# Formation of an organolithium derivative of 2-(α-aminobenzyl)-1-methylbenzimidazole in the reaction of 2-benzoyl-1-methylbenzimidazole oxime with lithium naphthalenide

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It was shown with the reaction of 2-benzoyl-1-methylbenzimidazole oxime with lithium naphthalenide that ketoximes can be used to obtain difficultly accessible organolithium derivatives of primary nonaromatic amines.

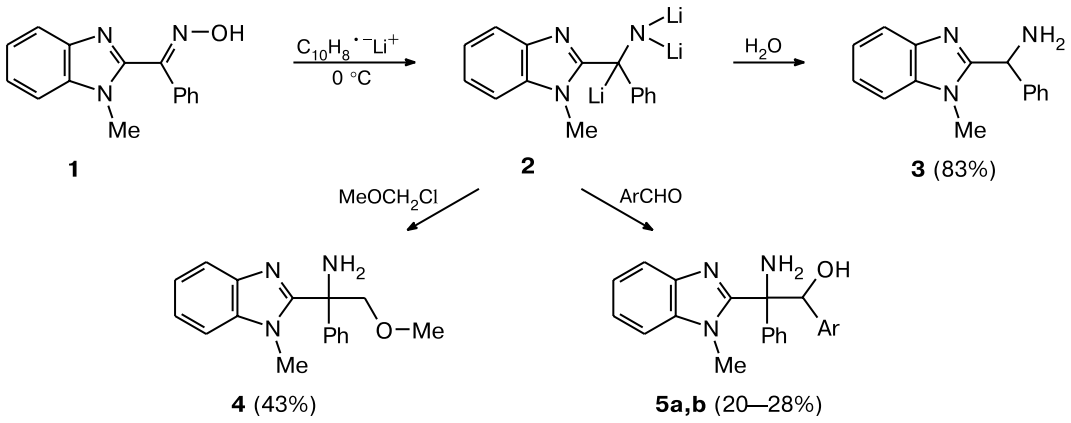
**Key words:** lithium naphthalenide, benzimidazole, ketoximes, primary amines, organolithium compounds, 2-methoxy-1-(1-methylbenzimidazol-2-yl)-1-phenylethylamine, 2-amino-2-(1-methylbenzimidazol-2-yl)-1,2-diphenylethanol.

Organometallic derivatives of nonaromatic primary amines are not easily accessible since metallation of these amines is impeded by their low CH acidity, which makes the formation of *N*-metal derivatives preferable. They are usually replaced by so-called synthetic equivalents,[1] namely, *C*-metal derivatives, in which the amino group is protected by an appropriate electron-withdrawing substituent. These compounds are readily obtained by metallation since the protecting group substantially polarizes the C—H bond under attack and occasionally prevents the formation of *N*-metal derivatives. However, this approach involves additional steps (protection of an amino group and elimination of the protection after the reaction with a synthetic equivalent is completed). For this reason, development of effective methods for the synthesis of organometallic derivatives of primary amines seems to be topical.

In this respect, salts of arene radical anions, $ArH^{\bullet -}M^{+}$, are promising reagents capable of forming organometallic compounds through both metallation and various reductive processes (*e.g.*, see Refs. 2, 3).

We showed with compound **1** as an example that lithium naphthalenide $C_{10}H_8^{\bullet -}Li^{+}$ can be used to convert ketoximes into an α-*C*-lithium derivative of primary amines. Indeed, when treated with lithium naphthalenide in THF at 0 °C, oxime **1** undergoes multielectron reduction with cleavage of the N—O bond to give a *C*,*N*,*N*-trilithium derivative **2** of 2-(α-aminobenzyl)-1-methylbenzimidazole **3**. Hydrolysis of compound **2** affords the known amine **3** in good yield, while its alkylation with

**Scheme 1**




Ar = Ph (**a**), *p*-$MeOC_6H_4$ (**b**)

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methoxymethyl chloride gives amino ether **4**. With aromatic aldehydes as electrophilic reagents, amino alcohols of type **5** are formed (Scheme 1).

## Experimental

$^1$H NMR spectra were recorded on a Varian XL-300 spectrometer (300 MHz) at ~20 °C. IR spectra were recorded on a Specord IR75 instrument (Nujol).

**Trilithium derivative 2 and 2-(α-aminobenzyl)-1-methylbenzimidazole (3).** A suspension of oxime **1** [4] (1.3 g, 5.2 mmol) in 10 mL of THF was added at 0 °C over 10 min to a solution of lithium naphthalenide obtained from lithium (0.3 g, 43 mmol) and naphthalene (5.5 g, 43 mmol) in 30 mL of anhydrous THF in an atmosphere of argon (*e.g.*, see Ref. 2). The reaction mixture was kept for an additional 5 min, and the resulting solution of a trilithium derivative was hydrolyzed. The organic layer was concentrated and treated with 15 mL of $Et_2O$ and 20 mL of 10% HCl. The acid extract was alkalified with aqueous ammonia, and the product was extracted with ether. The yield of compound **3** was 1.0 g (83%), m.p. 116—117 °C (from benzene).[4] Found (%): C, 75.77; H, 6.55; N, 18.06. $C_{15}H_{15}N_3$. Calculated (%): C, 75.92; H, 6.37; N, 17.71.

**2-Methoxy-1-(1-methylbenzimidazol-2-yl)-1-phenylethylamine (4).** A solution of lithium derivative **1** was treated with methoxymethyl chloride (3.0 g, 37 mmol) in 8 mL of THF at 0 °C. The mixture was hydrolyzed and compound **4** was routinely isolated from the hydrochloric acid extract. The yield of compound **4** was 0.6 g (43%), m.p. 145—146 °C (heptane—propan-2-ol). Found (%): C, 72.84; H, 6.56; N, 15.06. $C_{17}H_{19}N_3O$. Calculated (%): C. 72.57; H, 6.81; N, 14.94. $^1$H NMR (DMSO-$d_6$), δ: 2.21 (br.s, 2 H, $NH_2$); 3.35 and 3.45 (both s, 3 H each, MeN and MeO); 4.13 and 4.33 (both d, 1 H each, $CH_2$, $J$ = 9.2 Hz); 7.23—7.74 (m, 8 H, H arom.); 7.78—7.84 (m, 1 H, C(4)H of the benzimidazolyl fragment).

**2-Amino-2-(1-methylbenzimidazol-2-yl)-1,2-diphenylethanol (5a) and 2-amino-1-(4-methoxyphenyl)-2-(1-methylbenzimidazol-2-yl)-2-phenylethanol (5b).** Under similar conditions, amino alcohol **5a** was obtained from benzaldehyde (4 g, 37.7 mmol). The yield of compound **5a** was 0.5 g (28%), m.p. 181—182 °C (MeCN). Found (%): C, 76.84; H, 6.03; N, 11.97. $C_{22}H_{21}N_3O$. Calculated (%): C, 76.94; H, 6.16; N, 11.24. IR, ν/cm$^{-1}$: 3130 (OH); 3288 and 3362 ($NH_2$). $^1$H NMR ($CDCl_3$), δ: 2.15 and 3.39 (both s, 2 H and 3 H, $NH_2$ and MeN); 5.66 and 6.11 (both d, 1 H each, CH and OH, $J$ = 2.5 Hz); 6.71—7.27 (m, 12 H, 2 Ph + C(5)H (C(6)H) of the benzimidazolyl fragment); 7.31—7.39 (m, 1 H, C(7)H of the benzimidazolyl fragment); 7.66—7.74 (m, 1 H, C(4)H of the benzimidazolyl fragment).

Similarly, amino alcohol **5b** was obtained from anisaldehyde. The yield of compound **5b** was 20%, m.p. 160—162 °C (EtOH). Found (%): C, 73.86; H, 6.00; N, 11.46. $C_{23}H_{23}N_3O_2$. Calculated (%): C, 73.97; H, 6.21; N, 11.25. $^1$H NMR ($CDCl_3$), δ: 1.98 (br.s, 2 H, $NH_2$); 3.38 (s, 3 H, MeN); 3.73 (s, 3 H, MeO); 5.75 (s, 1 H, CH); 6.38 (br.s, 1 H, OH); 6.60—7.33 (m, 12 H, H arom.); 7.78—7.85 (m, 1 H, C(4)H of the benzimidazolyl fragment).

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