (br s, 4H), 5.77 (s, 1H), 7.04-7.36 (m, 12H), 7.64 (d, J = 8.1 Hz, 2H), 10.84 (s, 1H); UV (MeOH) λ_{max} 340 nm (ε = 26,725); Mass (70 eV) *m/z* (rel intensity) 77 (40), 130 (21), 143 (22), 233 (43), 234 (42), 262 (M^+-TsOH, 100).
   4d: 57%, yellow solid, mp 52-53 °C; IR (KBr) 3201, 3032, 2943, 1631, 1554 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 (br s, 2H), 2.74 (br s, 4H), 5.78 (br s, 1H), 7.12-7.40 (m, 10H), 8.79 (s, 2H of picric acid), 10.02 (br s, 2H); UV (MeOH) λ_{max} 343 nm (ε = 36,947).
   5a: 52%, brown solid, mp 147-149 °C; IR (KBr) 3016, 2954, 2866, 1570, 1539 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.93 (quintet, J = 6.0 Hz, 2H), 2.45 (t, J = 6.0 Hz, 4H), 4.44 (br s, 1H), 5.74 (s, 1H), 6.89-7.27 (m, 10H); ^{13}C NMR (DMSO-d_6) δ 21.59, 30.28, 93.86, 121.14, 122.37, 128.80, 145.86, 160.40; UV (MeOH) λ_{max} 338 nm (ε = 26,629).