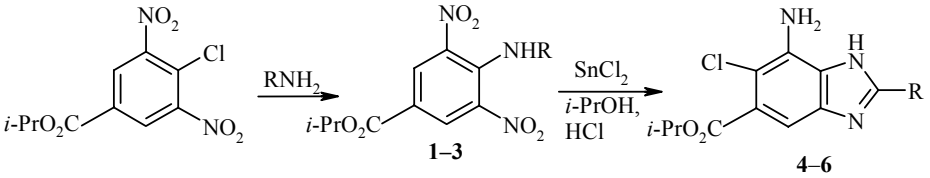
Chemistry of Heterocyclic Compounds, Vol. 40, No. 4, 2004

NOVEL SYNTHESIS OF SUBSTITUTED BENZIMIDAZOLES BY REDUCTION OF ESTERS OF 4-ALKYLAMINO-3,5-DINITRO-BENZOIC ACIDS BY TIN CHLORIDE

A. V. Vlaskina and V. P. Perevalov

Keywords: esters of 4-alkylamino-3,5-dinitrobenzoic acids, esters of 7-amino-6-chloro-2-R-1H-benzimidazole-5-carboxylic acids, tin chloride, reduction of nitro group.

We have established that in reduction of isopropyl esters of 4-benzylamino-, 4-β-phenethylamino-, and 4-butylamino-3,5-dinitrobenzoic acids **1-3** by tin chloride in isopropyl alcohol in the presence of hydrogen chloride, closure of the imidazole ring occurs, leading to formation of isopropyl esters of 7-amino-6-chloro-2-R-1H-benzimidazole-5-carboxylic acids **4-6**.



1, **4** R = Ph, **2**, **5** R = Bn, **3**, **6** R = Pr

Under the same conditions, the substituted benzimidazole is not formed from the methyl ester of 2-benzylamino-3,5-dinitrobenzoic acid.

We hypothesize that, in accordance with the data in [1, 2], in compounds **1-3** initially intermediate reduction of the nitro group to the hydroxylamine occurs, followed by its rearrangement accompanied by introduction of a chlorine atom into the position *ortho* to the amino group formed. In the second step, intramolecular cyclization of the intermediate *o*-nitroso-N-alkylamino compound when treated with tin chloride occurs more rapidly than further reduction to the amino compound.

The ^{1}H NMR spectra were recorded on a Bruker WP-200 (200 MHz) spectrometer in DMSO-d_6 solutions; chromato-mass spectral studies of the isolated compounds were conducted using a Hewlett Packard 6890 gas chromatograph/mass spectrometer with a 5973 mass spectrometric detector, an HP-5MS column (30 m × 0.25 mm), phase layer thickness 0.25 μm, helium as the carrier gas (40 cm/s), 20:1 flow splitter, source temperature 150°C, injector temperature 230°C, temperature gradient from 40°C to 320°C (25°C/min), ionization by electron impact.

3,5-Dinitro-4-chlorobenzoic acid was obtained according to the procedure in [3]; the isopropyl ester was obtained as for the methyl ester in [3].

D. I. Mendeleev Russian Chemical Technological University, Moscow 125047; e-mail: sark@muctr.edu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 620-622, April, 2004. Submitted October 17, 2003.

Isopropyl Ester of 4-Benzylamino-3,5-dinitrobenzoic Acid (1). A solution of benzylamine (1.8 ml, 16.5 mmol) in *i*-PrOH (10 ml) was poured into a boiling solution of the isopropyl ester of 3,5-dinitro-4-chlorobenzoic acid (5.0 g, 16.5 mmol) and Et_3N (2.3 ml, 16.5 mmol) in *i*-PrOH (50 ml). This was held for 20 min, and then the suspension formed was poured into hot water and boiled for 20 min, then acidified with a 10% HCl solution (pH 6), and cooled down. The yellow precipitate was filtered out. After recrystallization from *i*-PrOH, we obtained 5.2 g (88%) of compound **1**; mp 93-95°C.

Compounds 2 (yield 98%; mp 112-115°C) and **3** (yield 67%; mp 64-65°C) were obtained by a similar procedure.

Isopropyl Ester of 7-Amino-6-chloro-2-phenyl-1H-benzimidazole-5-carboxylic Acid (4). A reducing solution was prepared by passing HCl through a suspension of $SnCl_2 \cdot 2H_2O$ (4.3 g, 16.0 mmol) in *i*-PrOH (15 ml) until the precipitate was completely dissolved. Compound **1** (1.5 g, 4.0 mmol) in *i*-PrOH (20 ml) was dissolved by heating; the solution was saturated with HCl, and the reducing solution was slowly added dropwise over a period of 1.5 h. The reaction mass first had a dark red color, and then the color became lighter. When the reaction was complete, the solvent was distilled off under vacuum and the residue was mixed with a 10% HCl solution, and then the precipitated flocs were filtered out. After recrystallization from dilute AcOH, we obtained 0.6 g (44%) of compound **4**; mp 202-205°C. ^{1}H NMR spectrum, δ, ppm (*J,* Hz): 8.30-8.33 (2H, m, Ph); 7.66-7.69 (3H, m, Ph); 7.23 (1H, s, H_{arom}); 5.14 (1H, m, J = 6.48, CH); 1.35 (6H, d, J = 6.48, CH_3). Mass spectrum, *m/z*: 329, 331 $[M]^+$. Found, %: C 61.70; H 4.90; N 12.70. $C_{17}H_{16}ClN_3O_2$. Calculated, %: C 61.91; H 4.86; N 12.75.

Compound 5 was obtained similarly. Yield 22%; mp 211-214°C. ^{1}H NMR spectrum, δ, ppm (*J,* Hz): 7.37-7.46 (5H, m, Ph); 7.20 (1H, s, H_{arom}); 5.15 (1H, m, J = 6.01, CH); 4.49 (2H, s, CH_2); 1.33 (6H, d, J = 6.01, CH_3). Mass spectrum, *m/z*: 343, 345 $[M]^+$. Found, %: C 62.90; H 5.22; N 12.20. $C_{18}H_{18}ClN_3O_2$. Calculated, %: C 62.88; H 5.24; N 12.23.

Compound 6 was obtained as for compound **4**. Yield 11%; mp 189-192°C. ^{1}H NMR spectrum, δ, ppm (*J,* Hz): 7.18 (1H, s, H_{arom}); 5.15 (1H, m, J = 6.48, CH); 3.04 (2H, t, J = 7.40, $\underline{CH_2}CH_2CH_3$); 1.91 (2H, q, J = 7.40, $CH_2\underline{CH_2}CH_3$); 1.34 (6H, d, J = 6.48, CH_3); 0.97 (3H, t, J = 7.40, $CH_2CH_2\underline{CH_3}$). Mass spectrum, *m/z*: 295, 297 $[M]^+$. Found, %: C 56.88; H 6.00; N 14.20. $C_{14}H_{18}ClN_3O_2$. Calculated, %: C 56.85; H 6.09; N 14.21.

REFERENCES

1. C. C. Price, D. B. Guthrie, *J. Am. Chem. Soc.*, **68**, 1592 (1946).
2. H. E. Heller, E. D. Hughes, C. K. Ingold, *Nature*, **168**, 909 (1951).
3. F. Ullmann, *Ann.,* **366**, 82 (1909).