Electrochemical Oxidation of Substituted Amide Oximes and 4,5-Dihydro-1,2,4-Oxadiazoles

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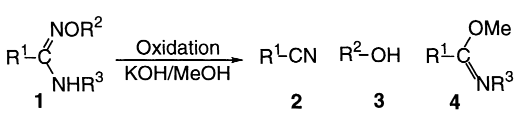
The electrooxidation of several substituted amide oximes to yield the corresponding nitriles, alcohols, and imidate was successfully carried out. The reaction products were dependent on the substituents. Additionally, 4,5-dihydro-1,2,4-oxadiazoles derived from amide oximes were electro-oxidized to afford 1,2,4-oxadiazoles in good yields.

We previously reported on the electrooxidations of various nitrogen-containing organic compounds, such as enamines,[1] hydrazones,[2] and imines.[3] As a continuation of this series of studies, we carried out the direct electrooxidation of amide oximes and its derivatives. Shono and co-workers have reported[4] on the indirect electrooxidation of aldoxime using halide ion as the electron carrier in forming the corresponding nitriles; however, to the best of our knowledge, the direct electrooxidation of amide oxime (**1**) has not been reported to date. In this study, we observed that the type of product formed from **1** was remarkably dependent on the substituents (R^1, R^2, and R^3; Table 1). In the cases of $R^2 = R^3 = H$ and $R^1 = Ph$, $PhCH_2$, and *iso*-C_5H_{11} (**1a**, **1b**, and **1c**, respectively), the corresponding nitriles (**2a**, **2b**, and **2c**) were isolated in good yields. In the cases of $R^1 = Ph$, $R^3 = H$, and $R^2 =$ *iso*-C_5H_{11}, $PhCH_2$, and PhCO (**1d**, **1e**, and **1f**, respectively), mixtures of benzonitrile and corresponding alcohols (**3d** and **3e**) were obtained, while and in the case of **1f**, methyl benzoate instead of the alcohol was formed. On the other hand, in the case of $R^1 = Me$, $R^2 = H$, and $R^3 = Ph$ (**1g**), imidate **4g** was obtained as the main product. As a note, **4g** was produced previously by a two-step photochemical reaction of an alkoxytungstencarbene complex with azobenzene[5] and an alkoxychromiumcarbene complex with sulfilimines.[6] However, this two-step method was limited by a somewhat troublesome preparation of the starting materials; in contrast, **4g** could be obtained in reasonable yields using readily available substrates in our electrooxidation method. Although the detailed reaction mechanisms are not clear, based on our observations that these oxidation reactions were almost complete after the consumption of 1.2 F/mol of electricity, it can be assumed that the electrooxidation of **1** to **2**, **3**, and **4** proceeded through one-electron transfer oxidation.

In addition, as shown in Fig. 1, amide oxime readily reacted with certain aldehydes to give 4,5-dihydro-1,2,4-oxadiazoles (**5**).[7] Although the electroreductions of 1,3,4-oxadiazoles have been reported,[8] the electrooxidative behavior of **5** was not examined. Typically, the compounds are oxidized using strong oxidizing agents, such as potassium permanganate[9] or sodium hypochlorite,[10] to yield the corresponding oxadiazoles (**6**).[11] In our case, electrooxidation was successful in affording **6** in 72–85% isolated yields, as shown in Table 2. In every case, the substrates were almost completely consumed after 2.2 F/mol of electricity had been passed. The electrooxidation reaction of **5** could also be carried out without any substituent effects at the 3- and 5-positions under the conditions described in the experimental section. In conclusion, although amide oximes, unlike aldoximes, are relatively stable towards solvolysis in the presence of strong acid or base catalysts, even at

Table 1. Electrochemical Oxidation of Amide Oximes[a)]



	R^1	R^2	R^3	Yield[b)]/%		
				2	**3**	**4**
1a	Ph	H	H	85		
1b	$PhCH_2$	H	H	70		
1c	*iso*-C_5H_{11}	H	H	80		
1d	Ph	*iso*-C_5H_{11}	H	(81)	(75)	
1e	Ph	$PhCH_2$	H	(88)	(78)	
1f	Ph	PhCO	H	(85)	(58)[c)]	
1g	Me	H	Ph			72

a) 1.2–1.5 F/mol of electricity was passed. b) Values in parenthesis were determined by GLC analysis. c) Yield of methyl benzoate.

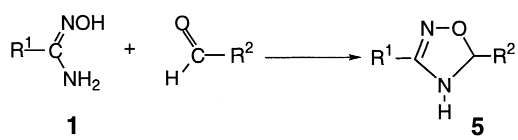
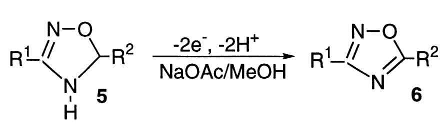


Fig. 1.

Table 2. Electrochemical Oxidation of 4,5-Dihydro-1,2,4-oxadiazoles[a)]



	R^1	R^2	Yield[b)] of **6**/%
5a	*iso*-C_5H_{11}	Et	72
5b	Ph	Et	78
5c	Ph	*iso*-C_3H_7	82
5d	Ph	*n*-C_5H_{11}	80
5e	*p*-ClC_6H_4	Et	81
5f	$PhCH_2$	Et	85
5g	$PhCH_2$	*iso*-C_3H_7	84

a) 2.2 F/mol of electricity was passed. b) Isolated yield.

elevated temperatures, they readily underwent electrooxidation to yield nitriles, alcohols, and imidate under very mild conditions. Moreover, 4,5-dihydro-1,2,4-oxadiazoles that were obtained by a simple condensation reaction between an amide oxime and an aldehyde were electrooxidized to afford the corresponding 1,2,4-oxadiazoles in good yields.

Experimental

Amide oximes **1a–c** were prepared by reactions between hydroxylamine and the corresponding nitriles.[12] **1d–f** were prepared by the reaction of benzamide oxime with alkyl halide.[13a] **1g** was synthesized by the reaction of acetamide oxime hydrochloride with aniline.[13b] 4,5-dihydro-1,2,4-oxadiazoles **5** were prepared by refluxing the corresponding amide oximes and aldehydes in EtOH.[7] Preparative-scale electrooxidation was carried out in a tall 50- or 100-mL beaker equipped with a fine frit cup as the cathode compartment, a cylindrical platinum net anode (diameter, 33 mm; height, 40 mm), and a nickel coil cathode. The electrooxidation of amide oxime **1** was carried out in MeOH (80 mL) containing **1** (20 mmol) and KOH (20 mmol) under a constant current (0.4 A). The electrooxidation of 4,5-dihydro-1,2,4-oxadiazoles **5** was carried out in MeOH (40 mL) containing **5** (5 mmol) and NaOAc (10 mmol) under a constant current (0.3 A). In both cases, the anolyte was stirred using a magnetic stir bar, and the temperature of the solution was maintained at ca. 15 °C. After completion of the electrooxidation, treatment of the reaction mixture was achieved as follows. The anolyte was concentrated in vacuo at ca. 30 °C to approximately one-fifth of its original volume. The resulting residue was treated with water (50 mL), then extracted with ether (3 $\times$ 50 mL). The ethereal extracts were combined, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was purified either by distillation in vacuo or by recrystallization from MeOH.

3-Isopentyl-5-ethyl-1,2,4-oxadiazole (6a). Bp 110–111 °C/44 hPa. IR (neat) 2959, 2872, 1583, 891 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.95 (d, 6H, J = 7Hz), 1.39 (t, 3H, J = 7Hz), 1.4–1.8 (m, 3H), 2.71 (t, 2H, J = 7 Hz), 2.89 (q, 2H, J = 7 Hz). ^{13}C NMR ($CDCl_3$) δ 10.8 (CH_3), 20.2 (CH_2), 22.3 (CH_3), 24.1 (CH_2), 27.8 (CH), 36.0 (CH_2), 170.7 (C), 180.2 (C). MS m/z (rel intensity): 168 (M^+), 125 (24), 113 (49), 112 (100), 97 (31), 57 (57), 41 (38), 29 (45). HRMS m/z Found: 168.1262 (M^+), Calcd for $C_9H_{16}N_2O$: 168.1263.

3-Phenyl-5-pentyl-1,2,4-oxadiazole (6d). Bp 138–139 °C/5.3 hPa. IR (neat) 2959, 1595, 1572, 1447, 1364, 907, 721, 694 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 7 Hz), 1.1–1.5 (m, 4H), 1.6–2.1 (m, 2H), 2.89 (t, 2H, J = 7 Hz), 7.3–7.6 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 13.8 (CH_3), 22.2 (CH_2), 26.4 (CH_2), 26.6 (CH_2), 31.2 (CH_2), 127.2 (C), 127.4 (CH), 128.8 (CH), 131.0 (CH), 168.3 (C), 180.0 (C). MS m/z (rel intensity) 216 (M^+, 34), 173 (40), 160 (74), 119 (100), 118 (78), 103 (53), 91 (37). HRMS m/z Found: 216.1270 (M^+), Calcd for $C_{13}H_{16}N_2O$: 216.1263.

3-Benzyl-5-ethyl-1,2,4-oxadiazole (6f). Bp 112–113 °C/5.3 hPa. IR (neat) 2986, 2943, 1580, 1497, 1456, 887, 733, 696 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.28 (t, 3H, J = 7 Hz), 2.78 (t, 2H, J = 8 Hz), 4.00 (s, 2H), 7.0–7.6 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 10.6 (CH_3), 20.2 (CH_2), 32.3 (CH_2), 127.0 (CH), 128.6 (CH), 129.0 (CH), 135.7 (C), 169.3 (C), 180.7 (C). MS m/z (rel intensity) 188 (M^+, 28), 173 (40), 132 (100), 131 (25), 103 (25), 91 (25), 77 (18), 57 (17), 29 (20). HRMS m/z Found: 188.0911 (M^+), Calcd for $C_{11}H_{12}ON_2$: 188.0950.

3-Benzyl-5-isopropyl-1,2,4-oxadiazole (6g). Bp 114–115 °C/5.3 hPa. IR (neat) 2978, 2937, 1576, 1498, 1456, 891, 727, 696 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.24 (d, 6H, J = 7 Hz), 2.8–3.4 (m, 1H), 4.00 (s, 2H), 7.0–7.6 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 20.0 (CH_3), 27.4 (CH), 32.3 (CH_2), 126.9 (CH), 128.6 (CH), 129.0 (CH), 135.8 (C), 169.2 (C), 183.8 (C), 168.3 (C). MS m/z (rel intensity) 202 (M^+, 21), 132 (100), 117 (20), 103 (21), 91 (26), 77 (16), 43 (39). HRMS m/z Found: 202.1115 (M^+), Calcd for $C_{12}H_{14}ON_2$: 202.1106.

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