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Cathodic Reduction of Phenacyl Azides

Belén Batanero, José Escudero, and Fructuoso Barba*

Department of Organic Chemistry, University of Alcalá, 28871 Alcalá de Henares, Madrid, Spain

fructuoso.barba@uah.es

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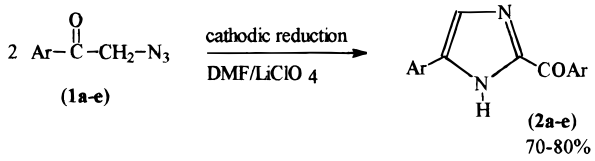
ABSTRACT



Ar= **a**: Ph, **b**: p-MeO-Ph, **c**: p-Me-Ph, **d**: p-Cl-Ph, **e**: p-Br-Ph

The electrochemical reduction of phenacyl azides (1a–e) leads to the formation of 2-aroyl-4-arylimidazoles (2a–e) (70–80% yield). 1a–e were prepared from phenacyl bromides and sodium azide and were reduced in aprotic DMF-$LiClO_4$ medium at the mercury cathode in a divided cell and under controlled potential.

Little attention has been paid to the cathodic reduction of azides. The electroreduction of azides was studied under protic conditions.[1] In this paper it was concluded that depending on the group directly linked to the azide function, one can obtain either an amine group with extrusion of dinitrogen or a loss of azide anion.

Recently we have studied the cathodic reduction of phenacyl azide thiosemicarbazones under aprotic conditions.[2] They afford N-substituted imidazolethiones in good yield.

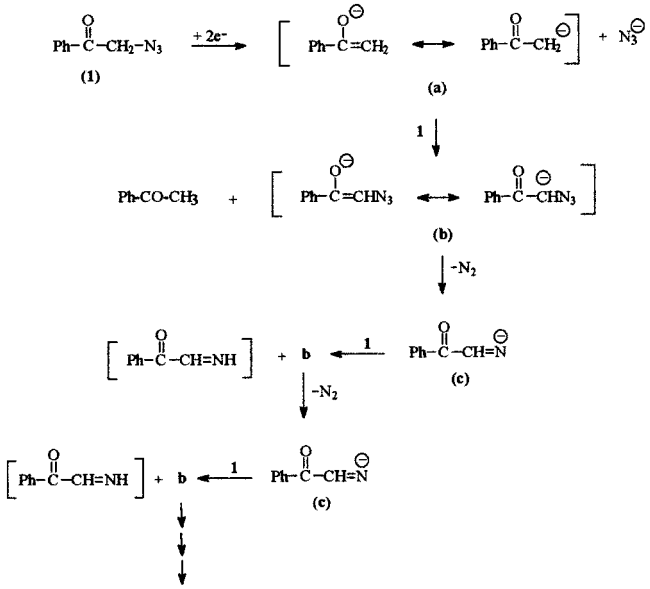
Due to the interest in these reactions and the mechanistic uncertainty, we have further studied the cathodic reduction of phenacyl azides (**1**) under aprotic conditions.

After only 10% of the expected current for a theoretical 2F process, the current fell to zero. At this point, analysis of the cathodic solution was performed. Surprisingly, no phenacyl azide remained; the products were 2-aroyl-4-arylimidazole (**2**) (70−80%), 2-(2-aroyl-1-arylethenyl)-4-arylimidazole (**3**), and other minority products (e.g., acetophenone).

The rationalization of these results is sumarized as follows: In a first step, the cleavage of the C−N_3 bond takes place in a 2F process as was demonstrated in a previous paper.[2] In this way an amount of the corresponding enolate (**a**) is formed.

The enolate **a** acts as an electrogenerated base,[3] which abstracts a proton from another substrate molecule to give a new enolate (**b**). This new enolate loses a N_2 molecule to be transformed into anion **c**, which is a strong base. Reaction with the starting azide affords phenyl glyoxal imino inter-

Scheme 1



(1) Lund, H. *Oesterreich. Chem. Z.* **1967**, *68*, 43.
(2) Batanero, B.; Escudero, J.; Barba, F. *Synthesis* **1999**, in press.
(3) Baizer, M. M. *Organic Electrochemistry*, 3rd ed.; Lund, H., Baizer, M. M., Eds.; Marcel Dekker: New York 1991; pp 1265−1272.

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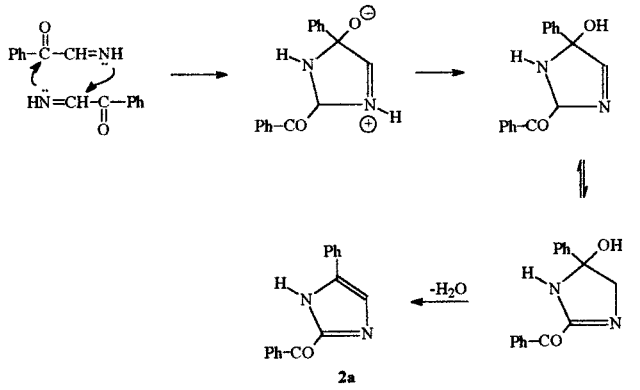
mediate and the enolate **b**, which continues reacting according to Scheme 1 until all the substrate is consumed.

Pinner[4] described the formation of 2-benzoyl-4-phenylimidazole (**2a**) when phenyl glyoxal was heated in the presence of ammonia. The reaction is believed to involve a dimerization of the phenyl glyoxal imino intermediate followed by dehydration.

Boyer and Straw[5] prepared **2a** by pyrolysis of phenacyl azide. In this case, the postulated intermediate was again the phenyl glyoxal imino derivative.

To confirm our electrochemical proposal, the acetophenone enolate was prepared from acetophenone and sodium hydride. This enolate was added in small amounts to a solution of phenacyl azide in DMF. N_2 evolution was observed inmediately, and a check on the reaction medium showed that the starting azide had disappeared. The products and their distribution were closely similar to those of the electrochemical reduction. The dimerization and dehydration are shown in Scheme 2.

Scheme 2



Formation of the secondary product **3** is possible via condensation of **2** with an acetophenone enolate. However when a solution of **2** was chemically treated with acetophenone sodium enolate in DMF, no reaction was observed. For this reason condensation before cyclization is proposed for the formation of **3**.

A series of 2,4-disubstituted imidazoles have been prepared using this efficient and convenient procedure.[6]

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(4) Pinner, A. *Ber. Dtsch. Chem. Ges.* **1905**, *38*, 1531.

(5) Boyer, J. H.; Straw D. *J. Am. Chem. Soc*. **1952**, *74*, 4506.

(6) **General Experimental Information.** Electrolyses were carried out using an Amel potentiostat Model 552 with an electronic integrator Amel Model 721. Mass spectra (EI, ionizing voltage 70 eV) were determined using a Hewlett-Packard Model 5988A mass-selective detector equipped with a Hewlett-Packard MS Chem Station. IR spectra of the compounds were recorded as dispersions in KBr or as film on NaCl plates, using Perkin-Elmer Model 583 spectrometer. ^{1}HNMR (300 MHz) and ^{13}CNMR (75.4 MHz) spectra were recorded using a Varian Unity 300 apparatus with $CDCl_3$ or DMSO-d_6 (^{1}H, ^{13}C) as internal standard. Melting points (mp) were determined on a Reichert Thermovar microhot stage apparatus and are uncorrected. Elemental analyses were performed using a Perkin-Elmer model 240-B analyzer. Cyclic voltammetry was run on a Metrohm apparatus Model 663 VA Stand and a Scanner VA E612. The potential values are given in volts (vs SCE). Analytical HPLC was performed on a Hewlett-Packard 5033 instrument, using a reverse-phase column and 80% methanol/water as the eluent. All products were purified by silica gel 60 (230−400 mesh) using toluene/methanol (20/1 or 40/1) as eluent. Phenacyl bromides are commercially available and have been used without purification. Phenacyl azides (**1**) were prepared according to Boyer and Straw (Boyer, H. J.; Straw D. *J. Am. Chem. Soc*. **1953**, *75*, 1642) with the following modifications: solutions of phenacyl bromides (25 mmol) in methanol (40 mL) were poured over an aqueous solution of sodium azide (1.63 g, 25 mmol, 40 mL) in an ice bath. After 2 h, the phenacyl azides were obtained in almost quantitative yields by removing the solvent under reduced pressure to dryness (azides can be *explosive* compounds and appropiate *caution* should be taken with these and related compounds), extracting the crude reaction mixture with Et_2O (80 mL) and water (80 mL), and drying the ethereal solution with $MgSO_4$. The electrochemical reductions were carried out at −1 V (vs SCE) using a concentric cell with two compartments separated by a porous (D3) glass tubing diaphragm and equipped with a magnetic stirrer. The solvent supporting electrolyte (SSE) was DMF−$LiClO_4$. Anhydrous solid K_2CO_3 (2.0 g, 145 mmol) was added to the anodic compartment for "in situ" neutralization of the generated perchloric acid. Other details: anode, platinum; anolyte, $LiClO_4$ (0.42 g, 4.0 mmol) in dry DMF (10 mL); Cathode, mercury pool (20 cm^2); catholyte, $LiClO_4$ (1.5 g, 14 mmol) containing the corresponding phenacyl azide (2.0 mmol) in dry DMF (30 mL). At the end of the electrolysis (it was considered finished when the current fell to zero) the cathodic solution was poured onto ice water (500 mL). After 12 h, the precipitated solid was filtered and dried under reduced pressure and chromatographed on a silica gel (17× 2.5 cm) column, using toluene/methanol (40/1)as eluent. **2-Benzoyl-5-phenylimidazole** (**2a**): 70%; mp 197−199 °C (lit.[4] mp 196−198 °C); IR (KBr) ν 3274, 1618, 1290, 1168, 690; ^{1}H NMR (300 MHz, DMSO) δ 13.6 (bs, 1H), 8.58 (d, 2H, J = 7 Hz), 8.08 (s, 1H, CH═), 7.92 (m, 2H), 7.2−7.8 (m, 6H);^{13}C NMR (75.4 MHz, DMSO) δ 118.7, 125.0, 127.3, 128.4, 128.7, 130.7, 133.2, 133.8, 136.1, 143.0, 144.8, 180.9; MS *m*/*e* (relative intensity) EI 249 (M^+ + 1, 4), 248 (M^+, 26), 220(26), 142(9), 116(21), 105(58), 77(100), 51(40). **2-(*p*-Methoxybenzoyl)-5-(*p*-methoxyphenyl)imidazole** (**2b**): 71%; mp 216−218 °C; IR (KBr) ν 3271, 1607, 1250, 1164, 832; ^{1}H NMR (300 MHz, DMSO) δ 13.4 (bs, 1H), 8.7 (d, 2H, J = 8.7 Hz), 7.8−8 (m, 3H), 6.9−7.2 (m, 4H), 3.87 (s, 3H, MeO), 3.78 (s, 3H, MeO);^{13}C NMR (75.4 MHz, DMSO) δ 55.2, 55.5, 113.5, 113.7, 114, 114.4, 117.0, 126.1, 126.5, 127.1, 128.6, 132.9, 133.1, 142.7, 144.7, 158.5, 163.2, 178.9; MS *m*/*e* (relative intensity) EI 309 (M^+ + 1, 10), 308 (M^+, 52), 280 (13), 265 (20), 135 (100), 107 (13), 92 (32), 77 (40), 63 (13). Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.13; H, 5.19; N, 9.09. Found: C, 69.87; H, 5.31; N, 9.12. **2-(*p*-Methylbenzoyl)-5-(*p*-methylphenyl)imidazole** (**2c**): 80%; mp 198−200 °C; IR (KBr) ν 3275, 1617, 1289, 1168, 821; ^{1}H NMR (300 MHz, DMSO) δ 13.5 (bs, 1H), 8.68 (d, 2H, J = 8.1 Hz),), 8.16 (s, 1H, CH═), 7.9−8.1 (m, 2H), 7.2−7.6 (m, 4H), 2.67 (s, 3H, Me), 2.58 (s, 3H, Me); ^{13}C NMR (75.4 MHz, DMSO) δ 20.8, 21.2, 117.8, 124.7, 125.6, 127, 128.9, 129.1, 130.7, 133.4, 136.2, 142.8, 144.6, 180.2; MS *m*/*e* (relative intensity) EI 277 (M^+ + 1, 17), 276 (M^+, 80), 248 (100), 119 (84), 91 (77), 77 (10), 71 (58), 57 (69). Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.26; H, 5.79; N, 10.14. Found: C, 77.97; H, 5.91; N, 9.92. **2-(*p*-Chlorobenzoyl)-5-(*p*-chlorophenyl)imidazole** (**2d**): 76%; mp 218−220 °C. IR (KBr) ν 3272, 1613, 1291, 1167, 833; ^{1}H NMR (300 MHz, DMSO) δ 13.65 (bs, 1H), 8.64 (d, 2H, J = 8.4 Hz), 8.18 (s, 1H, CH═), 7.45−8.1 (m, 6H);^{13}C NMR (75.4 MHz, DMSO) δ 119.5, 126.7, 127.5, 128.5, 131.3, 131.6, 132.5, 135, 138.2, 142, 144.6, 179.5; MS *m*/*e* (relative intensity) EI 318 (M^+ + 2, 23), 316 (M^+, 36), 290 (30), 288 (46), 141 (34), 139 (100), 113 (28), 111 (82), 89 (9), 75 (36). Anal. Calcd for $C_{16}H_{10}N_2OCl_2$: C, 60.57; H, 3.15; N, 8.83. Found: C, 60.87; H, 3.15; N, 8.71. **2-(*p*-Bromobenzoyl)-5-(*p*-bromophenyl)-imidazole** (**2e**): 77%; mp 252−254 °C (lit.[4] mp 245−247 °C); IR (KBr) ν 3271, 1613, 1290, 1169, 830; ^{1}H NMR (300 MHz, DMSO) δ 13.7 (bs, 1H), 8.53 (d, 2H, J = 8.5 Hz), 8.19 (s, 1H, CH═), 7.8−8. (m, 4H), 7.6−7.7. (m, 2H);^{13}C NMR (75.4 MHz, DMSO) δ 119.5, 126.9, 127.2, 131.5, 131.6, 131.9, 132.6, 132.8, 134.8, 141.8, 144.5, 179.6; MS *m*/*e* (relative intensity) EI 408 (M^+ + 4, 21), 406 (M^+ + 2, 44), 404 (M^+, 22), 380 (21), 378 (42), 376 (22), 299 (11), 297 (11), 185 (100), 183 (100), 157 (90), 155 (90), 76 (48), 75 (48). **2-(2-benzoyl-1-phenylethenyl)-4-phenylimidazole** (**3a**): 18%; mp 158−160 °C; IR (KBr) ν 3066, 1686, 1625, 1584, 1278, 1229, 1021; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.4 (bs, 1H), 7.9−8.1 (m, 6H), 7.43−7.63. (m, 10H), 6.4 (s, 1H, ═CH); ^{13}C NMR (75.4 MHz, DMSO) δ 101.5, 118.5, 126, 128.0, 128.2, 128.4, 128.6, 128.8, 129.0, 129.3, 130.1, 131.1, 133.4, 133.6, 134.6, 144.2, 152.3, 192.7; MS *m*/*e* (relative intensity) EI 351 (M^+ + 1, 1), 350 (M^+, 3), 250 (25), 105 (100), 77 (38), 51 (7). Anal. Calcd for $C_{24}H_{18}N_2O$: C, 82.28; H, 5.14; N, 8.0. Found: C, 82.48; H, 5.1; N, 8.1.