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THE REACTION OF LITHIATED 2-ALLYLOXYBENZIMIDAZOLES WITH ALKYL HALIDES

Teruaki MUKAIYAMA and Masahiko YAMAGUCHI
Department of Chemistry, Faculty of Science,
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

The treatment of 2-allyloxybenzimidazoles, derived from allyl alcohols and 2-chlorobenzimidazoles, with butyllithium generates the oxy allylic anions, which in turn were alkylated predominantly at α-carbon with alkyl halides to form allyl ethers as major products.

Since the introduction of strong bases into organic chemistry, much effort has been devoted to the generation of carbanions from various types of rather weakly acidic compounds such as allyl ether. Most interests were centered on the formation of γ-alkylated products, vinyl ethers1), on the reaction of lithiated allylic ethers with alkyl halides. We have investigated an effective method for the alkylation of allylic ether at α-carbon of the allyl group yielding a new allyl alcohol derivatives, which act as allylating reagent toward some nucleophiles.

The formation of allyl ethers were achieved by treating alkyl halides with lithiated allylic ether(2) derived from 2-allyloxy-1-methylbenzimidazoles(1a) and 2-allyloxy-1-(3,6,9-trioxadecyl)benzimidazoles(1b) as illustrated in the following equation.

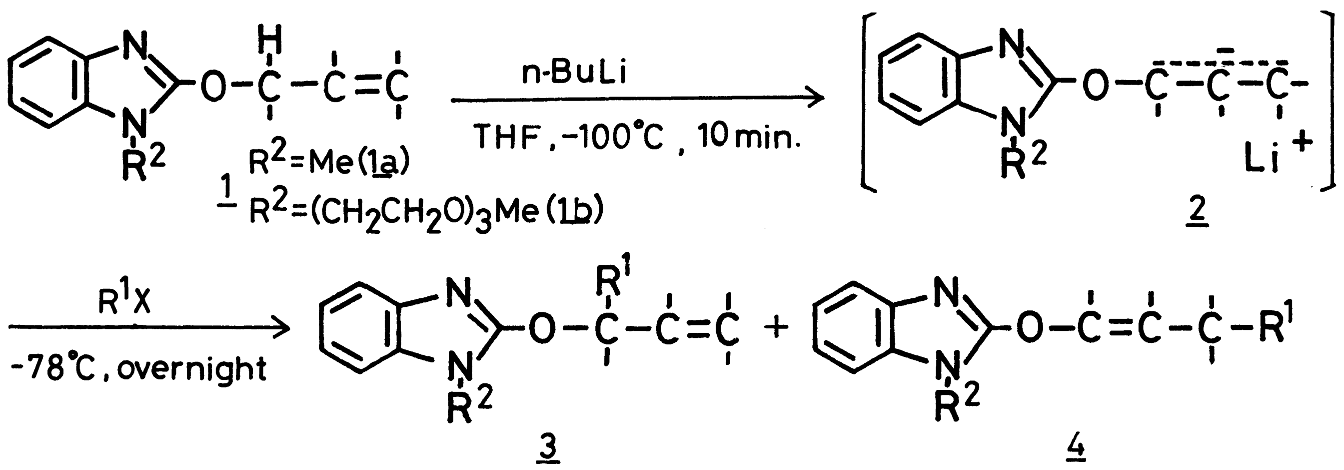


Table. Alkylation of the Oxy Allylic Anions.

		R^2=Me				R^2=$(CH_2CH_2O)_3$Me			
$O\text{-}\overset{H}{C}\text{-}C\text{=}C$	R^1X	Yield(%)	3	:	$4^{a)}$	Yield(%)	3	:	$4^{a)}$
$OCH_2CH=CH_2^{c)}$	MeI[2)]	87	68	:	32	87	70	:	30
	BuI[2)]	71	70	:	$30^{b)}$	80	70	:	$30^{b)}$
	i-PrI	63	71		29	66	73	:	27
	$PhCH_2Br$	81	73	:	$27^{b)}$	79	76	:	$24^{b)}$
	$CH_2=CHCH_2Br$	82	57	:	43	83	$56^{d)}$	:	$44^{e)}$
	t-$BuMe_2SiCl$	42	73	:	$27^{b),f)}$	69	68	:	$32^{b)}$
$OCH_2\underset{CH_3}{C}=CH_2$	MeI	88	65	:	35	87	66	:	$34^{b)}$

a) Each isomer was isolated by TLC , and all compounds gave satisfactory spectra.

b) The ratio was determined by NMR.

c) Physical data for 2-(2-propenyloxy)-1-(3,6,9-trioxadecyl)benzimidazole are as follows.

NMR($CDCl_3$) δ 3.28(3H,s), 3.42(4H,s), 3.50(4H,s), 3.71(2H,t,J=5Hz), 4.08(2H,t,J=5Hz), 5.1-5.5(2H,m), 5.7-6.4(1H,m), 6.9-7.3(3H,m), 7.3-7.5 (1H,m); Found: C, 63.48; H, 7.81; N, 8.59%. Calcd for $C_{17}H_{24}N_2O_4$: C, 63.73; H, 7.55; N, 8.74%.

d) NMR($CDCl_3$) δ 2.4-2.6(2H,m), 3.26(3H,m), 3.43(4H,s), 3.49(4H,s), 3.69(2H,t,J=5Hz), 4.07(2H,t,J=5Hz), 4.8-6.2(7H,m), 6.8-7.2(3H,m), 7.2-7.5(1H,m); Found: C, 66.70; H, 7.83; N, 7.77%. Calcd for $C_{20}H_{28}N_2O_4$: C, 66.64; H, 7.83; N, 7.77%.

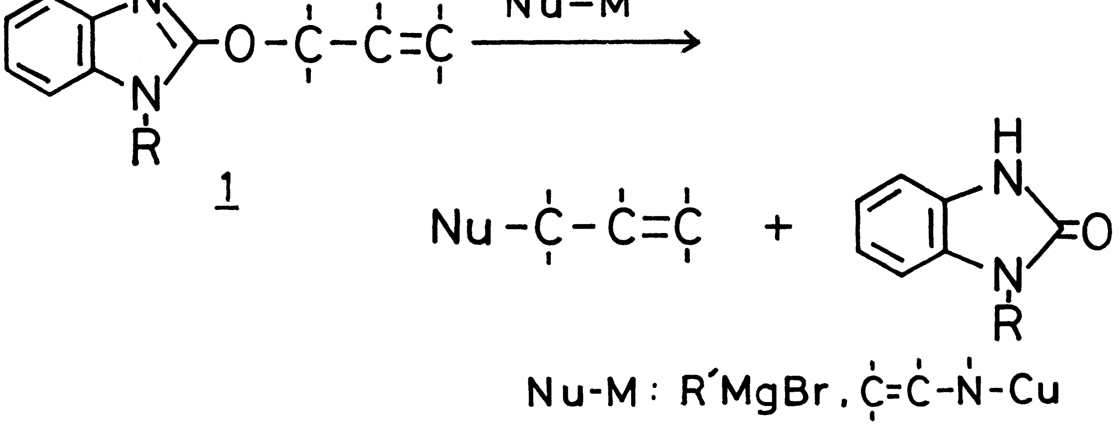
e) NMR($CDCl_3$) δ 2.1-2.4(4H,m), 3.23(3H,s), 3.40(4H,s), 3.48(4H,s), 3.73(2H,t,J=5Hz), 4.13(2H,t,J=5Hz), 4.7-5.2(3H,m), 5.4-6.0(1H,m), 6.8-7.5(5H,m); IR(neat) 1670 cm^{-1}; Found: C, 66.64; H, 8.13; N, 7.63%. Calcd for $C_{20}H_{28}N_2O_4$: C, 66.64; H,7.83; N,7.77%.

f) Disylilated product was isolated in 25% yield.

As shown in the table, lithiated allylic ethers(2a) derived from 2-allyloxy-1-methylbenzimidazoles(1a) reacted with a variety of alkyl halides to afford alkylated allyl ethers(3), as major products (α-alkylation). Polyether function on the nitrogen atom of benzimidazole in place of methyl group was introduced in order to activate the organolithium compounds and to stabilize the α-lithiated oxy allylic ethers. The results were not so different from those obtained in the reaction using N-methylbenzimidazoles(1a). Thus, it seems that coordination of nitrogen atom (3 postion) of benzimidazole ring with lithium atom of lithiated allylic ether plays an important role in the regioselectivity of the above reation.

A typical procedure is described for the reaction of 2-(2-propenyloxy)-1-(3,6,9-trioxadecyl)benzimidazole[3] with methyl iodide: Under argon atomosphere, to a THF (4 ml) solution of 2-(2-propenyloxy)-1-(3,6,9-trioxadecyl)benzimidazole (160 mg, 0.5 mmol) was added a hexane solution of butyllithium (0.37 ml, 0.6 mmol) at -100°C (methanol-liquid nitrogen bath), and the pale solution was stirred for 10 minutes. Then, a THF (2 ml) solution of methyl iodide (105 mg, 0.75 mmol) was added and the solution was stirred at -78°C overnight[4]. The reaction was quenched with water, and organic substances were extracted with ethyl acetate (3 times). The combined extracts were dried over $MgSO_4$. 2-(1-Methyl-2-propenyloxy)-1-(3,6,9-trioxadecyl)-benzimidazole (100 mg, 60%) and 2-(1-butenyloxy)-1-(3,6,9-trioxadecyl)benzimidazole (45 mg, 27%) were isolated by thin layer chromatography on silica gel.

Recently, in our laboratory it was found that 2-allyloxybenzimidazole derivatives (1) were effected with nucleophiles such as Grignard reagants[5] or enaminometallic compounds[6] to afford alkenes or unsaturated ketones. Thus, α-alkylated products obtained here may be transformed into the above mentioned substituted products by the effect of these nucleophiles, as shown in the following equation,



It is noted that α-alkylated products were obtained as major products by the reaction of alkyl halides with lithiated allylic ethers derived from 2-allyloxybenzimidazoles. These alkylated products are useful intermidiates for the preparation of alkenes or unsaturated ketones by the effect of some nucleophiles.

REFERENCES AND NOTES

1) D. A. Evans, G. C. Andrews, and B. Buckwalter, J. Am.Chem. Soc., 96, 5560 (1974); W. Clark Still and T. L. Macdonald, ibid, 96, 5561 (1974); W. Oppolzer and R. L. Snowden, Tetrahedron Lett., 1976, 4187 ; A. P. Kozikowski and K. Isobe, Tetrahedron Lett., 1979, 833.
2) The use of butyl bromide or methyl tosylate instead of butyl or methyl iodide lowered the total yield (less than 60%), and the amount of the product of the Wittig rearrangement increased.
3) 2-Allyloxybenzimidazoles were synthesized from 2-chlorobenzimidazoles and sodium alcoholate in good yields according to the method of G. H. Schmid and A. W. Wolkoff, Can.J. Chem., 50, 1181 (1972).
4) Usually the reaction is completed in a shorter time (about 30 minutes) except when i-PrI was used as an electrophile.
5) For example, the reaction of 2-(2-propenyloxy)-1-(3,6,9-trioxadecyl)-benzimidazole with 2-phenylethyl magnesium bromide in THF afforded 5-phenyl-1-pentene in 95% yield.
6) It will be reported in the following paper.

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