IMIDAZO[2,1-b]BENZOTHIAZOLE. NUCLEOPHILIC SUBSTITUTION REACTION ON SULFUR BY n-BUTYL LITHIUM

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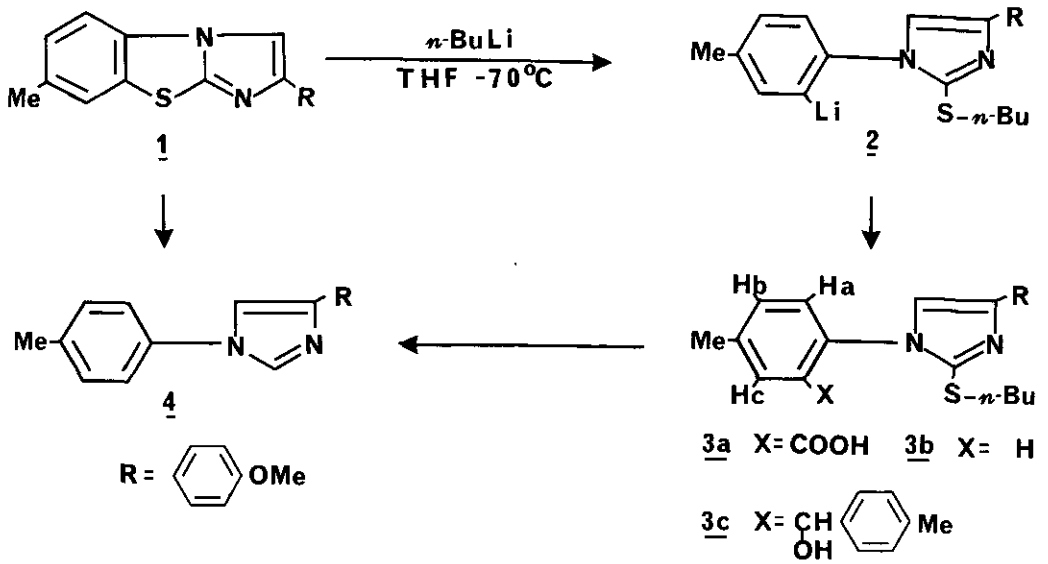
Abstract ——— The nucleophilic substitution reaction on sulfur of 2-(p-methoxyphenyl)-7-methylimidazo[2,1-b]benzothiazole by n-butyl lithium affords the C-S bond cleaved compound in excellent yield.

Nucleophilic substitution reactions on sulfur by organolithium compounds have been reported.[1-3] The nucleophilic cleavage of S-S bond by organolithium compounds is well known.[1] However, there are few reports on the similar nucleophilic cleavage of C-S bond.[3]

We now present an example of the nucleophilic substitution reaction on sulfur of 2-(p-methoxyphenyl)-7-methylimidazo[2,1-b]benzothiazole 1[4] by n-butyl lithium(n-BuLi).

1 was treated with n-BuLi in tetrahydrofuran at -70°C, and then quenched with carbon dioxide below -60°C. An oil 3a was obtained as the sole product, which was purified by silica gel chromatography (toluene : ethyl acetate = 7 : 3) as a yellow oil (96% yield); MS: m/z 396 (M^+); Anal. Calcd. for $C_{22}H_{24}N_2O_3S$; 396.1507; C,66.64; H,6.10; N,7.07; S,8.09. Found: 396.1497; C,66.80; H,6.09; N,7.10; S,8.14; IR: ν_{max}^{neat} 3400cm^{-1}(OH), 1700cm^{-1}(C=O); ^{1}H NMR (90MHz,$CDCl_3$,TMS): δ 0.76(3H,t,CH_3), 1.00-1.60(4H,m,CH_2CH_2), 2.46(3H,s,CH_3), 2.96(2H,t,CH_2), 3.77(3H,s,OCH_3), 6.40(1H,s,OH), 6.81 and 7.60 (4H,ABq,J_{AB}= 10Hz, aromatic protons of p-methoxyphenyl group), 7.10(1H,s, an aromatic proton of imidazole ring), 7.17 (1H,d,J_{ab}= 8Hz,Ha), 7.43(1H,dd,J_{ab}= 8Hz, J_{bc}= 2Hz,Hb), 7.98(1H,d,J_{bc}= 2Hz,Hc). Based on these spectral data, 3a was determined as 2-n-butylthio-1-(2-carboxy-4-methylphenyl)-4-(p-methoxyphenyl)imidazole.

The intermediate 2 was quenched with water to give 2-n-butylthio-4-(p-methoxyphenyl)-1-(p-methylphenyl)imidazole 3b (98% yield) as an oil; MS: m/z 352 (M^+); ^{1}H NMR (90MHz,$CDCl_3$,TMS): δ 0.88(3H,t, CH_3), 1.08-1.80(4H,m,CH_2CH_2), 2.40(3H,s,CH_3), 3.12(2H,t,CH_2), 3.80(3H,s,OCH_3), 6.90, and 7.74(4H, ABq, J_{AB}= 10Hz, aromatic protons of p-methoxyphenyl group), 7.24(5H,s, aromatic protons of p-tolyl group and imidazole ring). 3b was treated with Raney-Ni to give 4-(p-methoxyphenyl)-1-(p-methyl-



phenyl)imidazole 4 (69% yield); mp 127-129°C; MS: m/z 264(M^+); ^{1}H NMR (90MHz,$CDCl_3$,TMS): δ 2.40(3H, s,CH_3), 3.84(3H,s,OCH_3), 6.96 and 7.78(4H,ABq,J_{AB}= 10Hz, aromatic protons of p-methoxyphenyl group), 7.45 (1H,d,J_{24}= 2Hz, an aromatic proton at 4-position of imidazole ring), 7.85(1H,d, J_{24}= 2Hz, an aromatic proton at 2-position of imidazole ring). The disappearance of n-butyl hydrogens and the appearance of one hydrogen at 2-position of imidazole ring in the ^{1}H NMR spectra support that n-butyl group was located on sulfur and n-butylthio group was attached to 2-position of imidazole ring. 4 was also obtained from 1 by treatment with Raney-Ni in 91% yield. 2 was quenched with p-tolualdehyde to give 3c[6] (94% yield), an oil. Further work on this reaction is now in progress.

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4) 1 was prepared from p-methoxyphenacyl bromide and 2-amino-6-methylbenzimidazole in 56% yield by the known method.[5]

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6) 3C; ^{1}H NMR (90MHz,$CDCl_3$,TMS): δ 0.90(3H,t,CH_3), 1.10-1.90(4H,m,CH_2CH_2), 2.28(3H,s,CH_3), 2.48 (3H,s,CH_3), 3.16(2H,t,CH_2), 3.84(3H,s,OCH_3), 5.62(1H,s,CH), 6.72-7.80(12H,m,aromatic protons); MS: m/z 472(M^+).

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