Electrooxidative Conversion of Aldehyde and Ketone Phenylhydrazones into the Methoxy(phenylazo) alkanes

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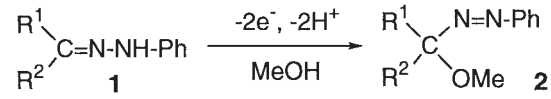
Several aldehyde and ketone phenylhydrazones were converted into the corresponding methoxy(phenylazo)alkane derivatives by electrochemical oxidation in MeOH.

The oxidative conversions of aldehyde and ketone phenylhydrazones into the corresponding alkoxy(phenylazo)alkanes or acetoxy(phenylazo)alkanes have been reported in several studies. Investigations on the oxidation of acetone phenylhydrazones to the alkoxy(phenylazo) derivatives have been reported by Schantl,[1] using iodine as an oxidant in various alcohols with yields of 23–50%, and by Chiusoli and co-workers,[2] using a palladium catalyst, thiourea, and a stream of carbon monoxide, with yields of less than 20%. Harrison and co-workers[3] have reported on the oxidation of benzophenone phenylhydrazones in dichloromethane, using lead tetraacetate as the oxidant. However, this application was limited to only benzophenone phenylhydrazones. Based on previous studies on the electrooxidation of various hydrazones,[4–9] we carried out our investigations on the oxidation of several aldehyde and ketone phenylhydrazones by means of an electrochemical method.

Our investigations on the electrooxidation of phenylhydrazones began with the determination of the optimal reaction conditions. Consequently, for the ketone phenylhydrazones (Table 1, **1c**–**1h**), the use of an equimolar amount of KI as the electrolyte was favorable in affording the corresponding methoxy(phenylazo) compounds (**2c**–**2h**). In contrast, for the aldehyde phenylhydrazones (**1a**, **1b**), the corresponding methoxy(phenylazo) compounds were not obtained when using KI as the electrolyte. Subsequently, it was found that the corresponding phenylazo products can be produced from aldehyde phenylhydrazones in nearly 50% yields by using the tetraethylammonium salt of *p*-toluenesulfonic acid (*p*-$TsONEt_4$) as the electrolyte, and also by employing carbon poles instead of a platinum net as the anode. As shown in Table 1, aldehyde phenylhydrazones **1a** and **1b** afforded methoxy(phenylazo) compounds **2a** and **2b** in 52% and 44% yields, respectively, whereas ketone phenylhydrazones **1c**–**1h** afforded compounds

Table 1. Electrooxidation of Aldehyde and Ketone Phenylhydrazones[a)]



Compound	R^1	R^2	Supporting electrolyte[b)]	Current passed	Yield[c)] of **2**
				$F\,mol^{-1}$	%
1a	Me	H	$TsONEt_4$	2.4	(52)
1b	*n*-Pr	H	$TsONEt_4$	3.2	(44)
1c	Me	Me	KI	2.1	67
1d	*i*-Bu	Me	KI	2.1	74
1e	*n*-Pr	*n*-Pr	KI	2.0	72
1f	$-(CH_2)_5-$		KI	2.0	75
1g	$-(CH_2)_7-$		KI	2.1	70
1h	$-(CH_2)_8-$		KI	3.2	60

a) **1**: 10 mmol, MeOH: 80 mL, reaction temp: ca. 15 °C. b) $TsONEt_4$: 6 mmol, KI: 10 mmol. c) Isolated yield. Values in parenthesis were determined by GLC analysis.

2c–**2h**, respectively, in 60–75% isolated yields, after 2.0–3.2 F of electricity had been passed. As a note, in the case of the aldehyde phenylhydrazones, significant amounts of a tar-like material was observed during ether extraction steps. Although details of the reaction mechanism of the electrooxidation are not clear, it can be assumed that, in the case of oxidation of ketone phenylhydrazones, the iodide ions serve as the electron carriers. In fact, the phenylazo compounds were hardly preparable when using NaOMe, NaCN, NaOAc, or $NaClO_4$ as the electrolyte instead of iodide ion from KI or NaI. In conclusion, we have found that methoxy(phenylazo)alkanes can be obtained in reasonable to good yields by the electrooxidation of phenylhydrazones in MeOH using *p*-$TsONEt_4$ or KI as the electrolyte without the use of special oxidizing agents under very mild conditions.

Experimental

All electrooxidation products were identified from their physical and spectral data. Substrates were synthesized through typical condensation reactions[10] using equimolar amounts of phenylhydrazine and the corresponding carbonyl compounds. The subsequent electrooxidations were carried out immediately, since all phenylhydrazones prepared in this study were relatively unstable, gradually giving a dark tar-like material within a few weeks even under storage in a refrigerator. Other reagents were obtained from commercial suppliers and used without further purifications. Preparative-scale electrooxidations were carried out in a tall 100-mL beaker, equipped with a fine frit cup as the cathode compartment, with either four pieces of carbon poles (diameter, 5 mm; height, 80 mm) for electrooxidation of **1a** and **1b**, or a cylindrical platinum net (diameter, 33 mm; height, 40 mm) for electrooxidation of **1c**–**1h** used as the anode, and a nickel coil cathode. Aldehyde phenylhydrazones **1a** and **1b** and ketone phenylhydrazones **1c**–**1h** were oxidized under conditions as follows: a solution of substrate **1a**–**1h** (10 mmol) and *p*-$TsONEt_4$ (6 mmol) for **1a** and **1b** or KI (10 mmol) for **1c**–**1h** in MeOH (80 mL) was electrooxidized under a constant current (0.3 A). During the course of the electrooxidation, the anolyte was magnetically stirred while maintaining the

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temperature of the cell at approximately 15 °C. After completion of the electrooxidation, the reaction mixture was treated with a threefold amount of the anolyte solution. After concentrating the combined anolyte solution in vacuo at approximately 30 °C to roughly one-fifth of its original volume, the resulting residue was treated with water (50 mL), and the oily layer was extracted with ether (3 × 40 mL). The combined ether extracts were washed with aqueous sodium thiosulfate solution (20% w/w, 30 mL), and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was purified by distillation under reduced pressures or by silicagel column chromatography (diameter, 3.5 cm; height, 30 cm) with ether as the eluent.

1-Methoxy-1-phenylazoethane (2a): bp 80–82 °C/1.8 hPa. IR (neat): 692, 768, 1132, 1607, 2934, 2988 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.44 (3H, d, $J = 6$ Hz, Me), 3.43 (3H, s, MeO), 4.64 (1H, t, $J = 6$ Hz, CH), 7.3–7.8 (5H, m, Ar). ^{13}C NMR ($CDCl_3$) δ 19.22 (Me), 56.52 (MeO), 101.56 (CH), 122.57 (CH), 129.04 (CH), 131.12 (CH), 151.52 (C). MS m/z (rel intensity %) 164 (M^+, 2), 77 (21), 58 ($(M - PhN_2)^+$, 100), 50 (16), 26 (16). HRMS m/z found: 164.1002 M^+, calcd for $C_9H_{12}N_2O$: 164.0950.

1-Methoxy-1-phenylazobutane (2b): bp 76–78 °C/1.8 hPa. IR (neat): 691, 768, 1121, 1456, 2874, 2961 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.94 (3H, t, $J = 7$ Hz, Me), 1.2–2.0 (4H, m, $CH_2 \times 2$), 3.40 (3H, s, MeO), 4.51 (1H, t, $J = 7$ Hz, CH), 7.4–7.9 (5H, m, Ar). ^{13}C NMR ($CDCl_3$) δ 13.97 (Me), 17.59 (CH_2), 35.67 (CH_2), 56.72 (MeO), 105.02 (CH), 122.61 (CH), 129.49 (CH), 131.04 (CH), 151.60 (C). MS m/z (rel intensity %) 192 (M^+, 3), 87 ($(M - PhN_2)^+$, 60), 77 (27), 54 (16), 44 (100). HRMS m/z found: 192.1327 M^+, calcd for $C_{11}H_{16}N_2O$: 192.1263.

2-Methoxy-4-methyl-2-phenylazopentane (2d): bp 88–90 °C/1.4 hPa. IR (neat): 691, 764, 1090, 1454, 2870, 2955 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.90 (3H, d, $J = 6$ Hz, Me), 0.94 (3H, d, $J = 6$ Hz, Me), 1.40 (3H, s, Me), 1.6–2.2 (3H, m, $CHCH_2$), 3.48 (3H, s, MeO), 7.3–7.8 (5H, m, Ar). ^{13}C NMR ($CDCl_3$) δ 20.93 (Me), 23.82 (Me), 24.19 (Me), 24.60 (CH), 46.83 (CH_2), 50.58 (MeO), 100.42 (C), 122.37 (CH), 128.96 (CH), 130.63 (CH), 151.93 (C). MS m/z (rel intensity %) 115 ($(M - PhN_2)^+$, 100), 77 (32), 73 (50), 58 (57), 41 (27), 39 (23). HRMS m/z found: 115.1208 $(M - PhN_2)^+$, calcd for $C_7H_{15}O$: 115.1123. CIMS m/z 221 $(M + 1)^+$.

4-Methoxy-4-phenylazoheptane (2e): bp 103–105 °C/1.4 hPa. IR (neat): 692, 764, 1086, 1456, 2871, 2961 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.89 (6H, t, $J = 7$ Hz, Me × 2), 1.2–1.6 (4H, m, $CH_2 \times 2$), 1.7–1.9 (4H, m, $CH_2 \times 2$), 3.45 (3H, s, MeO), 7.4–7.8 (5H, m, Ar). ^{13}C NMR ($CDCl_3$) δ 14.58 (Me), 16.25 (CH_2), 36.81 (CH_2), 50.49 (MeO), 101.19 (C), 122.28 (CH), 128.96 (CH), 130.55 (CH), 152.05 (C). MS m/z (rel intensity %) 129 ($(M - PhN_2)^+$, 100), 77 (29), 54 (39), 44 (48), 39 (20). HRMS m/z found: 129.1327 $(M - PhN_2)^+$, calcd for $C_8H_{17}O$: 129.1279. CIMS m/z 235 $(M + 1)^+$.

1-Methoxy-1-phenylazocyclohexane (2f): bp 110–112 °C/1.4 hPa. IR (neat): 691, 766, 1088, 1452, 2858, 2936 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.3–2.0 (10H, m, $CH_2 \times 5$), 3.45 (3H, s, MeO), 7.3–7.8 (5H, m, Ar). ^{13}C NMR ($CDCl_3$) δ 22.19 (CH_2), 25.41 (CH_2), 32.01 (CH_2), 49.92 (MeO), 98.71 (C), 122.33 (CH), 128.96 (CH), 130.63 (CH), 152.05 (C). MS m/z (rel intensity %) 113 ($(M - PhN_2)^+$, 100), 81 (78), 77 (31), 44 (32), 39 (18). HRMS m/z found: 113.1020 $(M - PhN_2)^+$, calcd for $C_7H_{13}O$: 113.0966. CIMS m/z 219 $(M + 1)^+$.

1-Methoxy-1-phenylazocyclooctane (2g): bp 132–134 °C/1.4 hPa. IR (neat): 691, 766, 1072, 1457, 2851, 2926 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.3–2.1 (14H, m, $CH_2 \times 7$), 3.45 (3H, s, MeO), 7.3–7.8 (5H, m, Ar). ^{13}C NMR ($CDCl_3$) δ 21.01 (CH_2), 24.43 (CH_2), 28.10 (CH_2), 30.58 (CH_2), 50.25 (MeO), 101.03 (C), 122.24 (CH), 128.92 (CH), 130.47 (CH), 151.97 (C). MS m/z (rel intensity %) 141 ($(M - PhN_2)^+$, 100), 109 (22), 77 (34), 67 (48), 44 (20), 39 (24). HRMS m/z found: 141.1343 $(M - PhN_2)^+$, calcd for $C_9H_{17}O$: 141.1279. CIMS m/z 247 $(M + 1)^+$.

1-Methoxy-1-phenylazocyclononane (2h): bp 156–158 °C/1.8 hPa. IR (neat): 691, 764, 1094, 1450, 2850, 2927 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.3–2.2 (16H, m, $CH_2 \times 8$), 3.36 (3H, s, MeO), 7.3–7.9 (5H, m, Ar). ^{13}C NMR ($CDCl_3$) δ 18.94 (CH_2), 22.44 (CH_2), 27.57 (CH_2), 28.59 (CH_2), 50.53 (MeO), 102.17 (C), 122.28 (CH), 128.92 (CH), 130.51 (CH), 151.97 (C). MS m/z (rel intensity %) 155 ($(M - PhN_2)^+$, 100), 81 (60), 77 (34), 67 (27), 55 (26), 41 (24). HRMS m/z found: 155.1389 $(M - PhN_2)^+$, calcd for $C_{10}H_{19}O$: 155.1436. CIMS m/z 261 $(M + 1)^+$.

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