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Novel and chemoselective dehydrogenation of 2-substituted imidazolines with potassium permanganate supported on silica gel

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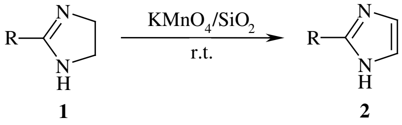
Abstract—Various types of 2-imidazolines are efficiently oxidized to the corresponding imidazoles using potassium permanganate supported on silica gel under mild conditions at room temperature. 2-Alkylimidazolines are selectively converted to their corresponding imidazoles in the presence of 2-arylimidazolines. Chemoselective oxidation of 2-imidazolines in the presence of other oxidizable functional groups such as sulfide, ether, aldehyde, acetal, and THP ether was also achieved by this reagent system.

The oxidation of 2-imidazolines to imidazoles is biologically and pharmaceutically very important, since many imidazole derivatives possess antihypertensive, antiinflammatory, antibacterial, and antidiabetic activities.[1] 2-Imidazolines can be easily prepared from nitriles and ethylenediamine.[2] Therefore, dehydrogenation of 2-imidazolines by an oxidizing agent should provide an efficient method for the preparation of imidazole derivatives. Several reagents such as Zn–Al_2O_3,[3] Ni,[4] Se,[5] Pd/C,[6] MnO_2,[7] $BaMnO_4$,[8] and DMSO[9] have been previously reported for this purpose. These reagents suffer from limitations such as low yields of the products, very long reaction times, toxicity, the use of large excess of the reagents, and harsh reaction conditions. Also, some of these reagents are not effective for the oxidation of 2-alkylimidazolines. Therefore, the discovery of a novel, mild, and efficient method using an inexpensive reagent for excellent-yielding oxidation of 2-imidazolines to their corresponding imidazoles is of general interest.

Potassium permanganate has been used for the oxidation of 2-imidazolines,[10] but this method also suffers from disadvantages such as low yields of the products (40–72%), long reaction times (12–16 h), and harsh reaction conditions (reflux in dioxane).

The use of supported reagents has gained popularity because of the improved selectivity, reactivity, and associated ease of manipulation.[11] On the other hand, it was recently shown that adsorption onto solid supports can change the reactivity and selectivity of $KMnO_4$ in oxidation reactions.[12] We now report that $KMnO_4$ adsorbed on the very inexpensive and readily available support, silica gel,[13] oxidizes 2-imidazolines to imidazoles efficiently (Scheme 1).

Our goals in undertaking this work were: (a) to achieve rapid reaction rates, higher yields, and milder reaction conditions; (b) to overcome the drawbacks of the reported methods; (c) to develop a high-yielding synthesis of imidazoles using a cheap commercially available



Scheme 1.

Keywords: 2-Imidazolines; Imidazoles; Dehydrogenation; Potassium permanganate.

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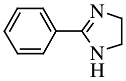
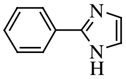
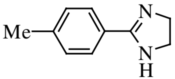
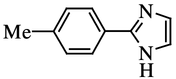
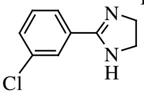
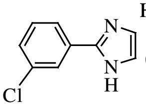
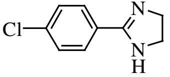
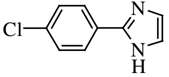
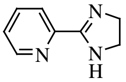
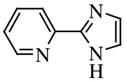
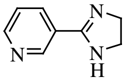
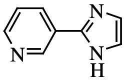
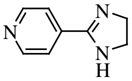
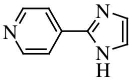
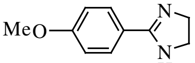
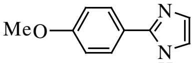
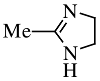
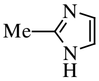
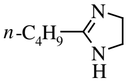
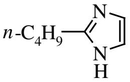
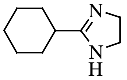
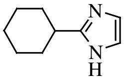
Table 1. Dehydrogenation of 2-imidazolines with $KMnO_4/SiO_2$ in CH_3CN at room temperature

Substrate (**1**)	Time (h)	$KMnO_4$/Imidazoline[a,b]	Product[c] (**2**)	Yield[d] (%)
 **(1a)**	2.5	2.5	 **(2a)**	85
 **(1b)**	2.3	3[e]	 **(2b)**	89
 **(1c)**	2.5	2.5	 **(2c)**	95
 **(1d)**	3	3[e]	 **(2d)**	89
 **(1e)**	1.2	2.5	 **(2e)**	85
 **(1f)**	1.7	2.5	 **(2f)**	90
 **(1g)**	1.5	2.5	 **(2g)**	96
 **(1h)**	1.2	2.1	 **(2h)**	74
 **(1i)**	0.15	1.1	 **(2i)**	90
 **(1j)**	0.25	1.1	 **(2j)**	86
 **(1k)**	0.35	1.3	 **(2k)**	88

[a] Molar ratio.

[b] Five hundred milligrams of SiO_2 per mmol of 2-imidazoline was used.

[c] All products were characterized by comparison of their physical and spectral data with those of authentic samples.[8–10,15]

[d] Isolated yields.

[e] Eight hundred milligrams of SiO_2 per mmol of 2-imidazoline was used.

reagent. As shown in Table 1, different types of 2-arylimidazolines are oxidized to their corresponding imidazoles in good to excellent yields with $KMnO_4/SiO_2$ in acetonitrile at room temperature (entries **1a**–**h**).[14] Some of the reported reagents such as DMSO[9] and Pd/C[9] were not effective for dehydrogenation of 2-alkylimidazolines. Thus, efficient oxidation of 2-alkylimidazolines to their imidazoles by $KMnO_4/SiO_2$ system is an interesting feature of the presented method (entries **1i**–**k**).

In order to establish the general applicability of the method, we have performed several competitive oxidation reactions, results of which are shown in Scheme 2. As can be seen, interesting selectivities were observed. 2-Alkylimidazolines are oxidized in the presence of 2-arylimidazolines with high selectivity. Also, chemoselective oxidation of 2-imidazolines in the presence of other oxidizable functional groups such as sulfide, ether, aldehydes, acetal, and THP ether is achieved using this reagent system. To the best of our knowledge, such selectivities have not been reported previously in oxidation of 2-imidazolines.

In Table 2, some of the results of our experiments are compared with those reported by other methods. The results show that the reaction times are considerably lower and the yields of the products are higher using $KMnO_4/SiO_2$ system.

In summary, it is clear that the simplicity of this method, the low cost of the reagent, the ease of use, very mild reaction conditions, and high yields of the products accompanied with chemoselectivity make the reagent system described here very attractive.

Acknowledgements

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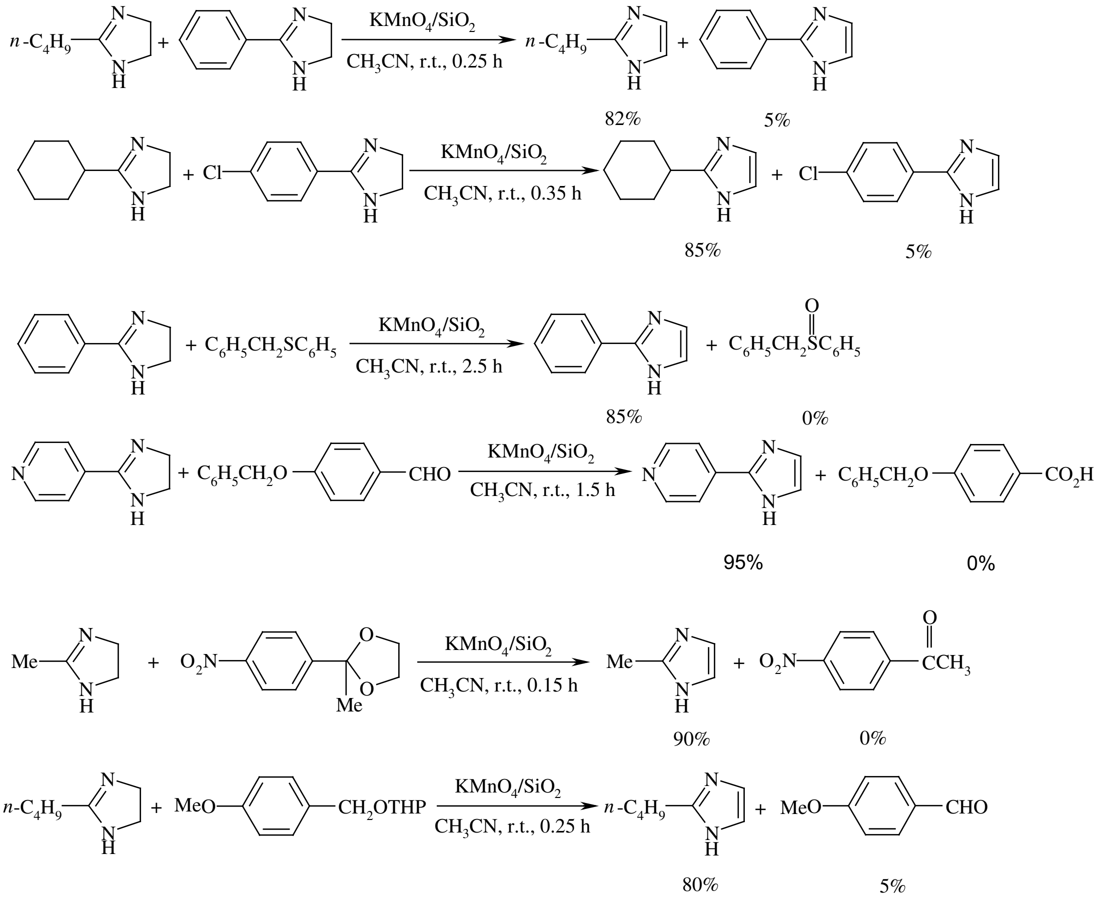
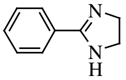
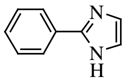
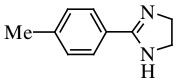
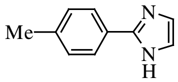
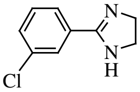
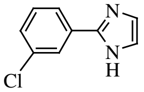
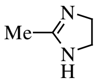
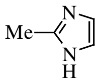


Scheme 2.

Table 2. Comparison of some of the results obtained from KMnO$_4$/SiO$_2$ (I) and some of those reported with DMSO (II),[9] 10%Pd/C (III),[9] and KMnO$_4$/refluxing dioxane (IV)[10]

Substrate	Product	Yield (%) (Time, h)			
		I	II	III	IV
		85 (2.5)	51 (48)	77 (48)	40 (16)
		89 (2.3)	71 (48)	57 (48)	–
		95 (2.5)	65 (48)	30 (48)	–
		90 (0.15)	0 (48)	0 (48)	72 (12)

Reference and notes

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13. Potassium permanganate (0.79 g) and SiO_2 (1 g) were ground together in a mortar until a fine homogeneous powder was obtained.
14. Typical procedure: To a solution of 2-phenylimidazoline **1a** (2 mmol) in CH_3CN (25 mL), $KMnO_4/SiO_2$ (1.79 g, 5 mmol) was added and the mixture was stirred at room temperature for 2.5 h. The progress of the reaction was monitored by TLC (eluent: EtOAc/MeOH: 4/1). Ethanol (1 mL) was added to reduce excess oxidant. The mixture was filtered and the solid material was washed with CH_3CN (10 mL). The filtrate was evaporated and the resulting crude material was purified by chromatography on alumina with the appropriate eluent to afford the pure 2-phenylimidazole **2a**. Yield 245 mg (85%). Mp 140–142 °C (lit.[8] mp 144–146 °C). IR (KBr) 3360, 3120, 3040, 1656, 1568, 1502, 1458, 1102, 944, 700 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ 7.01 (1H, br s), 7.22 (1H, br s), 7.31 (1H, t, $J = 7$ Hz), 7.42 (2H, t, $J = 7.4$ Hz), 7.92 (2H, d, $J = 8$ Hz,), 12.47 (1H, s).
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