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AMMONIUM SULPHATE- MAGNESIUM SELECTIVE REDUCTION OF N-2-NITROPHENYLMIDATES: SYNTHESIS OF 2-SUBSTITUTED BENZIMIDAZOLES

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**AMMONIUM SULPHATE-
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REDUCTION OF *N*-2-
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SYNTHESIS OF 2-SUBSTITUTED
BENZIMIDAZOLES**

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ABSTRACT

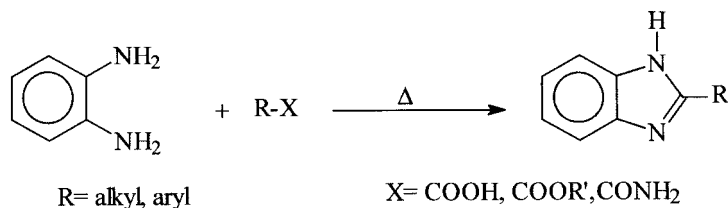
Various *N*-2-nitrophenylimidates were selectively reduced by (NH₄)₂SO₄-Mg to the non-isolated *N*-2-aminophenylimidates which cyclise to the corresponding 2-substituted benzimidazoles.

INTRODUCTION

Benzimidazoles derivatives are an important class of heterocyclic compounds which have biological activities^{1–3} and interesting pharmacological

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properties.^{4,5} In general, 2-substituted benzimidazoles depicted in Scheme 1 were prepared by the condensation of *o*-phenylenediamine with carbonyl-containing compounds, such as carboxylic acids, esters or amides.⁶⁻⁸



Scheme 1.

As a part of our continuing studies on *N*-substituted imidates,⁹⁻¹² we report in the present investigation the synthesis of some 2-substituted benzimidazoles, in a single step and under very mild conditions, by using *N*-2-nitrophenylimidates as starting materials.

RESULTS AND DISCUSSION

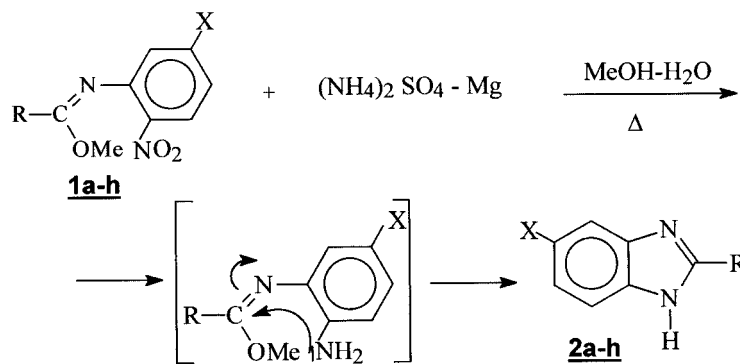
Treatment of *N*-2-nitrophenylimidates **1a-h** with the reducing system (NH₄)₂SO₄-Mg described by Prajapati and Al.,¹³ using methanol and water as solvent and heating at 60°C during 0.5 h gives respectively benzimidazoles **2a-h** in good yield (table). The formation of compounds **2** proceeds

Table. Reduction of *N*-2-nitrophenylimidates by (NH₄)₂SO₄-Mg and Formation of Benzimidazoles **2**

Product	R	X	Yield (%)	M.P. (°C)	Reported (M.P.) ¹⁴
2a	CH ₃	H	92	168–170	169–171
2b	C ₂ H ₅	H	88	177–179	178–180
2c	Ph	H	85	265–267	266–269
2d	H	H	76	106–108	108–110
2e	CH ₃	CH ₃	86	198–200	280–301
2f	C ₂ H ₅	CH ₃	82	216–218	218–220
2g	Ph	CH ₃	85	231–233	232–234
2h	H	CH ₃	78	121–122	119–121



presumably by selective reduction of the functional group -NO₂ and formation of the non-isolated intermediary *N*-2-aminophenylimidates which undergo cyclization (Scheme 2).



Scheme 2.

The structures of compounds **2a-h** have been unambiguously characterized on the basis of their IR, NMR (¹H, ¹³C) and mass spectra.

The IR spectra show the characteristic bands of NH, C=N and C=C aromatic, the ¹H and ¹³C NMR spectra display the characteristic signals of protons and carbons of all the substituents (aromatics, R and X), their spectral data are presented in the experimental part. It is noteworthy that the EI-MS spectra of the compounds **2** record the existence of the molecular ion peaks as the base peaks indicating that the heterocycle skeletons are stable under the EI-MS conditions.

In conclusion, these results demonstrated a versatile and selective reducing system for *N*-2-nitrophenylimidates; the *N*-2-aminophenylimidates were not isolated and the reaction afforded directly the corresponding 2-substituted benzimidazoles **2** in good yield.

EXPERIMENTAL

The uncorrected melting points were determined by a Büchi 510 apparatus. IR spectra were recorded on a Perkin-Elmer 681 and band positions were reported in wave numbers (cm⁻¹) (KBr pellet). NMR spectra of compounds **2** (¹H at 300 MHz (CDCl₃) and ¹³C at 75 MHz (CDCl₃)) were carried out on a VARIAN unity spectrometer using tetramethylsilane as the

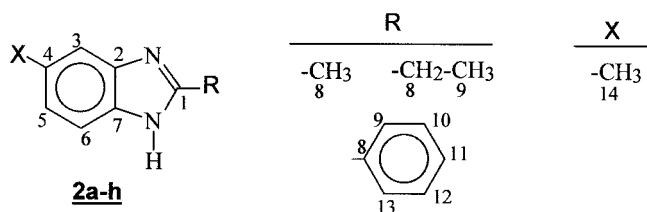


internal standard. Mass spectra were recorded on a HP micromass 5890A instrument.

Synthesis of *N*-2-Nitrophenylimidates 1a–h: The *N*-2-nitrophenylimidates 1 were obtained according to the literature^{16,17} by the following procedure: A solution of 2-nitroaniline (1.38 g, 10 mmol) in triethylorthoacetate (30 mL) was refluxed until TLC (ethyl acetate:hexane:1:1) indicated that the starting material was converted. Excess of orthoacetate was removed *in vacuo*, and the resultant nearly pure 1a obtained on more than 80% was used without further purification.

Synthesis of 2-Substituted Benzimidazoles 2a–h: General procedure: A solution of the *N*-2-nitrophenylimidate 1a (5.12 g, 20 mmol) was added to a mixture of magnesium (2.19 g, 120 mmol) and ammonium sulphate (26.40 g, 200 mmol dissolved in 6 ml of water) in methanol (50 mL). The reaction mixture was stirred at 60°C for about 30 min and then quenched by addition of water and ether. The product was extracted with ether (3 × 50 mL), washed with water and dried over Na₂SO₄. After evaporation of the solvent the residual oily material was chromatographed on a silica gel 60 (Fluka) (ether:ethylacetate:70:30) to yield 2-substituted benzimidazoles 2a as a solid recrystallized from ethanol.

Spectroscopic data (IR: ν (cm⁻¹), ¹H-NMR: δ (ppm), J (Hz), ¹³C-NMR: δ (ppm), MS: (*m/z* (%)) of benzimidazoles 2a–h are given here:



2a: IR: 3360 (NH), 1630 (C=N), 1580 (C=C); ¹H-NMR: 3.0 (s, 3H), 7.4–7.8 (m, 4H), 9.6 (s, 1H, NH); ¹³C-NMR: 149.5 (C1), 136.8 (C2), 131.6 (C7), 18.9 (C8), 114.5–126.4 (other C. arom.); MS: 132 (M⁺, 100), 131 (79), 104 (12), 133 (12), 77 (8).

2b: IR: 3350 (NH), 1635 (C=N), 1560 (C=C); ¹H-NMR: 1.1 (t, 3H, J = 7.5), 3.1 (q, 2H, J = 7.5), 7.3–7.9 (m, 4H), 9.0 (s, 1H, NH); ¹³C-NMR: 149.3 (C1), 137.4 (C2), 130.2 (C7), 20.0 (C9), 54.5 (C8), 115.5–124.5 (other C. arom.); MS: 146 (M⁺, 100), 145 (95), 147 (10), 77 (6), 56 (10).

2c: IR: 3370 (NH), 1640 (C=N), 1560 (C=C); ¹H-NMR: 7.2–8.1 (m, 9H), 9.5 (s, 1H, NH); ¹³C-NMR: 149.7 (C1), 136.8 (C2), 131.6 (C7), 118.8–128.2 (other C. arom.); MS: 194 (M⁺, 100), 193 (92), 166 (9), 77 (8), 104 (12).



2d: IR: 3350 (NH), 1640 (C=N), 1550 (C=C); ¹H-NMR: 6.4 (s, 1H), 7.3–7.7 (m, 4H), 8.5 (s, 1H, NH); ¹³C-NMR: 150.6 (C1), 136.8 (C2), 131.6 (C7), 119.2–127.0 (other C. arom.); MS: 118 (M⁺, 100), 117 (85), 77 (12), 104 (6).

2e: IR: 3365 (NH), 1635 (C=N), 1560 (C=C); ¹H-NMR: 2.4 (s, 3H), 3.0 (s, 3H), 7.3–7.9 (m, 3H), 10.2 (s, 1H, NH); ¹³C-NMR: 150.1 (C1), 137.7 (C2), 129.6 (C7), 20.2 (C8), 13.8 (C14), 112.5–121.7 (other C. arom.); MS: 146 (M⁺, 92), 145 (100), 77 (18), 104 (15), 51 (16).

2f: IR: 3360 (NH), 1630 (C=N), 1550 (C=C); ¹H-NMR 1.1 (t, 3H, J = 7.2), 3.2 (q, 2H, J = 7.2), 2.5 (s, 3H), 7.2–8.0 (m, 3H), 9.2 (s, 1H, NH); ¹³C-NMR: 149.8 (C1), 136.8 (2), 128.8 (C7), 19.6 (C8), 57.0 (C9), 14.5 (C14), 120.0–128.5 (other C. arom.); MS: 160 (M⁺, 100), 159 (90), 104 (12), 77 (15).

2g: IR: 3340 (NH), 1640 (C=N), 1560 (C=C); ¹H-NMR: 2.4 (s, 3H), 7.1–8.0 (m, 8H), 8.5 (s, 1H, NH); ¹³C-NMR: 150.5 (C1), 135.8 (C2), 130.2 (C7), 13.0 (C14), 118.8–128.2 (other C. arom.); MS: 208 (M⁺, 100), 207 (77), 209 (18), 104 (22), 77 (20).

2h: IR: 3355 (NH), 1640 (C=N), 1550 (C=C); ¹H-NMR: 2.4 (s, 3H), 6.5 (s, 1H), 7.2–7.7 (m, 3H), 9.0 (s, 1H, NH); ¹³C-NMR: 150.4 (C1), 136.6 (C2), 130.2 (C7), 13.5 (C14), 122.5–126.0 (other C. arom.); MS: 132 (M⁺, 100), 131 (83), 77 (18), 133 (12), 77 (8).

REFERENCES

- Joshi, K.; Jain, R.; Dandia, A.; Sharma, K. J. Fluorine Chem. **1992**, *56*, 1.
- Parmar, S.S.; Misra, R.S.; Chaudhari, A.; Gupta, T.K. J. Pharm. Sci. **1972**, *61*, 1322.
- Antonini, I.; Martelli, S.J. J. Med. Chem. **1988**, *31*, 260.
- Kaliszan, R.; Milczarska, B.; Lega, B.; Szefer, P.; Janowiec, M. Pol. J. Pharmacol. Pharm. **1978**, *30*(4), 585; Chem. Abstr. **1979**, *90*, 197398y.
- Winn, M.; Kyncl, J. U.S. 4,093, 726; Chem. Abstr. **1978**, *99*, 197600n.
- Philips, M.A.; J. Chem. Soc. **1928**, 2393.
- Hein, D.W.; Alheim, R.S.; Leavitt, J.J. J. Am. Chem. Soc. **1957**, *79*, 427.
- Alcalde, E.; Dinares, I.; Perez-Garcia, L.; Roca, T.; Synthesis **1992**, *4*, 395.
- Hajjem, B.; Chihi, A.; Baccar, B. Synth. Commun. **1992**, *28*, 133.
- Harizi, A.; Hajjem, B.; Baccar, B. Revue Roumaine de Chimie **1998**, *43*, 35.
- Dridi, K.; El Efrat, M.L.; Baccar, B.; Zantour, H. Synth. Commun. **1999**, *29*(11), 2026.



12. Harizi, A.; Hajjem, B.; Zantour, H.; Baccar, B. J. Soc. Chim. Tunisie **1995**, *10*, 683; Chem. Abstr. **1996**, *124*, 289482v.
13. Prajapathi, D.; Borah, H.N.; Sandhu, J.S.; Ghosh, A.C. Synth. Commun. **1995**, *25*(24), 4025.
14. The products were identified by comparison of M.P. and spectral data with the literature (15).
15. Pretsch, E.; Cherc, T.; Seibel, J.; Simon, W. Tables of Spectral Data for Structure Determination of Organic Compound. ^{13}C NMR, ^1H NMR, IR, MS, UV/Vis, (Springer-Verlag, Berlin, 1976).
16. Younes, M.I.; Metwally, S.A.M.; Atta, A.H. Synthesis **1990**, 704.
17. Gatta, F.; Giudice, M.R.D.; Borioni, A. J. Het. Chem. **1993**, *30*(1), 11.

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